women & children's
health research institute

2014 Research Day
Online Abstract Book

UNIVERSITY OF ALBERTA

Alberta Health Services

STOLLERY CHILDREN'S HOSPITAL FOUNDATION

Royal Alexandra HOSPITAL FOUNDATION

Acknowledgments

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The University of Alberta and the Faculty of Medicine & Dentistry

The University of Alberta strives to create and support an environment of research excellence across the university to fuel knowledge advancement, discovery and innovation; all of which provide significant contributions to society provincially, nationally and globally. It is through the continued support of the University of Alberta's Faculty of Medicine & Dentistry (FoMD), that WCHRI can house many of its core groups and its entire administrative staff. FoMD also provides partial funding for WCHRI's operating expenses, without which WCHRI would not be able to manage its many grants programs and research support initiatives.

Alberta Health Services

Alberta Health Services is a strong and active supporter of W
women's health and Alberta Health Services' standards in the delivery of clinical care, wellness and prevention in Alberta remain a focus of WCHRI's mandate.

The Stollery Children's Hospital Foundation

The Stollery Children's Hospital Foundation is dedicated to raising funds for specialized equipment, sub-specialty medical education to train the best of the best, research to pave the way to the discovery of new treatments or cures for child health issues and specialized programs that improve patient and family outcomes at the Stollery Children's Hospital.

The Royal Alexandra Hospital Foundation

The Royal Alexandra Hospital Foundation inspires community support for their healthcare facilities. The Foundation empowers compassionate, leading-edge patient care through education, research, technology and facility enhancements. They provide support for the Lois Hole Hospital for Women and a growing number of specialized centres of healthcare located at the Royal Alexandra Campus.

Presenter Name	Ab #	Time	Room
Al Jabri, Basma	153	15:15-16:45	Ballroom
Al Jishi, Taher	84	10:30-12:00	Ballroom
Al Yousef, Habib	178	15:15-16:45	Ballroom
Albrecht, Lauren	172	15:15-16:45	Ballroom
Alipour, Misagh	66	10:30-12:00	Ballroom
Aljunaidy, Mais	92	10:30-12:00	Ballroom
Alsahafi, Zaki	4	09:00-10:30	Chairman
Alzaben, Abeer	51	10:30-12:00	Ballroom
Amith, Ray	108	10:30-12:00	Ballroom
Andrews, Colin	165	15:15-16:45	Ballroom
Androschuk, Alaura	81	10:30-12:00	Ballroom
Antony, Nikytha	127	15:15-16:45	Ballroom
Araujo, Carolina	57	10:30-12:00	Ballroom
Assmus, Mark	137	15:15-16:45	Ballroom
Auch, Shieva	93	10:30-12:00	Ballroom
Avis, Jillian	52	10:30-12:00	Ballroom
Azad, Abul Kalam	105	10:30-12:00	Ballroom
Aziz, Sarah	58	10:30-12:00	Ballroom
Baghirova, Sabina	158	15:15-16:45	Ballroom
Bahitham, Wesam	2	09:00-10:30	Chairman
Bal, Jasmin	89	10:30-12:00	Ballroom
Bannar-Martin, Katherine	164	15:15-16:45	Ballroom
Bao, Bo	138	15:15-16:45	Ballroom
Barghout, Samir H	173	10:30-12:00	Ballroom
Becerra, Lina	136	15:15-16:45	Ballroom
Bedi, Prabhjot	6	09:00-10:30	Chairman
Beka, Qendresa	163	15:15-16:45	Ballroom
Benesch, Matthew	109	10:30-12:00	Ballroom
Bording-Jorgensen, Michael	17	09:00-10:30	Leduc
Brennan, Lesley	96	10:30-12:00	Ballroom
Bridgman, Sarah	85	10:30-12:00	Ballroom
Buka, Irena	102	10:30-12:00	Ballroom
Cabeza Gonzalez, Jose Luis	139	15:15-16:45	Ballroom
Cao, Amanda	182	15:15-16:45	Ballroom
Carias, Vanessa	150	15:15-16:45	Ballroom
Carroll, Allison	131	15:15-16:45	Ballroom
Carvalho Henriques, Beatriz	133	15:15-16:45	Ballroom
Castro Codesal, Maria	132	15:15-16:45	Ballroom
Chadha, Vikas	187	15:15-16:45	Ballroom
Chahal, Harneet	183	15:15-16:45	Ballroom
Champagne, Chantelle	43	13:45-15:15	Turner
Chan, Brandon	159	15:15-16:45	Ballroom
Chan, Michelle	184	15:15-16:45	Ballroom
Chaurasiya, Shyambabu	110	10:30-12:00	Ballroom
Chiu, Anthony	140	15:15-16:45	Ballroom
Choi, Sangho	190	15:15-16:45	Ballroom
Chomyn, Alanna	10	09:00-10:30	Chancellor
Cooke, Christy-Lynn	83	10:30-12:00	Ballroom
Corriveau-Bourque, Catherine	23	09:00-10:30	Turner
Crick, Katelynn	103	10:30-12:00	Ballroom
Croden, Jennifer	188	15:15-16:45	Ballroom
Crosley, Powel	111	10:30-12:00	Ballroom
Danesh, Ghazal	179	15:15-16:45	Ballroom
DeBruyne, Beth	47	13:45-15:15	Turner
Dhillon, Santokh	122	15:15-16:45	Ballroom
Ding, FangChao	154	15:15-16:45	Ballroom
Djordjevic, Gordana	44	13:45-15:15	Turner
du Toit, Nadia	191	15:15-16:45	Ballroom

Presenter Name	Ab #	Time	Room
Echigoya, Yusuke	37	13:45-15:15	Leduc
Elahi, Shokrollah	16	09:00-10:30	Leduc
Elboraee, Mohamed	82	10:30-12:00	Ballroom
Eldeeb, Mohamed	35	13:45-15:15	Chancellor
Elgendi, Mohamed	119	15:15-16:45	Ballroom
Elliott, Sarah	115	10:30-12:00	Ballroom
Elyasi, Maryam	104	10:30-12:00	Ballroom
Ewing, Christopher	24	09:00-10:30	Turner
Figueiredo, Vívian	59	10:30-12:00	Ballroom
Flynn, Rachel	166	15:15-16:45	Ballroom
Foisy, Michelle	167	15:15-16:45	Ballroom
Fortin-Pellerin, Etienne	19	09:00-10:30	Turner
Frello Roque, Ariane Thaise	91	10:30-12:00	Ballroom
Fu, Allen	64	10:30-12:00	Ballroom
Germani, Tamara	67	10:30-12:00	Ballroom
Gill, Jasmeena	3	09:00-10:30	Chairman
Gonzalez de Armas, Aimee	168	15:15-16:45	Ballroom
Guo, Long	20	09:00-10:30	Turner
Gyoba, Jennifer	76	10:30-12:00	Ballroom
Hamza, Deena	79	10:30-12:00	Ballroom
Hariharan, Shine	41	13:45-15:15	Leduc
Hejazi, Maryam	39	13:45-15:15	Leduc
Heywood, Brodie	160	15:15-16:45	Ballroom
Hirani, Saima	112	10:30-12:00	Ballroom
Hoppenbrouwers, Ernst	118	15:15-16:45	Ballroom
Hu, Rongfang	186	15:15-16:45	Ballroom
Huang, Vivian	28	13:45-15:15	Chairman
Hussein, Abbeir	46	13:45-15:15	Turner
Hyshka, Elaine	113	10:30-12:00	Ballroom
Isaac, Andre	130	15:15-16:45	Ballroom
Jackman, Alex	45	13:45-15:15	Turner
Janetzki-Flatt, Cassandra	55	10:30-12:00	Ballroom
Japoni, Sara	7	09:00-10:30	Chancellor
Kaddoura, Tarek	121	15:15-16:45	Ballroom
Kamaludin, Ain	151	15:15-16:45	Ballroom
Kar, Preeti	152	15:15-16:45	Ballroom
Kaur, Harmanpreet	54	10:30-12:00	Ballroom
Kircher, Janeva	22	09:00-10:30	Turner
Klinger, Christen	18	09:00-10:30	Leduc
Krishnan, Devishree	94	10:30-12:00	Ballroom
Krishnan, Preethi	106	10:30-12:00	Ballroom
Kumaran, Mahalakshmi	107	10:30-12:00	Ballroom
Kuzik, Nicholas	95	10:30-12:00	Ballroom
Labonte, Katrina	40	13:45-15:15	Leduc
Lam, Vanessa	125	15:15-16:45	Ballroom
Leduc, Renee	142	15:15-16:45	Ballroom
Lee, Clara	9	09:00-10:30	Chancellor
Lee, Sarah	117	10:30-12:00	Ballroom
Leimert, Kelycia	98	10:30-12:00	Ballroom
Lim, David	1	09:00-10:30	Chairman
Lissinna, Brittany	75	10:30-12:00	Ballroom
Lodhi, Rohit	149	15:15-16:45	Ballroom
Long, Rebecca	77	10:30-12:00	Ballroom
Luck, Chloe	68	10:30-12:00	Ballroom
Lukasewich, Megan	12	09:00-10:30	Chancellor
Mann, Jasdeep	180	15:15-16:45	Ballroom
Mansour, Yael	13	09:00-10:30	Leduc
Marensi, Vanessa	86	10:30-12:00	Ballroom

Presenter Name	Ab #	Time	Room
Meneksedag, Deniz	177	15:15-16:45	Ballroom
Mian, Qaasim	69	10:30-12:00	Ballroom
Mills, Lindsay	120	15:15-16:45	Ballroom
Monteiro, Juliana	87	10:30-12:00	Ballroom
Moorhouse, Cadence	38	13:45-15:15	Leduc
Nasralla, Awrad	42	13:45-15:15	Leduc
Nguyen, Antoinette	15	09:00-10:30	Leduc
Norris, Allison	162	15:15-16:45	Ballroom
O'Reilly, Megan	5	09:00-10:30	Chairman
Ou, Joe	63	10:30-12:00	Ballroom
Parmar, Manoj	175	15:15-16:45	Ballroom
Peat, Rebecca	123	15:15-16:45	Ballroom
Pereira, Leticia C. R.	116	10:30-12:00	Ballroom
Perez, Arnaldo	49	10:30-12:00	Ballroom
Przyslupski, Ann-Marie	74	10:30-12:00	Ballroom
Quintanilha, Maira	27	13:45-15:15	Chairman
Rashid, Marghalara	148	15:15-16:45	Ballroom
Raza, Hasnain	50	10:30-12:00	Ballroom
Rengan, Supraja	70	10:30-12:00	Ballroom
Revill, Ann L.	129	15:15-16:45	Ballroom
Reyes, Laura	126	15:15-16:45	Ballroom
Ricci, Florencia	21	09:00-10:30	Turner
Richard, Caroline	14	09:00-10:30	Leduc
Robinson, Tristan	80	10:30-12:00	Ballroom
Roper, Leslie	156	15:15-16:45	Ballroom
Rossolatos, David	155	15:15-16:45	Ballroom
Rosychuk, Rhonda	26	13:45-15:15	Chairman
Sacrey, Lori	11	09:00-10:30	Chancellor
Saltaji, Humam	169	15:15-16:45	Ballroom
Samoluk, Carissa	170	15:15-16:45	Ballroom
Schmidt, Sydney	97	10:30-12:00	Ballroom
Scott, Shannon	171	15:15-16:45	Ballroom
Shah, Amin	124	15:15-16:45	Ballroom
Shenouda, Suzan	134	15:15-16:45	Ballroom
Sivananthajothy, Tharsini	100	10:30-12:00	Ballroom
Siyam, Tasneem	185	15:15-16:45	Ballroom
Skow, Rachel	71	10:30-12:00	Ballroom
Smyth, Samantha	8	09:00-10:30	Chancellor
So, Iyla	60	10:30-12:00	Ballroom
Soleymani Abyaneh, Hoda	176	15:15-16:45	Ballroom
Soon, Sue Rene	56	10:30-12:00	Ballroom
Suleman, Raheem	36	13:45-15:15	Chancellor
Sullivan, Ginger	88	10:30-12:00	Ballroom
Sun, Luxin	31	13:45-15:15	Chancellor
Sun, Rose	99	10:30-12:00	Ballroom
Sydora, Beate	25	13:45-15:15	Chairman
Tamana, Sukhpreet	145	15:15-16:45	Ballroom
Tang, Xiaoyun	161	15:15-16:45	Ballroom
Tiffinger, Alexandria	143	15:15-16:45	Ballroom
Tsang, Conrad	147	15:15-16:45	Ballroom
Usselman, Charlotte	72	10:30-12:00	Ballroom
Usselman, Charlotte	29	13:45-15:15	Chairman
Valencia Serna, Juliana	174	15:15-16:45	Ballroom
Veltri, Nicole	189	15:15-16:45	Ballroom
Venkateswaran, Geetha	157	15:15-16:45	Ballroom
Venkatraman, Ganesh	32	13:45-15:15	Chancellor
Verstraeten, Barbara	30	13:45-15:15	Chairman
Virk, Punit	146	15:15-16:45	Ballroom

Presenter Name	Ab #	Time	Room
Vo, Quang	135	15:15-16:45	Ballroom
Watkins, Elise	53	10:30-12:00	Ballroom
Weinstangel, Hannah	48	13:45-15:15	Turner
Widen, Sonya	144	15:15-16:45	Ballroom
Wine, Osnat	101	10:30-12:00	Ballroom
Wood, Melissa	61	10:30-12:00	Ballroom
Wyper, Katherine	114	10:30-12:00	Ballroom
Yang, Ning	181	15:15-16:45	Ballroom
Yin, Nanlin	90	10:30-12:00	Ballroom
Yoon, Jenny	73	10:30-12:00	Ballroom
Young, Michelle	141	15:15-16:45	Ballroom
Yuen, Yue	33	13:45-15:15	Chancellor
Zagozewski, Jamie	78	10:30-12:00	Ballroom
Zaidi, Deenaz	65	10:30-12:00	Ballroom
Zhang, Han	62	10:30-12:00	Ballroom
Ziegler, Kirby A.	34	13:45-15:15	Chancellor

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Abstract #:	1
Presenter:	David W. Lim
Supervisor:	Justine M. Turner
Title:	Exogenous glucagon-like peptide-2 therapy promotes adaptation in a translational piglet model of neonatal short bowel syndrome.
Authors:	David W. Lim, Paul W Wales, Donna F. Vine, Patricia L. Brubaker, Patrick N. Nation, Pamela R. Wizzard, David L. Sigalet, David L. Bigam, Justine M. Turner
Affiliations:	University of Alberta
Research Activity:	Child and Youth Development : Nutrition
Investigation Type:	Quantitative Research

Purpose

To study the efficacy of exogenously administered glucagon-like peptide-2 (GLP-2) on intestinal growth and adaptation in a translational piglet model of neonatal short bowel syndrome (SBS); and how treatment is related to the expression of other gut-derived trophic peptides with a known role in perinatal intestinal development, including insulin-like growth factor-1 (IGF-1), epidermal growth factor (EGF) and fibroblast growth factor-2 (FGF-2).

Methods

Piglets 3-5 days old were block randomized to either a 75% mid-intestinal resection or no resection (sham control) and either saline or GLP-2 (11 nmol/kg/d) treatment. Piglets were pair-fed for 7 days until terminal lapartomy. Structural adaptation was assessed by measurement of final bowel lengths, mucosal weights and histopathologic analysis. Jejunal permeability *ex vivo* as a surrogate of functional adaptation was assessed using Üssing techniques. Assessment of peptide growth factors and their receptors (designated 'R') were performed in jejunum and ileum for GLP-2R, IGF-1, IGF-1R, EGF, EGFR, FGF-2, FGFR2b, and 18S (control) using qRT-PCR. Data are analyzed by two-way ANOVA for a 2x2 factorial design of surgery and treatment factors at a significance level of $p < 0.05$.

Results

The study groups are as follows: sham-saline (n=4), sham-GLP-2 (n=4), resection-saline (n=7) and resection-GLP-2 (n=5). There was no difference in the percent change in small bowel length between groups (p=0.14). Bowel weight per length (p<0.01), and jejunal (p<0.01) and ileal (p<0.001) mucosal weights increased with GLP2 treatment. Jejunum and ileum villus height both increased with resection and GLP2 treatment (p<0.01 for both). There was a significant decrease in jejunal permeability to mannitol as a function of both resection and GLP2 treatment (p<0.01). The relative gene expression of GLP-2R and IGF-1 mRNA were significantly increased in the ileum with GLP-2 treatment (p=0.01 and 0.0004 respectively). There was a trend towards increased ileal IGF-1R mRNA expression with GLP-2 treatment (p=0.055). There was no difference in the relative expression of EGF, EGFR, FGF-2 or FGF-2R mRNA in either jejunum or ileum with GLP-2 treatment.

Conclusion

The exogenous administration of glucagon-like peptide-2 in a translational model of neonatal SBS with mid-intestinal resection results in structural and functional changes consistent with intestinal adaptation. Histologic changes translate to increased surface area for absorption while permeability changes decrease the risk for bacterial translocation and ensuing sepsis. The IGF-1 system may mediate some of observed changes. These findings have the highest potential for translation to human neonates with SBS, especially those with mid-intestinal resection anatomy.

Funded By: Trainee Travel Grant

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Abstract #: 2
Presenter: Wesam Bahitham
Supervisor: Richard Lehner

Title: Liver-specific expression of Es-x (Ces1g) reduces hepatic steatosis and improves dyslipidemia and glucose metabolism

Authors: Wesam Bahitham, Russell Watts, Randy Nelson, Richard Lehner
Affiliations: University of Alberta

Research Activity: Other
Investigation Type: Quantitative Research

Introduction

Triacylglycerol (TG) accumulation in liver is a hallmark of nonalcoholic fatty liver disease (NAFLD). Several factors are associated with an increase in liver TG content including obesity, insulin resistance and alcohol ingestion. NAFLD includes a spectrum of pathological changes ranging from simple hepatic steatosis to advanced abnormalities such as nonalcoholic steatohepatitis (NASH), fibrosis, and cirrhosis. We have shown previously that ectopic expression of Es-x (Ces1g) in McArdle-RH7777 cells decreases cellular TG and increases fatty acid oxidation. Es-x is only expressed in the liver and in the small intestine in the mouse. Importantly, we have demonstrated that ablation of *Es-x* expression in mice results in weight gain, insulin resistance, fatty liver, and hyperlipidemia by upregulation of de novo lipogenesis and by oversecretion of TG-rich lipoproteins. The objective of this study was to elucidate the effect of liver specific Es-x expression to lipid metabolism in mice lacking Es-x expression in the intestine.

Methods

To directly address this question, female *Es-x*$^{-/-}$ mice (12-14 weeks old) fed a standard chow diet, were injected with an adenovirus harboring Es-x cDNA or a control adenovirus encoding GFP. At 7 days post-infection blood and selected tissues were harvested for further analysis including blood biochemistry, hepatic lipid content, liver histology, insulin sensitivity, expression of lipogenic and fatty acid oxidation genes.

Results

Liver-specific expression of Es-x results in decreased hepatic lipogenesis and secretion of TG-rich lipoproteins (hepatic very-low density lipoproteins), which leads to improve dyslipidemia and glucose metabolism. Hepatic Es-x expression significantly reduced liver TG concentration accompanied by decreased size of lipid droplets and improved insulin-mediated signal transduction. Plasma alanine aminotransferase levels were reduced in Ad-Es-x mice.

Conclusion

Collectively, this work demonstrates that Es-x plays a critical role in limiting hepatic steatosis, which could have implications for treatments of metabolic and liver diseases.

Funded By: CIHR

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Abstract #:	3
Presenter:	Jasmeena Gill
Supervisor:	Andrea Haqq
Title:	Association between macronutrient intake and fasting levels of ghrelin in children with and without Prader-Willi Syndrome.
Authors:	Jasmeena Gill, Michelle Mackenzie, Diana Mager, Michael Thorner, Andrea Haqq
Affiliations:	University of Alberta
Research Activity:	Child and Youth Development : Nutrition
Investigation Type:	Quantitative Research

Introduction

High ghrelin levels in children with Prader-Willi Syndrome (PWS) are thought to contribute to the insatiable appetite characteristic of the genetic condition. Previous studies have indicated that fasting levels of total ghrelin are associated with nutritional factors including body weight and habitual dietary intake. However, the association with the specific isoform of ghrelin (acyl ghrelin) that stimulates hunger is not known. We examined the relationship between usual dietary intake and fasting levels of the two isoforms of ghrelin (acyl and desacyl ghrelin) in children with and without PWS.

Methods

In this study, there were 10 PWS subjects (9 female, 1 male) and 7 controls (1 female, 6 male) that participated in three study visits. At each study visit, participants completed a 3-day food record and a fasting blood sample was obtained. Three 3-day food records were analyzed using Food Processor (version 10.9.0). Fasting acyl and desacyl ghrelin levels were measured using a two-site sandwich assay. Average dietary intake from the three 3-day food records and the three fasting ghrelin levels were used to examine the associations using Spearman rank-order correlations. Groups were compared using the Mann-Whitney U Test.

Results

Fasting acyl ($p=0.03$) and desacyl ($p=0.007$) ghrelin were significantly higher in the PWS group compared to the control group. Fasting acyl and desacyl ghrelin are negatively associated with percent body fat ($r_s = -0.886$, $p = 0.019$ for both) but not body mass index, and positively associated with usual energy intake ($r_s = 0.857$, $p = 0.014$ for both) in control children. The absolute intake of carbohydrates, sugar, protein and fat in control children was also positively associated with fasting levels of both isoforms of ghrelin. This association was not present in children with PWS. However, fasting acyl and desacyl ghrelin was positively associated with fat intake expressed as a percent total energy intake ($r_s = 0.709$, $p = 0.022$ for acyl ghrelin and $r_s = 0.685$, $p=0.029$ for descayl gherelin) in children with PWS.

Conclusion

Macronutrient and energy intake is correlated with both fasting acyl and desacyl ghrelin levels in controls but not in children with PWS. It is known that children with PWS have higher than normal ghrelin levels, however the affect of macronutrient composition on ghrelin regulation needs to be further researched.

Key Words: children, Prader-Willi Syndrome, ghrelin, diet, obesity

Funded By: Innovation Grant

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Abstract #: 4
Presenter: Zaki Alsahafi
Supervisor: Silvia Pagliardini

Title: Optogenetic excitation of preBötzinger complex neurons potently drives inspiratory activity in vivo

Authors: Zaki Alsahafi, Clayton Dickson
Affiliations: University of Alberta

Research Activity: Child and Youth Development : Sleep and Breathing Disorders
Investigation Type:

Introduction

Understanding the sites and mechanisms underlying respiratory rhythmogenesis is of fundamental interest in the field of respiratory neurophysiology. Compelling evidence from lesioning and inactivation studies suggests that the preBötzinger Complex (preBötC) is necessary and sufficient to generate inspiratory rhythms *in vitro* and *in vivo*. However, the influence of precisely timed activation of the preBötC network *in vivo* is as yet unknown given the experimental approaches previously used and available.

Methods

By unilaterally infecting neurons of the preBötC region using an adeno-associated virus expressing channelrhodopsin and the fluorescent protein EYFP driven by the synapsin promoter we photo-activated this neural network in a spatially and temporally precise manner in order to assess the influence on ongoing breathing rhythms and related muscular activity in urethane-anesthetized rats.

Results

Stimulation of preBötC neurons consistently increased respiratory rate and entrained respiration up to 180 breaths per minutes in both the presence and absence of spontaneous respiration. While minute ventilation remained unaffected, tidal volume and diaphragmatic activity decreased, while genioglossus activity increased. Furthermore, brief pulses of photostimulation delivered at random phases between inspiratory events robustly and consistently induced respiratory reset and recruited inspiratory muscle activity at short delays whereas little effect was observed when stimulation was delivered during inspiration itself.

Conclusion

These data provide strong evidence for a fine control of respiratory rhythmic activity in the preBötC region and are the final confirmation that the preBötC network constitutes the fundamental pacemaker of inspiratory rhythms.

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Abstract #:	5
Presenter:	Megan O'Reilly
Supervisor:	Bernard Thebaud
Title:	Enhanced healing capacity of MRL/MPJ mice in response to hyperoxia-induced neonatal lung injury
Authors:	Megan O'Reilly, Farah Eaton, John Greer, Bernard Thebaud
Affiliations:	University of Alberta
Research Activity:	Child and Youth Development : Lung Development
Investigation Type:	Quantitative Research

Background

Many preterm infants develop a chronic lung disease known as bronchopulmonary dysplasia (BPD), which interrupts lung development and results in long-term pulmonary complications that reach beyond childhood and into adult life. The MRL/MPJ strain of mouse has a unique capacity for accelerated and regenerative wound healing, but it is not known if the same healing process applies to the neonatal lungs. Our aim was to determine if MRL/MPJ mice are protected from, or capable of repair, following neonatal exposure to hyperoxic gas compared to the non-healer C57Bl/6 mouse strain.

Methods

Experimental BPD was achieved by exposing neonatal MRL/MPJ and C57Bl/6 mice to hyperoxic gas (95% O_2) from postnatal day (P) 4-10. Thereafter, mice were raised room air. Controls breathed only room air from birth. Lung structure was assessed at P10, P28, and P56. Lung function was assessed at P28 and P56.

Results

Immediately after O_2-exposure at P10, both MRL/MPJ and C57Bl/6 mice exhibited lung injury characterized by impaired alveolar growth with air-space enlargement ($p<0.05$). In O_2-exposed MRL/MPJ mice at P28, there was no significant difference in lung structure compared to room air controls. However, O_2-exposed C57Bl/6 mice displayed persistent structural lung injury ($p<0.05$). Despite the improvement in lung structure at P28, O_2-exposed MRL/MPJ mice exhibited functional differences (increased dynamic lung compliance; $p<0.05$). C57Bl/6 mice also displayed increased dynamic lung compliance at P28 ($p<0.05$). Structural lung injury persisted into adulthood at P56 in O_2-exposed C57Bl/6 mice ($p<0.05$), which was also associated with an increase in dynamic lung resistance ($p<0.05$). Conversely, at P56, MRL/MPJ mice were persistently protected from O_2-induced lung injury and displayed no significant difference in lung structure as well as no functional differences compared to controls.

Conclusion

MRL/MPJ mice display enhanced healing potential of the lung following neonatal O_2-exposure, which persists into adulthood. MRL/MPJ mice may be useful to identify new therapeutic strategies to promote injury resolution in BPD.

Funded By: Molly Towell Perinatal Fellowship, CIHR, OHRI, CHEO, CFI

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Abstract #:	6
Presenter:	Prabhjot Bedi
Supervisor:	Joanna MacLean
Title:	Long-term non-invasive ventilation in children in Alberta (2002-2014): clinical course and outcomes of the Edmonton cohort
Authors:	Prabhjot Bedi, Maria Castro Codesal , Joanna MacLean
Affiliations:	University of Alberta
Research Activity:	Child and Youth Development : Sleep and Breathing Disorders
Investigation Type:	Quantitative Research

Introduction

The use of non-invasive ventilation (NIV) in Alberta's pediatric population has risen exponentially over the last decade. Despite this, there is little data about outcomes and complications in Alberta. **The aim** of this study is to analyze the clinical course and outcomes of children on NIV at the Stollery Children's Hospital, Edmonton, over the last 12 years.

Methods

A retrospective chart review was performed on children receiving NIV ≥ 3 months at the Stollery's home-ventilation program. Medical charts from the NIV clinic and sleep laboratory records were reviewed. Underlying conditions were divided into 4 categories: upper airway obstruction (UAO), central nervous system (CNS), musculoskeletal (MSK), and pulmonary (PULM) categories.

Results

Over the last 12 years, 345 children have started NIV through the Stollery's home-ventilation program. Eighty-nine charts have been reviewed to date. Sixty percent of the children were male. The ethnic distribution noted was Caucasian (47.7%), Amerindian (12.8%), Asian (4.7%), African American (3.5%), Latin American (3.5%) and other (2.3%).Fifty-seven percent of children were classified into UAO, 23% CNS, 12.8% MSK, and 7.0% PULM categories. Additional supportive therapies including G-tube and supplemental oxygen were received by 23.3% and 22% of children respectively.

Data about patients/parents reported change in clinical outcomes were collected 6-12 months after NIV initiation and the most current clinical visit. At 6-12 months visit, outcome improvement was recorded in 72.9% of subjects. Seventy-one percent stated improvements in sleep, 72.9% nocturnal breathing, 40.7% mood/behaviour, 37.3% learning/school performance, and 64.4% in quality of life (QOL). Outcome data from the most current visit was available in 86.6% of subjects, with 75.6% reporting improved sleep, 84.1% breathing, 31.7% mood/behaviour, 39.0% learning/school, and 63.4% QOL. There were no statistically significant differences in improvements between time points or by disease category. Complications during NIV were reported by 63% of patients, with only hospitalizations having difference among disease categories (Chi-square 25.1, $p<0.05$)

Thirty-five percent of children to date have discontinued ventilation due to improvement of underlying condition (4.9%), patient/family's refusal or complications (7.3%), switch to invasive ventilation (2.4%), death (1.2%), transfer to adult services (12.2%) or transfer out of province (3.7%). There were no differences by disease category.

Conclusion

NIV use in children often improved sleep, breathing, and QOL. Data on clinical outcomes was not collected systematically. Complications were frequent in NIV use. Most children continued to require long-term NIV. Disease category did not seem to impact clinical outcomes or complications except hospitalizations.

Funded By: Trainee Research Grant

women & children's health research institute

Abstract #: 7
Presenter: Sara Japoni
Supervisor: David Eisenstat

Title: DLX transcriptional regulation of neural progenitor cell fate in the developing forebrain

Authors: Sara Japoni, Michelle Casey, Jamie Zagozewski, David Eisenstat
Affiliations: University of Alberta

Research Activity: Child and Youth Development : Neuro-cognitive Development
Investigation Type: Mixed Methods

Introduction

Balance between excitation and inhibition in the forebrain is crucial for proper neural function. Differentiation of inhibitory interneurons from neural precursor cells and their migration to the appropriate regions of the forebrain contributes to maintaining this balance. *Dlx* genes are required for central nervous system development. They encode transcription factors that bind to TAAT/ATTA motifs of regulatory regions and activate or repress target gene expression. Of the six *Dlx* genes in mice, *Dlx1, Dlx2, Dlx5* and *Dlx6* are expressed in the developing forebrain. In the *Dlx1/2* double knockout (DKO) mouse, tangential migration of inhibitory interneurons to the neocortex from the ganglionic eminences is disrupted. Our goal is to identify DLX2 transcriptional targets required for interneuron migration and/or differentiation. *Nkx2.2* is required for oligodendrocyte differentiation. Disruption of signaling by the CXCR4 chemokine receptor and/or its ligand CXCL12 results in improper migration of interneurons in the forebrain. This proposed research study will contribute to the emerging evidence supporting a role for the DLX transcription factors and their downstream target genes in maintaining the balance of excitation to inhibition during brain development by actively repressing oligodendrocyte differentiation while promoting interneuron differentiation and migration.

Methods

We have used chromatin immunoprecipitation (ChIP) of embryonic mouse forebrain (E13.5) using a specific polyclonal antibody to DLX2 followed by PCR using oligonucleotide primers flanking candidate homeodomain binding motifs. Targets are characterized using gel shift and reporter gene assays *in vitro* and validated by gene expression studies *in vivo* comparing wild-type and DKO forebrain tissues.

Results

ChIP-based PCR of embryonic mouse forebrain demonstrated that DLX2 binds to regions containing putative DLX2 binding sites upstream of the transcriptional start sites of *Nkx2.2* and *Cxcr4*. *Dlx2* significantly affected luciferase reporter gene expression *in vitro* when co-expressed with the regulatory regions of *Cxcr4* and *Nkx2.2* occupied by DLX2 *in vivo*. Furthermore, site directed mutagenesis revealed the critical sites on *Cxcr4* and *Nkx2.2* necessary for DLX2 binding. Quantitative RT-PCR showed an increase in transcript level of *Nkx2.2* in the *Dlx1/2* DKO tissues compared to the WT supporting a repressive role of DLX2 on *Nkx2.2* expression *in vivo*.

Conclusion

Our results support the hypothesis that DLX2 regulates expression of *Cxcr4* and *Nkx2.2* in order to maintain proper differentiation and migration of interneurons and concurrently repress oligodendrocyte cell fate in the developing forebrain. Specific molecules affecting the expression of DLX transcriptional targets may be a novel means to treat patients with autism spectrum disorders.

women & children's health research institute

Abstract #:	8
Presenter:	Samantha Smyth
Supervisor:	Khalid Aziz
Title:	The effect of delayed cord clamping on neurodevelopment in preterm and low weight infants
Authors:	Samantha Smyth, Amber Reichert, Jennifer Toye, Khalid Aziz
Affiliations:	University of Alberta
Research Activity:	Child and Youth Development : Neuro-cognitive Development
Investigation Type:	Quantitative Research

Introduction (Purpose)

This retrospective cohort study looks at the effects delayed umbilical cord clamping has on neurodevelopmental outcomes at 18 months adjusted age in infants born <29 weeks or ≤1250g.

Methods

Data was abstracted from existing databases for babies born without major congenital abnormalities at the Royal Alexandra Hospital from December 1st, 2008 to December 31st, 2011. Delayed cord clamping (DCC) was defined as a delay of ≥45 seconds. The major outcome of severe neurological impairment was a composite outcome comprised of scores on the Bayley III, diagnosis of cerebral palsy (CP) as well as the presence of neurosensory deficits. Secondary outcomes included ambulatory and non-ambulatory CP (GMFCS level 1-2 and level 3-5, respectively), developmental quotient 3 SD below mean, developmental quotient 2-3 SD below mean, hearing impairment, visual impairment (acuity <20/60 in the best corrected eye) and legal blindness (acuity <20/200 in the best corrected eye).

Results

Complete data was available for 303 infants (n=303). 143 (47%) babies received DCC while 160 (53%) babies received immediate cord clamping (ICC). Analysis of DCC and ICC populations pre-intervention found a difference in number of cesarean and vaginal deliveries (p=0.010). Post-intervention, the DCC and ICC populations differed in the timing of ventilation (p=0.00), and red blood cell transfusions (p=0.006) as well as with scores of illness severity. Outcomes analysis found no difference between the type of cord clamping received and the incidence of severe neurological impairment (p=0.315). Secondary analysis found no difference between the incidence of secondary outcomes and the type of umbilical cord clamping received.

Conclusion

Neurological development at 18 months adjusted age was not affected by delayed cord clamping. Results of short-term effects are also consistent with current evidence.

Funded By: Northern Alberta Clinical Trials and Research Centre, Northern Alberta Neonatal Program

women & children's health research institute

Abstract #:	9
Presenter:	Clara Lee
Supervisor:	Jacqueline Pei
Title:	Working memory in children born pretermIntroduction Research showed that children born preterm have higher risk of working memory (WM) impairments. Ho
Authors:	Clara Lee, Jacqueline Pei, Gail Andrew, Kim Kerns, Carmen Rasmussen
Affiliations:	University of Alberta
Research Activity:	Child and Youth Development : Neuro-cognitive Development
Investigation Type:	Quantitative Research

Introduction

Research showed that children born preterm have higher risk of working memory (WM) impairments. However, the profile of their WM abilities and challenges has yet to be clearly understood. Therefore, in this study, we examined the WM profile of preterm children using a model-driven measure in an effort to identify the developmental pattern of WM in preterm children.

Methods

Two groups of children were recruited: a Preterm group comprised of 24 children (mean age = 78.75 weeks, SD = 23.85; mean GA = 27.96 weeks, SD = 1.99; mean BW = 1106.45 grams, SD = 328.33) and a Control group comprised of 22 children (mean age = 77.18 weeks, SD = 19.89; mean GA = 39.09 weeks, SD = 1.51; mean BW 3183.93 grams, SD = 603.62). The Automated Working Memory Assessment (AWMA) was administered to measure WM abilities. Attention was assessed by the NEPSYII Auditory Attention subtest and the Test of Variables of Attention (TOVA). ANOVAs were used to compare WM performance between the two groups, and the developmental profile of WM within the Preterm group was examined using Pearson correlations between short-term memory (STM) and WM skills.

Results

Significant group differences were found between the two groups in all WM (all $p < .05$) but not STM (all $p > .05$) subtests, with controls outperforming preterms. However, after controlling for attention, these group differences became insignificant. Preterm and Control groups had different patterns in the correlations between verbal ST (VST) and visuospatial ST (VSST) (Preterm group: rs range from .561 to .717; Control group: r word-dot matrix = .430, others n.s.), and between VST and visuospatial WM (VSWM) (Preterm group: rs range from .520 to .591, r digit-spatial = n.s.; Control group: all rs n.s.). These findings suggested that preterm children may rely on VST to support VS tasks. Moreover, preschool preterm children (n =5) were found to have high correlations between auditory attention (omission errors) and VSWM (rAA-Mr.X = -.789, rAA-spatial =-.698) and between auditory attention (omission errors) and digit recall (r = -.762).

Conclusion

Consistent with previous research, children born preterm presented with WM impairments. The correlations between VST and VSST and between VST and VSWM in Preterm group revealed that preterm children may rely on VST to support VS tasks. Findings showed that preschool preterm children also rely on sustained auditory attention to support VS performance, which consistent with literature that younger children draw more executive resources (controlled attention) for VS tasks.

Funded By: Innovation Grant

women & children's health research institute

Abstract #:	10
Presenter:	Alanna Chomyn
Supervisor:	Jennifer Toye
Title:	Evaluating the combined influence of socioeconomic position and preterm birth on child language development
Authors:	Alanna Chomyn, Jennifer Toye, Amber Reichert, Linda Carroll, Mosarrat Qureshi
Affiliations:	University of Alberta
Research Activity:	Child and Youth Development : Neuro-cognitive Development
Investigation Type:	Qualitative Research

Introduction

As neonatal care advances, an increasing number of infants survive the immediate complications of preterm birth. In addition to ongoing physical health problems associated with preterm birth, these babies have been shown to be more prone to delays in multiple domains of child development including cognitive, behavioral, and language development. Delay in these domains may impact future success in both academic and social endeavors. Compounding the issue is that preterm birth is most common, and increasing most rapidly, in low socioeconomic populations- a group already disadvantaged in the same domains of child development. In our study, we look to establish if very preterm birth (≤28 weeks gestation) and living in an area of Edmonton with low socioeconomic status (SES) at time of birth negatively influences language development in infants 18-36 months, born between 2008-2011. We hope our research will help inform early intervention programs and support targeted multidisciplinary intervention of children most vulnerable to language delay.

Methods

Using combined data from the Edmonton Neonatal Database and the Edmonton Neonatal Follow Up Database, we assessed the relationship between socioeconomic status, preterm birth, and language outcomes by comparing language scores of very preterm babies at 18 and 36-month follow up visits on the Bayley III and WPPSI, validated language tools administered during neonatal follow up care, and looking for developmental differences between high, average, and low socioeconomic status groups. Socioeconomic status was determined using the CPHI deprivation index, a tool that combines social and material factors to establish area-based socioeconomic position. Univariate analysis was then performed to identify developmental risk factors present in high, average, and low SES groups, and then multivariable logistic regression was performed to evaluate language development outcomes between groups.

Results

We found that our low SES population had lower average gestational age and birth weight, and were less likely to survive preterm birth than average and high SES infants. These infants also performed more poorly on all assessed domains of language development on both language assessment tools by 36 months.

Conclusion

Our results are consistent with previous findings that preterm infants born to low SES backgrounds are more likely to experience greater delays in language development compared to average and high SES infants. Further study is needed to assess the role of intervention programs in improving developmental outcomes in socially disadvantaged very preterm babies.

Funded By: Department of Pediatrics, Undergraduate Research Initiative

women & children's health research institute

Abstract #:	11
Presenter:	Lori Sacrey
Supervisor:	Lonnie Zwaigenbaum
Title:	Can parents' concerns predict a later autism spectrum disorder outcome:
Authors:	Lori Sacrey, Lonnie Zwaigenbaum, Susan Bryson, Jessica Brian, Isabel Smith, Wendy Roberts, Peter Szatmari, Caroline Roncadin, Nancy Garon, Christopher Novak
Affiliations:	University of Alberta
Research Activity:	Child and Youth Development : Neuro-cognitive Development
Investigation Type:	Mixed Methods

Introduction (purpose)

Little is known about the utility of parent concerns in predicting a subsequent diagnosis of ASD, since concerns are generally ascertained in retrospect. This longitudinal study is the first to describe prospective parent concerns in infants at high-risk of developing ASD (each with an older sibling with ASD) at multiple time points in the first two years of life.

Methods

Parents of low-risk controls (LR; do not have a family history of ASD) and high-risk infant siblings (HR; infant siblings of children diagnosed with ASD) were asked to report any concerns they had regarding their children's development when the children were 6, 9, 12, 15, 18, and 24 months of age. Parents reported on ten aspects of development: sleep, diet, responses to sensory stimulation, gross and fine motor skills, repetitive movements, communication development, communication regression, social skills, play, and behavioral problems using a Parent Concern Form designed for this study. At 36 months of age, an independent, gold standard diagnostic assessment for ASD was conducted for all children.

Results

As predicted, parents of HR children who received an ASD diagnosis at 36 months of age reported more concerns than parents of LR children and HR children who were not diagnosed with ASD at 36 months of age. The total number of concerns predicted a subsequent diagnosis of ASD as early as 12 months of age within the HR group.

Conclusion

Parent reports of concern can improve earlier recognition of ASD in HR children. This is important for the development of interventions for children at-risk for ASD.

Funded By: Trainee Travel Grant

women & children's health research institute

Abstract #:	12
Presenter:	Megan Lukasewich
Supervisor:	Cindy Jardine
Title:	"We came out of our shells": Aboriginal youth's perspective on health changes occurring through participatory research approaches
Authors:	Megan Lukasewich, Shyanne Ewaskow, Cindy Jardine
Affiliations:	University of Alberta
Research Activity:	Child and Youth Development : Mental Health
Investigation Type:	Qualitative Research

Introduction

Promoting health and wellbeing through community-based participatory research (CBPR) projects is particularly effective for socially excluded populations such as Aboriginal youth in Canada. Using CBPR facilitates inclusion through participation and is an effective empowerment strategy. However, youth's perspectives of being participants in CBPR projects are rarely assessed. This limits our knowledge on how the process of participation in research truly impacts youth's health. This study explored youth's perspective and the perceived health changes resulting from participation in a CBPR project on smoking prevention/cessation.

Methods

Aboriginal youth (ages 13-18 years) from Edmonton, AB and N'dilo, NWT used video production to promote smoking cessation/prevention in their communities. The research team used a constructivist qualitative approach and assessed from the youth's perspectives the effect of participating in a CBPR on their health and wellness. Group interviews were conducted with the youth at three points throughout 2013; March (n=28), May (n=18), and October (n=11). Through content analysis we inductively developed a code book and formed themes.

Results

Through cooperation and team work, youth supported and encouraged each other as they participated in the research project. Active engagement in the research, created a context where youth were able to go on an empowering journey. Through this journey youth contributed their ideas and actively participated in solving problems. The youth described a sense of belonging and connectedness to each other. This facilitated youth bonding where they took responsibility to lead the project, which increased their agency. Youth from Edmonton described the importance of coming together as Aboriginal peoples to pursue traditional teachings and practices to promote health. N'dilo youth emphasised the importance of gaining leadership skills and described motivation to be healthy role models for their peers and family. A positive sense of identity and a greater leadership role improved their self-esteem and self-efficacy.

Conclusion

Actively participating in research processes builds a foundation for youth to have positive health and wellness outcomes. It is important to develop programs that foster a sense of belonging and cultural identity, provide opportunities for youth empowerment, and increase youth self-esteem. These social determinants of health are all known to be prerequisites to become an agent of change in one's own life. Building youth's capacity to act as agents of change is necessary for true community development. These areas need to be addressed in future programs if we are to see health and wellness changes in Aboriginal youth.

Funded By: Trainee Travel Grant

women & children's health research institute

Abstract #:	13
Presenter:	Yael Mansour
Supervisor:	Stephane Bourque
Title:	Prenatal iron deficiency in the absence of maternal anemia causes fetal hypoxia
Authors:	Yael Mansour, Ferrante Gragasin, Stephane Bourque
Affiliations:	University of Alberta
Research Activity:	Maternal Research : Fetal Origins of Adult Disease
Investigation Type:	Quantitative Research

Introduction

Iron deficiency (ID) is the most common nutritional deficiency in the world, and the population most at risk is pregnant women, due to volume expansion during pregnancy as well as demands from the fetal-placental unit. Fetal ID is associated with pre-term birth and fetal growth restriction, both of which have important implications for the long-term health of the offspring. Current assessments for fetal anemia rely on maternal haematological indices. However, it is not presently known whether modest ID (with no overt anemia) in mothers would cause adverse fetal outcomes. Here, we tested the hypothesis that modest ID in dams would cause adverse fetal outcomes in rats.

Methods

To study this effect, female Sprague Dawley rats (12 wk) were fed a control diet (70mg/kg iron), or an identical diet with no added iron (3mg/kg iron) 2 wk prior and throughout pregnancy. Dams were treated with pimonidazole (PIMO) (60mg/kg) at gestational day 20; PIMO forms covalent adducts to tissues in low oxygen conditions (<10mmHg). Tissues were harvested and fixed, and adduct formation was quantified by immunofluorescence.

Results

Iron restriction resulted in fetal anemia ($P<0.05$), albeit no evidence of fetal growth restriction or maternal anemia was observed. PIMO staining was evident in fetal tissues of iron restricted dams (including the liver [$P=0.01$], kidneys [$P=0.01$]), but was not observed in maternal tissues nor in the placenta.

Conclusion

The reduced fetal Hb, but not maternal Hb levels due to modest ID in dams coincided with indices of hypoxia in the fetus, but no in the dam. These results suggest that modest prenatal ID compromises oxygen transport in the fetus. In conclusion, the prevalence of fetal ID anemia may be higher than previously estimated and therefore, novel diagnostic approaches independent of maternal hematological indices are needed.

Funded By: Summer Studentship

women & children's health research institute

Abstract #:	14
Presenter:	Caroline Richard
Supervisor:	Catherine Field
Title:	Effect of feeding a docosahexaenoic acid rich diet on immune system development during the suckling period of the offspring
Authors:	Caroline Richard, Susan Goruk, Catherine Field
Affiliations:	University of Alberta
Research Activity:	Child and Youth Development : Infection, Inflammation, Immunology
Investigation Type:	Quantitative Research

Background

The early postnatal period is a critical time for immune system development (particularly T cells) in infants. Althoughit is well established that long chain polyunsaturated fatty acids (LCPUFA) modulate T cell function, no study has documented the effect of a docosahexaenoic acid (DHA) rich diet on the immune system development early in life. The objective of this study was to determine the effect of feeding a high DHA maternal diet on immune system development and function in suckled offspring.

Methods

Sprague-Dawley dams were randomized to one of the two nutritionally adequate experimental diets 24-48h prior to parturition: control diet (N=12, 0% DHA) or high DHA diet (N=8, 2.2% DHA of total fatty acids). Diets were fed ad libitum throughout the suckling period and matched for macronutrient, micronutrient and LCPUFA content differing only in the composition of LCPUFA. At 3 weeks, two of the suckled pups from each dam were terminated and pooled to represent each dam. Immune cells from spleen were isolated and phenotypes and cytokine production by mitogen-stimulated splenocytes were measured by direct immunofluorescence assay and ELISA respectively.

Results

Pups from dams fed the DHA a higher proportion of 18:3n-3, 22:5n-3 and 22:6n-3, and a lower proportion of 18:1n-9 in their stomach contents compared to pups from dams fed the control diet (all $P<0.01$). Pups from dams fed the control diet vs. DHA diet did not differ in final body weight, spleen weight, liver weight or gut length. There were no effects of feeding a high DHA diet on *ex vivo* cytokine production (IL-2, IL-1B, IL-6, IL-10, IFN-γ and TNF-α) by splenocytes stimulated with either Concanavalin A (Con A) or lipopolysaccharide (LPS). Feeding a high DHA diet had no impact on major T cell types ($CD3^+$, $CD4^+$, $CD8^+$, $CD25^+$ or $CD28^+$) compared with the control diet.

Conclusion

Our findings suggest that although feeding the dams a high DHA diet during the suckling period lead to higher proportion of omega-3 in the stomach contents of the pups, it appears to have no impact on the immune system development and function in suckled offspring.

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women & children's health research institute

Abstract #:	15
Presenter:	Antoinette Nguyen
Supervisor:	Jerome Yager
Title:	Investigating the effects of broccoli sprouts on inflammatory cytokines and oxidative stress in a neonatal model of the fetal inflammatory response
Authors:	Antoinette Nguyen, Tremayne Peart, Edward Armstrong, Po-Yin Cheung, Richard Schulz, Jerome Yager
Affiliations:	University of Alberta
Research Activity:	Child and Youth Development : Neuro-cognitive Development
Investigation Type:	Quantitative Research

Introduction

Infection and inflammation during late pregnancy leads to a fetal inflammatory response (FIR), characterized by enhanced production of cytokines and oxidative stress. Newborns exposed to a FIR may develop brain damage leading to neurodevelopmental disabilities and cerebral palsy. Currently, no preventative intervention exists to deter brain injury caused by the FIR. However, studies have shown that broccoli sprouts (BrSp) contain powerful anti-inflammatory and anti-oxidative properties, and in our hands, have reduced developmental delays associated with FIR. Thus, we hypothesized that BrSp dietary supplementation will reduce the inflammation and oxidative stress.

Methods

Dams received intraperitoneal injections of either saline or lipopolysaccharide (LPS, 200 µg/kg) every 12 hours on gestational days 19 and 20. BrSp are added to their diet beginning at the third trimester, gestational day 14, and continued until delivery. Experimental groups included: 1) saline (control) 2) saline+BrSp 3) LPS, and 4) LPS+BrSp. Newborn pups were weighed, sexed, and euthanized on the day of birth. Brain tissues were harvested to evaluate alterations of cytokines and oxidative stress.

Results

Compared to control saline, the LPS group showed increased IL-1β and IL-10 levels, and significantly reduced KC/GRO ($p<0.05$) (neutrophil activating protein). Compared to LPS, LPS+BrSp had decreased levels of IL-10 and significantly reduced levels of IL-1β ($p<0.05$). LPS+BrSp pups also showed reduced concentrations of oxidized glutathione and increased concentrations of reduced glutathione. Furthermore, LPS+BrSp supplementation significantly reduced ($p<0.05$) the GSSG/GSH ratio compared to LPS. Analyses of matrix-metalloproteinase-2 did not show any significant differences between the two groups.

Conclusion

The results indicate subtle changes in inflammation and oxidative stress induced by our FIR model, and suggest that the reduction in prenatal brain injury by BrSp may be related to this effect. These alterations may occur, however over a short timeframe following LPS exposure. Further experiments are underway to determine the evolution of these changes.

Funded By: Trainee Travel Grant

women & children's health research institute

Abstract #: 16
Presenter: Shokrollah Elahi
Supervisor:
Title: Why are babies more susceptible to infections than the adults?
Authors: Shokrollah Elahi
Affiliations: University of Alberta
Research Activity: Maternal Research : Infection, Inflammation, Immunology
Investigation Type: Qualitative Research

Introduction

Newborn infants are uniquely susceptible to infection. According to a WHO estimate, almost 7 million children die each year before reaching their fifth birthday. Strikingly two thirds of these deaths are due to infectious diseases. The mechanisms underlying the susceptibility of neonates to infections and the molecular basis for the transition of immunologic function from fetal to postnatal life has remained a mystery. Although the neonatal immune cell immaturity has been ascribed as the underlying mechanism of susceptibility to infection, the discordance in the past illustrates the need for a more unifying explanation for why immunity is compromised in neonates.

Methods

Given the delayed immunological development at birth for mice, six day neonates in comparison with eight week adults were utilized. We reasoned if neonatal susceptibility reflects inadequate number or hyporesponsiveness of immune cells, adoptive cell transfer was performed. Furthermore, to interrogate potential suppressive properties among neonatal cells, cytokine production and activation of adult immune cells co-cultured with neonatal splenocytes was evaluated. We next investigated the neonatal splenocyte subset responsible for suppression. Cell ablation was used to further establish the relationship between suppression by these cells and neonatal infection susceptibility and digestive health. Finally, presence and function of these cells in human cord blood specimens was further studied.

Results

We discovered that physiologically enriched $CD71^+$ erythroid cells in neonatal mice and human cord blood have distinctive immune suppressive properties. Production of innate protective cytokines is diminished for adult cells transferred into newborn mice or after co-culture with neonatal splenocytes. Neonatal $CD71^+$ cells express arginase-2, and this enzymatic activity is essential as molecular inhibition or L-arginine supplementation overrides suppression. In turn, $CD71^+$ cell ablation or their progressive decline with postnatal development parallel loss of suppression with restored resistance to perinatal pathogens *Listeria monocytogenes* (Lm) or *Escherichia coli*. However, $CD71^+$ cell mediated susceptibility to infection is counterbalanced by protection against aberrant immune cell activation in the intestine where brisk postnatal colonization with commensal microbes occurs. Thus, $CD71^+$ cells quench excessive inflammation induced by abrupt commensal colonization after parturition.

Conclusion

Our results challenged the notion that neonatal infection susceptibility reflects immune cell intrinsic defects, but instead highlighted the presence of active immunosuppression which is developmentally more essential processes. We anticipate these results will spark renewed investigation addressing the unique necessity for immune suppression in neonates, and improved strategies for augmenting host defense in this vulnerable population.

Funded By: Innovation Grant

women & children's health research institute

Abstract #: 17
Presenter: Michael Bording-Jorgensen
Supervisor: Eytan Wine
Title: Enhanced enteric pathogen killing by inflammasome-activated macrophages
Authors: Michael Bording-Jorgensen, Misagh Alipour, Eytan Wine
Affiliations: University of Alberta
Research Activity: Child and Youth Development : Infection, Inflammation, Immunology
Investigation Type: Quantitative Research

Introduction

Interleukin (IL)-1β is a proinflammatory cytokine that is released from macrophages and monocytes through a class of protein complexes called inflammasomes. Nod-like receptor protein-3 (NLRP3) inflammasomes have been linked to various inflammatory conditions such as gout, asthma, and inflammatory bowel diseases (IBD). IBD is highly relevant to pediatrics where many cases are diagnosed in children with an increasing incidence, especially among Canadian children. Conditions associated with the inflammasomes are typically characterized by an overabundance of IL-1β with the exception of IBD, where the inflammasome is dysregulated, leading to an IL-1β reduction. The mouse pathogen *Citrobacter rodentium,* a common mouse model pathogen for enteropathogenic *Escherichia coli,* is used to understand the dynamic relationship between pathogens, the inflammasome and the epithelial barrier. We have previously shown that *NLRP3*$^{-/-}$ mice given exogenous IL-1β had improved ability to clear *C. rodentium* infections. Our hypothesis was that inflammasome activation increases macrophages ability to phagocytose and eliminate *C. rodentium*.

Methods

Gentamicin protection assay with J774A.1 cell line macrophages was used to determine the rate of phagocytosis and bacterial killing. ATP (5mM; NLRP-3 activator) was utilized to stimulate endogenous IL-1β production; YVAD (25μM) was used as a caspase 1 inhibitor. A multiplex ELISA kit was used on cell supernatants with and without the presence of bacteria to study cytokine production. Polarized epithelial (CMT-93) cells, grown in transwells, were employed to study the interplay between macrophages, bacteria, and epithelium.

Results

Activation of the inflammasome, using extracellular ATP, significantly increased the ability of J774A.1 macrophages to kill *C. rodentium*. Inhibition using YVAD resulted in a reduction of microbial death. Furthermore, inflammasome activation did not appear to affect the macrophage ability to phagocytose, nor did it illicit an increase in cell toxicity. Cytokine analysis showed that inflammasome activation by ATP induced a reduction in IL-6 and an increase in IL-12. For the epithelial cell experiment, the addition of IL-1β induces transepithelial migration of macrophages to the apical membrane where bacteria were adherent.

Conclusion

Inflammasome activation appears to play a critical role in the clearance of pathogens, whether it is in direct pathogen elimination or localizing the immune response. In relation to IBD, this dysregulation of the inflammasome may contribute to an increase in host susceptibility to pathogens. Studying the role of IL-1β on macrophage activity during an inflammatory state will lead to a better understanding of inflammatory diseases, especially in children.

Funded By: Trainee Travel Grant

women & children's health research institute

Abstract #:	18
Presenter:	Christen Klinger
Supervisor:	Joel Dacks
Title:	Characterization of membrane trafficking in the algae Chromera velia and Vitrella Brassicaformis reveals a complex ancestor of apicomplexan parasites
Authors:	Christen Klinger, Yong Woo, Arnab Pain, Joel Dacks
Affiliations:	University of Alberta
Research Activity:	Other
Investigation Type:	Qualitative Research

Introduction

The Apicomplexa are a group of unicellular eukaryotes and includes parasites of immense global importance. Plasmodium falciparum, the causative agent of cerebral malaria, contributes to high childhood mortality rates in areas like Sub-Saharan Africa. Toxoplasma gondii causes ocular lesions and is responsible for congenital defects in cases of infection during pregnancy. The presence of a relict plastid in several species of apicomplexan parasites hinted at the existence of a photosynthetic ancestor. Recent environmental surveys have revealed a large diversity of algae known as chromerids forming sister groups to the Apicomplexa, including the two described species Chromera velia and Vitrella brassicaformis. Despite vastly different morphologies and trophic strategies, chromerids possess structures reminiscent of the apical complex (a unique cytoskeletal apparatus in Apicomplexa), and organelles that bear similarities to micronemes and rhoptries (apical organelles critical to apicomplexan host cell invasion). Membrane trafficking, the process of moving proteins and lipids between compartments within the cell, is essential for formation of the apical complex and associated organelles. Work from the Dacks lab, as well as many others, has demonstrated modification of membrane trafficking machinery in Apicomplexa, mainly in the endocytic system. We hypothesize this to be an adaptation concurrent with a switch emphasizing the exocytic rather than endocytic function of these apical organelles. The completion of the C. velia and V. brassicaformis genomes affords an opportunity to better understand these modifications, in terms of whether they are pre-adaptive (i.e. present in the chromerid ancestor), or in fact represent specific adaptations within the Apicomplexa.

Methods

Utilizing multiple homology searching and phylogenetic and clustering algorithms, we searched for homologs of several endocytic trafficking protein families in both chromerid genomes and compared these results to those found in representative Apicomplexa and close outgroup taxa.

Results

We consistently identified a greater repertoire of trafficking machinery in chromerids than in Apicomplexa, suggesting that significant sculpting took place after the two lineages diverged. The most striking differences were identified in large regulatory gene families, suggesting that trafficking in Apicomplexa is a streamlined process.

Conclusion

This study provides the first characterization of membrane trafficking in the closest known free-living relative of apicomplexan parasites. Mapping of functions associated with homologous proteins in well-characterized systems such as humans and yeast provides insight into which trafficking pathways are maintained in the stripped down apicomplexan system and reveals the evolutionary path from free-living algae to deadly parasites.

Funded By: Graduate Studentship

women & children's health research institute

Abstract #:	19
Presenter:	Etienne Fortin-Pellerin
Supervisor:	Lisa Hornberger
Title:	Increased diastolic untwisting velocity in response to Tachycardia as evidence of Diastolic Reserve in the young infant heart
Authors:	Etienne Fortin-Pellerin, Lindsay Mills, James Y Coe, Nee S Khoo, Po Yin Cheung, Lisa Hornberger
Affiliations:	University of Alberta
Research Activity:	Child and Youth Development : Cardiology
Investigation Type:	Quantitative Research

Introduction

In response to exercise, the healthy adult left ventricle (LV) augments its filling through early untwisting, creating suction even before the AV valve opens. The role of untwisting in the immature heart remains controversial. Older infants have delayed and decreased LV untwisting rates at baseline, suggesting untwisting may play less of a role in LV filling at least at rest. Although no in vivo data exists, one in vitro investigation of human infant myocardium has suggested relaxation may be augmented during tachycardia which could suggest an element of diastolic reserve. In the present study, we sought to explore the diastolic function response to atrial tachycardia in a young piglet model.

Methods

Under general anesthesia (propofol, isoflurane), 1-15 day old piglets were instrumented intravascularly with Millar high-fidelity and pacing catheters in the LV and right atrium (RA), respectively. After stabilization, invasive hemodynamic and echocardiography parameters were acquired at baseline and at 230bpm (30-40% above baseline). LV twist was analyzed off-line by speckle tracking (226 ± 55 frames/s). Subjects were their own control and paired t-tests were used for comparisons after confirmation of normal distribution for each variable. Values were expressed as mean ± SD.

Results

Eight piglets of mean age 8.6 ± 6.8 days and weight 3.6 ± 2.18kg, and baseline heart rate of 157 ± 18bpm were assessed. With tachycardia, Tau decreased from 28 ± 9ms to 23 ± 9ms ($p = 0.03$). Peak untwisting rate increased from -247 ± 83 to -412 ± 179 degrees/s ($p = 0.04$) and the change correlated with Tau ($r=0.45$, $p=0.04$). Untwisting rate during isovolumic relaxation also increased from -146 ± 74 deg/s to -335 ± 205 deg/s ($p = 0.03$). There was a trend towards reduction in LV end diastolic pressure from 13 ± 6 to 10 ± 5 mmHg ($p = 0.067$).

Conclusion

The early infant heart has the capacity to maintain normal LV filling pressures during atrial tachycardia, and this is associated with increased LV untwisting performance suggesting diastolic reserve. The boundaries of this diastolic reserve, and whether this knowledge can be exploited to augment LV filling in the critically ill infant is the subject of ongoing investigations.

Funded By: Trainee Research Grant

women & children's health research institute

Abstract #:	20
Presenter:	Long Guo
Supervisor:	Ian Adatia
Title:	Hyperoxia reduces oxygen consumption in children with pulmonary hypertension.
Authors:	Long Guo, Prashant Bobhate, Shine Hariharan, Tarek Kaddoura, James Coe, Jennifer Rutledge, Andrea Wan, Ian Adatia
Affiliations:	University of Alberta
Research Activity:	Child and Youth Development : Cardiology
Investigation Type:	Mixed Methods

Introduction

High inspired oxygen concentration (FiO_2) and inhaled nitric oxide (iNO), either alone or in combination, are administered to test pulmonary vasoreactivity in children. Oxygen consumption (VO_2) cannot be measured accurately with conventional methods if the inspired FiO_2 >0.85 and it is usually assumed that (VO_2)does not changewith hyperoxia or iNO. We hypothesised that an inspired FiO2 >0.85 would change VO_2 compared with VO_2 in room air (RA) and iNO administered with room air and could influence the accuracy of flow calculations using the direct Fick's equation.

Methods

We reviewedretrospectivelythe cardiac catheterization data obtained between 2009-14 in children with pulmonary hypertension (PH) without cardiac shunts and cardiac output (CO) measured by thermodilution in 3 conditions of RA, with an FiO2 >0.85 and iNO in RA. VO_2 was calculated using the Fick equation CO= VO_2 / arterial-venous oxygen content difference. Dissolved O_2 was included in the calculation.

Results

Data was availablein20 subjects (median age 8.5 years, range 1 -18, median weight 27 kg range, 8 – 95, BSA median $1m^2$, range 0.4 – 1.8). The median VO_2 in RA was 147 (range 84-231) and decreased in hyperoxia to 134 (range 84-239) (p=0.03). The median percentage change in VO_2 from RA to FiO2>0.85 was 10% (range + 24 to - 42%). VO_2 was unchanged with iNO 139 (range 78-221) ml/min/m^2 (p=0.3). The cardiac index remained unchanged in all 3 conditions (room air: 3.5±1.0, FiO_2 >0.85: 3.5±1.0 and iNO: 3.6±1.0 L/min/m^2).

Conclusion

VO_2 decreased significantly during hyperoxia but not during iNO in children with PH. If VO_2 is assumed to remain constant during hyperoxia errors maybe introduced if the direct Fick equation is used to calculate pulmonary and systemic blood flow.

Funded By: Deloitte Clinical Research Fellowship

women & children's health research institute

Abstract #:	21
Presenter:	Florencia Ricci
Supervisor:	Charlene Robertson
Title:	Frequency and potentially modifiable predictors of major neuromotor disability following complex cardiac surgery in early infancy
Authors:	Florencia Ricci, John Andersen, Ari Joffe, Irina Dinu, Elham Moez, Gonzalo Garcia Guerra, Charlene Robertson
Affiliations:	University of Alberta
Research Activity:	Child and Youth Development : Cardiology
Investigation Type:	Quantitative Research

Background

Survival rates after neonatal complex cardiac surgery (CCS) for congenital heart disease (CHD) have increased. Surviving children face neurodevelopmental and neuromotor challenges. While neurocognitive difficulties have been reported; little research has been done on motor impairments. Permanent non-progressive motor impairments are cerebral palsy (CP) and acquired brain injury (ABI), including stroke. Major Neuromotor Disability (MND) is the umbrella term used here to include CP and ABI.

Objectives

1)To calculate the rate of MND among 4.5-year survivors, 2)To describe MND among 4.5-year survivors according to the current CP definition and classification, 3)To determine potentially modifiable acute care predictors that might lead to a reduction in the frequency of MND.

Methods

This prospective inception cohort study included 549 children with CHD of ≤6 weeks of age at the time of their first CCS requiring cardio-pulmonary bypass at the Stollery Children's Hospital, 1996-2009. Groups included those with only one CCS, mostly bi-ventricular CHD, and those with more than one CCS, predominantly single ventricle defects. After 4.5 years, 105(19.1%) children had died, 24(5.4%) were lost to follow up, and 420 survivors received multidisciplinary assessment. The frequency of MND is given as percentage (95% confidence interval(CI)) of assessed survivors. Operative and peri-operative predictors of MND were analyzed using univariate and multiple logistic regression analysis, expressed as odds ratios (OR) with 95%CI.

Results

MND occurred in 25 (5.9%)(CI 3.7%,8.2%) of 420 4.5-year survivors; for one CCS, 3.9%(CI 1.7%,6.1%) and more than one, 11.5%(CI 5.6%,17.4%). MND occurred in 10.9%(CI 5.1%,16.7%) of those with single ventricle defects. Unilateral MND was found in 18(72%); spasticity in 20(80%). According to the multiple regression model, statistically significant independent OR for MND are: age in days at first surgery, 1.084 (CI:1.040,1.131)(P<0.001); and prior to first surgery, highest plasma lactate (mmol/L), 1.127 (CI:1.024,1.230)(P=0.001) and highest inotrope score, 1.020 (CI:0.997,1.040)(P=0.054) (marginal significance). Adjusting for the presence of these predictors, OR for MND is 4.642 (CI:1.875,11.493)(P=0.001) if more than one CCS is needed.

Conclusion

MND is not uncommon among survivors after CCS, especially for those children needing more than one surgery. OR for MND is 1.08 for each day the neonatal CCS is delayed and 1.13 for each mmol/L of plasma lactate elevation in the pre-operative period at first surgery. Identification of these potentially modifiable predictors may assist in reducing the frequency of MND after life-saving CCS. This information will improve counselling for families of these children.

women & children's health research institute

Abstract #:	22
Presenter:	Janeva Kircher
Supervisor:	Samina Ali
Title:	Caregiver satisfaction with children's pain management in the emergency department
Authors:	Laura Weingarten, Amanda Newton, Kathryn Dong, Rhonda Rosychuk, Sarah Curtis
Affiliations:	University of Alberta
Research Activity:	Child and Youth Development : Pain Management
Investigation Type:	Quantitative Research

Introduction

Pain is a common reason for seeking care for a child in the emergency department (ED) and family members are generally considered the most appropriate proxy to interpret a child's pain. A better understanding of the caregiver's satisfaction is key to improving ED pain management.

Methods

This cross-sectional survey examined caregivers of children aged 0-17 years presenting to a general (GED) and pediatric ED (PED) with a complaint of pain as part of the triage-reported presenting problem. Trained research assistants approached caregivers prior to discharge and distributed a survey to measure caregiver-estimated pain scores, satisfaction with their child's pain management, perspectives on analgesia use, and recollection of discharge advice provided. Surveys were collected between May 2009-December 2011 using a convenience sample.

Results

Ninety-seven caregivers participated (GED, n=46; PED, n=51). Most caregivers were female (n=69, 71%). The mean patient age was 9.2 years (SD 5.2) and 52 (53%) were male. Children were predominantly treated for musculoskeletal pain (n=41, 42%), headache (n=16, 16%) and abdominal pain (n=7, 7%). Using a 100 mm Visual Analog Scale, the maximum mean reported pain score in the 24 hours prior to visiting the ED was 75 mm (95% CI: 70, 80) and the mean score at discharge was 39 mm (95% CI: 32, 46). Over half of respondents indicated they would not request a stronger dose of pain medicine if their child were still having pain (n=54, 57%). Caregivers at the PED were more likely to agree with the statement: "Did a physician/nurse make it clear to you that pain treatment is important?" (p=0.014). Eighty caregivers (90%) were satisfied with their child's pain management and nine (10%) were dissatisfied, with no difference between the PED and GED (p=0.172). At discharge, caregivers who rated their child's pain as severe were less likely to be satisfied than those who rated their child's pain as mild or moderate (p=0.034). Maximum reported pain score in the 24 hours prior to visiting the ED did not influence satisfaction (p=0.097).

Conclusion

Despite continued pain experienced by children at discharge, most caregivers report being satisfied with their child's ED pain management. The relationship between caregiver satisfaction and pain management should be explored further, as satisfaction does not necessarily correlate with use of the most appropriate analgesia. Further, parental triggers for requesting and withholding pain medications need to be better understood, as they are often the gatekeepers to their child's pain treatment.

Funded By: Support services

women & children's health research institute

Abstract #:	23
Presenter:	Catherine Corriveau-Bourque
Supervisor:	Aisha Bruce
Title:	The changing epidemiology of pediatric hemoglobinopathy patients in Northern Alberta, Canada
Authors:	Catherine Corriveau-Bourque, Aisha Bruce
Affiliations:	University of Alberta
Research Activity:	Other
Investigation Type:	Quantitative Research

Introduction

Sickle cell disease and transfusion dependent thalassemia (hemoglobinopathies) are disorders of hemoglobin production that are associated with significant morbidity and mortality. In Canada there are no accurate statistics reflecting the number of patients with a hemoglobinopathy. Canada's immigration patterns are changing and regions where these diseases were rare are seeing substantial increase. With the change in the healthcare population significant public health issues have arisen. There is a definite need to demonstrate the changing population and healthcare requirements in Canada in order to advocate for appropriate resources, educate healthcare providers, and increase awareness.

Methods

In order to better understand the epidemiology of our patient population given the provincial population growth and immigration patterns, a retrospective chart review was conducted of pediatric sickle cell disease and transfusion dependent thalassemia patients at the Stollery Children's hospital from 2004 to 2013. Ethics approval was obtained from the University of Alberta Health Research Ethics Board.

Results

There was acceleration in patient accrual after 2003 with a steady increase over each 5-year period and then approximately triple the number of new patients in 2013. Fifty-three percent were Canadian-born, with two-thirds of these patients having been born in Alberta. The majority of families originated from Africa (63%), the Caribbean (17%), and China/South East Asia (9%). There was a delay in the diagnosis of patients' conditions in 71% of all cases. In addition, while many of these patients were relatively well, one third developed at least one severe complication from their underlying diagnosis. Fifteen percent required at least one exchange transfusion, 18% received chronic transfusions, and an additional 22% needed at least 1 simple transfusion.

Conclusion

With this dramatic increase in our patient population, changes at the level of newborn screening, pediatric and adult multidisciplinary follow-up clinics, and education of health care providers will need to be implemented to meet the needs of our expanding hemoglobinopathy and thalassemia population. In addition, we hope to contribute to the development of a national database to better monitor this population, and further identify unmet clinical needs.

Funded By: Stollery Children's Hospital travel fund

women & children's health research institute

Abstract #:	24
Presenter:	Christopher Ewing
Supervisor:	Piushkumar Mandhane
Title:	Electronic screen usage is associated with decreased sleep duration among children with sleep-disordered breathing
Authors:	Christopher Ewing, Amanda Lau, Piushkumar Mandhane
Affiliations:	University of Alberta
Research Activity:	Child and Youth Development : Sleep and Breathing Disorders
Investigation Type:	Quantitative Research

Introduction

Television-viewing has been associated with sleep disturbances and reduced sleep duration in children. Information on the impact of widespread new electronic technologies such as smartphones and tablets on sleep duration among children with pre-existing sleep disturbances is limited. Our primary objective was to determine the association between time spent using electronic screens and sleep duration among children in a sleep-disordered breathing clinic. We hypothesized that increased time spent using electronic screens would be associated with reduced sleep duration. Additional analyses examined if the number of screens was associated with sleep duration.

Methods

We studied children in a pediatric sleep disorders clinic in Edmonton. Children were seen for sleep-disordered breathing (SDB) and obstructive sleep apnea (OSA) symptoms. The child and their caregivers completed several previously validated sleep related questionnaires including Children's Sleep Habits Questionnaire (CSHQ), Pediatric Sleep Questionnaire (PSQ), Sleep Disturbance Scale for Children (SDSC), and Childhood Television Viewing Habits Questionnaire (CTVHQ) as part of the assessment. The CTVHQ was modified to collect data on the presence and use of all types of electronic screens in the household. Sleep duration was measured on a 4-point scale in ordered groups of hours of sleep (5-7, 7-8, 8-9, and 9+). We used ordered logistic regression analysis to examine the association between screen use and sleep duration.

Results

We studied 113 children with mean age of 8 years (range 2 to 18) and mean BMI Z-score +1.17. One child had Down syndrome and thirteen had asthma (12%). Mean electronic screen number per household was 6. Mean duration of screen use was 3 hours on weekdays, and 5 hours on weekends. Number of electronic screens was neither significantly associated with duration of screen use ($p=0.51$) nor sleep duration (OR 0.94, $p=0.12$). After adjusting for age, children were 14% less likely to have longer sleep with each additional hour of weekday screen use (OR 0.86, 95% CI 0.73-1.00; $p=0.05$) and 15% less likely to have longer sleep with weekend screen use (OR 0.85, 95% CI 0.77-0.93; $p = 0.001$). Association between weekday screen use and sleep duration remained significant after adjusting for subjective measures of OSA including subscales of the PSQ ($p=0.02$), CSHQ ($p=0.01$), and SDSC ($p<0.01$).

Conclusion

In our study, the proliferation of electronic screens was not associated with increased duration of use. However,screen use was significantly associated with reduced sleep duration. For all children, including those assessed for sleep-disordered breathing, counseling on appropriate use of all electronic screens should be routine in order to optimize sleep duration.

Funded By: Trainee Research Grant

women & children's health research institute

Abstract #:	25
Presenter:	Beate Sydora
Supervisor:	Sue Ross
Title:	Outcomes of an interdisciplinary Menopause Clinic at the Lois Hole Hospital
Authors:	Beate Sydora, Nicole Veltri, Christoph Sydora, Hilary Fast, Justin Marillier, Lori Battochio, Nese Yuksel, Tami Shandro, Sue Ross
Affiliations:	University of Alberta
Research Activity:	Women's Health : Mature Women's Health
Investigation Type:	Qualitative Research

Background

The Menopause clinic at the Lois Hole Hospital for Women (LHHW) provides care for women suffering from severe menopause symptoms, following referral by their general practitioner or Ob/Gyn physician. Clinical care is provided by a range of disciplines including specialized physician, pharmacist, dietician, and nurses. Patients' health status and care received are recorded on Menopause Clinic Health Profile (MCHP) Charts including a 35 item patient-completed menopause symptom severity questionnaire filled in at each visit. Our goal is to evaluate the outcomes of treating patients at the LHWH Menopause Clinic.

Methods

Patients who had attended the menopause clinic during 2008 to 2013 were included in the analysis. We used the symptom questionnaires to compare scores from the first and follow-up visits. Scores ranged from 1-4 (none, mild, moderate, severe). Women who had not returned for follow-up visits for more than 1½ year were sent a follow-up questionnaire inquiring on their current state of menopause symptoms. Scores were then compared to their previous scores on file. All data from the initial MCHP and follow-up charts were entered into REDCap database for analysis. Changes in symptom severity scores were correlated to lifestyle and diet changes, medication use, and perception of wellbeing.

Results

The analysis included 164 charts entered into REDCap to date. Forty-one women (25%) had only one visit to the clinic during the study period and nine women (5.5%) attended the clinic seven times, the maximum number of total visits per patient. The majority of women (63/164, 34.4%) visited the clinic twice. Of the 110 patients with clinic follow-up charts, symptom severity scores were reduced between the first and the last follow-up for 84 patients (76.4%), scores were unchanged for 5 patients (4.5%) and were increased for 21 (19.1%). Additionally, 12 out of 40 patients responded to follow-up by mail. Of those 50% (6/12) had reduced symptom scores when the mailed-in questionnaire was compared to the one filled in at their first clinic visit; 33% (4/12) indicated no change and 17% (2/12) indicated an increase in symptom severity. Decrease in symptom scores were associated with positive lifestyle changes including increased exercise or weight reduction.

Conclusion

Our results demonstrate that the care received in the LHHW Menopause clinic has a positive impact on patient outcomes as judged by reduced menopause scores over time of follow-up visits. Further investigation will correlate clinic outcomes for groups of women with specific medical needs.

Funded By: Support services

women & children's health research institute

Abstract #:	26
Presenter:	Rhonda Rosychuk
Supervisor:	
Title:	Sex differences in outcomes After discharge from the emergency department for atrial fibrillation/flutter in Alberta
Authors:	Rhonda Rosychuk, Michelle Graham, Brian Holroyd, Xuechen Zhang, Brian Rowe
Affiliations:	University of Alberta
Research Activity:	Other
Investigation Type:	Quantitative Research

Introduction

Sex differences in atrial fibrillation/flutter (AFF) may influence the individual's decision to seek ED care for AFF-related symptoms and subsequent physician visits after an ED visit. We sought to examine the differences in outcomes between males and females discharged from the ED after an AFF presentation in the province of Alberta, Canada.

Methods

Retrospective, population-based, cohort study of patients during April 1, 1999, to March 31, 2011, linking multiple administrative databases. All Alberta residents aged ≥35 years who presented to the ED for AFF during the study period and whose presentation ended in discharge from the ED (one randomly selected per patient). Main outcomes and measures included time to ED return for AFF, the time to first follow-up visit (with a cardiologist or non-cardiologist), and time to death. Statistical analyses included descriptive statistics, Kaplan-Meier curves, and multivariable Cox proportional hazards models.

Results

There were 21,062 patients/ED presentations (10,007 [47.5%] female) that formed the discharged subset used for analyses. About 10% of patients returned to the ED for AFF after discharge and the time to return was similar for both sexes (P=0.39). Nearly 48% of females had at least one follow-up visit within 365 days of ED discharge and the median times to first follow-up visits were the same for each sex, 5 days. When adjusted by other variables, females with certain characteristics had longer times to the first follow-up visit than males (interactions with sex were present). Females had longer times to first follow-up visit with a cardiologist (unadjusted hazard ratio [HR]=0.89, 95% confidence interval [CI] 0.85 to 0.92) and when adjusted by other variables, longer times were also seen for females with some characteristics. At 30 and 90 days after ED discharge, there were 234 and 548 deaths, respectively. Females had more deaths than males at 30 (131 vs 103, P=0.009) and 90 (287 vs 261, P=0.02) days after ED discharge. The time between ED discharge and death was shorter for females than males (unadjusted HR=1.22, 95% CI 1.03 to 1.44).

Conclusion

We identified differences between women and men for time to ED return, time to follow-up visit, and time to death. These differences are not solely based on the longevity of women and multiple factors are involved. Further understanding these differences could lead to specific policies to address any bias in services to females.

Funded By: Innovation Grant

women & children's health research institute

Abstract #:	27
Presenter:	Maira Quintanilha
Supervisor:	Rhonda Bell
Title:	Coping with contrasts between “back home” and “here”: African-immigrant women’s pregnancy and postpartum experiences
Authors:	Maira Quintanilha, Jessica Thompson, Tatjana Alvadj-Korenic, Rhonda Bell, Maria Mayan
Affiliations:	University of Alberta
Research Activity:	Maternal Research : Nutrution
Investigation Type:	Qualitative Research

Introduction

Low socioeconomic status, language difficulties and sociocultural barriers can negatively affect many aspects of a healthy pregnancy, including dietary practices, physical activity and women’s receptivity to prenatal and postpartum care. Immigrant women in Canada (i.e., refugees and non-refugees) often have unmet social, economic and health needs during pregnancy and postpartum, and poorer birth outcomes. Given all the adaptation that migration requires, and the importance of pregnancy for women and infant’s health, this project sought to understand immigrant women’s perceptions of a healthy pregnancy, and their experiences during pregnancy and postpartum in the new host country.

Methods

A community-based research approach was used to engage African-immigrant women who participated in a prenatal/postnatal group offered through Multicultural Health Brokers Cooperative (MCHB) in Edmonton, Alberta. Focused ethnography was the method used in this study. Eight focus groups (n = ~8 women per group) were conducted with women from four African ethnicities (Eritrean, Ethiopian, Oromo and Somali) who had been living in Canada for between 1 and 36 months. This data was supplemented with direct observations, and analyzed through qualitative content analysis.

Results

Cultural clashes between “back home” and “here” (Canada), and various life adversities (e.g., poverty), in the absence of women’s family circle created a sense of isolation and increased stress, which were heightened by pregnancy and postpartum. African-immigrant women discussed that in their home countries they experienced political instability and persecution; nevertheless, they felt supported and cherished in pregnancy and postpartum as their family circle and friends provided them with “everything they needed” to be healthy. This included nutritious foods, opportunities to be physically active, and to get enough rest. Once in Canada, women acknowledged that their political rights are respected, and they are able to access healthcare throughout pregnancy and postpartum. Yet, without enough money to buy healthy foods, and to afford leisure activities and childcare, it becomes extremely challenging to be healthy during pregnancy and postpartum. On the other hand, women described that services and supports offered through MCHB (e.g., childcare, cooking classes, family activities) facilitated a healthy pregnancy and postpartum.

Conclusion

Community-based organizations such as MCHB that work with African-immigrant, pregnant and postpartum women have a valuable opportunity to improve women’s health through existing prenatal/postnatal programs. Policies that support these organizations and ensure adequate funding will make possible continuing services and supports that can assist immigrant women in being healthier during pregnancy and postpartum in their new country.

Funded By: Summer Studentship

women & children's health research institute

Abstract #:	28
Presenter:	Vivian Huang
Supervisor:	Richard Fedorak
Title:	Fecal calprotectin is elevated with clinical disease activity during pregnancy in women with inflammatory bowel disease
Authors:	Vivian Huang, Jasmin Bal, Rae Foshaug, Lindsy Ambrosio, Karen Kroeker, Levinus Dieleman, Brendan Halloran, Richard Fedorak
Affiliations:	University of Alberta
Research Activity:	Maternal Research : Infection, Inflammation, Immunology
Investigation Type:	Mixed Methods

Introduction

Women with inflammatory bowel disease (IBD) often have gastrointestinal symptoms during pregnancy. Fecal calprotectin (FCP) is a non-invasive biomarker that detects intestinal inflammation and therefore is being used to determine if gastrointestinal symptoms in patients with IBD are due to active disease. Nevertheless, the validation of FCP as a biomarker in pregnant women with IBD and gastrointestinal symptoms has not been studied.

Objective

To determine if an elevated FCP is associated with clinical disease activity during pregnancy among women with IBD.

Methods

Female IBD patients (18-45yrs) were enrolled pre-conception (PC) or at each trimester of pregnancy (T[n]). At each visit, a FCP measurement was determined and women were grouped by clinical disease activity using the modified Harvey Bradshaw index (HBI) for Crohn's disease and the partial Mayo score for ulcerative colitis. Women with a modified HBI score of $\geq$ 5 or a partial Mayo score of $\geq$ 2 were identified as having clinically active disease. FCP on a first morning stool was determined using the Quantum Blue High Range reader. To examine the assocation of FCP with clinical disease activity, we compared, at each visit, the median FCP of the women with clinically active disease to those with inactive dsiease.

Results

Sixteen patients (median age 34.5 (IQR 28.8 – 37.3) years provided 16 stool samples for analysis. The median FCP of the women with clinically active disease was numerically higher than the median FCP of women with inactive disease at each visit: PC (1800mg/kg vs 739mg/kg; *P*=.333), T1 (1298mg/kg, no inactive cases), T2 (1200mg/kg vs 180mg/kg; *P*=.100), and T3 (1510mg/kg vs 134mg/kg; *P*=.486), respectively.

Conclusion

Women with IBD who had clinically active disease during preconception and pregnancy had higher fecal calprotectin levels than women who had clinically inactive disease. This confirms that that fecal calprotectin can be used as a biomarker for assessing clinical disease activity during pregnancy in women with IBD.

Funded By: Summer Studentship

women & children's health research institute

Abstract #: 29
Presenter: Charlotte Usselman
Supervisor: Craig Steinback
Title: Sympathetic baroreflex sensitivity in normotensive pregnant women
Authors: Charlotte W. Usselman, Rachel J. Skow, Michael K. Stickland, Radha S. Chari, Colleen G. Julian, Margie H. Davenport, Craig D. Steinback
Affiliations: University of Alberta
Research Activity:
Investigation Type: Quantitative Research

Introduction

Muscle sympathetic nerve activity (MSNA) is increased during normotensive pregnancies while mean arterial pressure (MAP) is maintained or reduced. These data suggest baroreflex resetting; however, to date sympathetic baroreflex sensitivity (BRS) during healthy pregnancy has not been specifically investigated. We hypothesized that BRS would be reset in normotensive pregnant women (PREG) relative to similarly aged non-pregnant controls (CTRL).

Methods

Integrated MSNA (microneurography), MAP, systolic (SBP) and diastolic (DBP) blood pressures (Finometer) and cardiac output (Q; ModelFlow) were obtained on a beat-by-beat basis during 7-15 minutes of semi-recumbent rest in 10 PREG (gestation = 32±4 weeks; age = 31±3 yrs; pre-pregnancy BMI = 23 ± 3 kg/m^2) and 10 CTRL (age = 28 ± 6; BMI = 25 ± 7) women. Spontaneous BRS slope was calculated from the linear relationship between fluctuations in MSNA burst incidence and DBP, while BRS set-point was specifically determined through comparisons of prevailing burst incidence and DBP.

Results

Baseline MAP (87 ± 10 *vs* 90 ± 7 mmHg, PREG *vs* CTRL, P=0.4), SBP (112 ± 12 *vs* 120 ± 7 mmHg, P=0.1) and DBP (71 ± 9 *vs* 71 ± 8 mmHg, P=0.9) were not different between PREG *vs* CTRL, whereas MSNA burst frequency (38 ± 9 *vs* 22 ± 7 bursts/min, P<0.001) and burst incidence (43 ± 8 *vs* 30 ± 10 bursts/100hb, P=0.004) were higher in PREG than CTRL. Nevertheless, spontaneous sympathetic BRS slopes were similar between PREG and CTRL (-3.4 ± 1.5 *vs* -3.9 ± 1.0 bursts/100hb/mmHg, P=0.3). Total peripheral resistance (TPR; MAP/Q) tended to be lower and Q tended to be higher (both P=0.06) in PREG. *Post hoc* analysis of neurovascular transduction (TPR/MSNA) revealed that PREG was associated with a pronounced blunting of sympathetic transduction relative to CTRL (TPR/burst frequency: 0.32 ± 0.06 *vs* 0.72 ± 0.29 a.u., P=0.001; TPR/burst incidence: 0.28 ± 0.05 *vs* 0.52 ± 0.20 a.u., P=0.002).

Conclusion

These data indicate that the set-point (but not gain) of the sympathetic baroreflex is increased in normotensive pregnancy. Furthermore, the transduction of MSNA into a vascular outcome is significantly blunted in pregnancy, resulting in the maintenance of normal blood pressures. Ongoing research will determine whether the lack of this blunting of sympathetic transduction contributes to the development of hypertensive pregnancy disorders in some women.

Supported by the Women and Children's Health Research Institute, NSERC, & the Human Performance Scholarship Fund.

Funded By: Innovation Grant

women & children's health research institute

Abstract #:	30
Presenter:	Barbara Verstraeten
Supervisor:	David Olson
Title:	IL-1B and PGF2a stimulate IL-1 Receptor (R)1 and 2 and Accessory Proteins (AcP) as well as IL-6R in human myometrial smooth muscle cells (HMSMC).
Authors:	Barbara Verstraeten, Kelycia Leimert, Xin Fang, David Olson
Affiliations:	University of Alberta
Research Activity:	Maternal Research : Pre-term Birth
Investigation Type:	Quantitative Research

Introduction

Every delivery involves the transformation of the non-contractile uterus of pregnancy to the active uterus of labour. This process utilizes inflammatory mediators within the uterus including Prostaglandin (PG)$F_{2\alpha}$, Interleukin (IL)-1β and IL-6. The IL-1β receptors, IL-11 and IL-1R2, form a complex with IL-1R AcP for signalling. Previously, IL-1RAcPb mRNA expression had only been described in the brain. However, we recently found an increase in expression of IL-1R1, IL-1R2, IL-1RAcP and IL-1RAcPb in the rat uterus. IL-6 has a key role in the onset of parturition. The IL-6R binds IL-6, and complexes with glycoprotein (gp)130 for signal transduction, with gp130 being the common signalling component of the cytokine receptor within the IL-6 family. Recently, we showed that $PGF_{2\alpha}$ stimulation induces production of IL-6 by HMSMC. In this study, we hypothesize that HMSMC express the four IL-1R genes and that they are regulated by $PGF_{2\alpha}$ and IL-1β. We also investigate whether IL-1β, with or without $PGF_{2\alpha}$ treatment, stimulates the IL-6R and gp130.

Methods

HMSMC were retrieved from women not in labor at term, following caesarean section (n=5-9). The cells were pre-treated with 5 ng/ml IL-1β for 24h, followed by $PGF_{2\alpha}$ (10^{-7} and 10^{-5} M) for 6h, or treated only with $PGF_{2\alpha}$. mRNA abundance of IL-1R1, IL-1R2, IL-1RAcP, IL-1RAcPb, IL-6R, gp130 and GAPDH as housekeeping gene was evaluated by RT-PCR. ANOVA with Tukey HSD post-hoc tests or t-tests were performed for statistical evaluation after $\log_{10}$ transformation.

Results

Both IL-1R1 and IL-1R2 expression increased in a dose-response manner to PGF2α ($p<0.001$ and $p<0.05$). IL-1AcP displayed a similar trend (NS), while IL-1RAcPb demonstrated an inverse relationship, with $PGF_{2\alpha}$ stimulating expression at lower doses ($p<0.05$). IL-1β stimulated a significant increase in expression of these 4 genes ($p<0.001$). Addition of $PGF_{2\alpha}$ after IL-1b pre-treatment did not induce a further rise in expression. IL-6R expression was increased by IL-1β, with an additive effect of PGF2α ($p<0.001$). There was no effect on gp130 expression.

Conclusion

The expression of IL-1R1, IL-1R2, IL-1RAcP, IL-1RAcPb is regulated by $PGF_{2\alpha}$ and IL-1β in HMSMC. $PGF_{2\alpha}$ has an additive effect on IL-6R expression after IL-1β treatment. IL-1β stimulates its own receptors and accessory proteins, as well as IL-6R. Furthermore, these are the first data showing presence of IL-1RAcPb outside the human brain. Together, these observations add a level of complexity to the feed-forward aspect of uterine transformation for labour.

Acknowledgements: PhD Fellowship, Research Fund Flanders, CIHR, March of Dimes.

Funded By: Research Fund Flanders, CIHR, March of Dimes

women & children's health research institute

Abstract #:	31
Presenter:	Luxin Sun
Supervisor:	Mark Glover
Title:	Development of phosphomimetic inhibitors of the BRCA1 C-terminal domain for cancer therapy
Authors:	Luxin Sun, E.Railey White, Zhong Ma, Jason Beckta, Brittany Danzig, David. E. Hacker, Melissa Huie, J. N. Mark Glover, Kristoffer Valerie, Matthew C. T. Hartman
Affiliations:	University of Alberta
Research Activity:	Women's Health : Oncology
Investigation Type:	Mixed Methods

Introduction

The maintenance of genomic integrity during genotoxic events relies on nuclear signaling systems that coordinate the repair of DNA damage with regulation of the cell cycle and apoptosis. Breast cancer type 1 susceptibility (BRCA1) protein is a nuclear protein that facilitates DNA repair through the formation of a large complex called BASC after DNA double strand break (DSB). The carboxyl terminus of BRCA1 contains a phospho-protein binding motif comprised of two repeating BRCA1 C-terminal (BRCT) domains. Through its BRCT domains, BRCA1 recognizes a conserved pSer-x-x-Phe(pSxxF) motif of BRCA1-associated carboxyl terminal helicase (BACH1)in phosphorylation dependent manner and this interaction is essential for its function in DSB DNA damage repair.2Since many current cancer therapies employ DNA damaging chemotherapy or ionizing radiation that primarily cause DSBs leading to cell cycle arrest or cell death, development of small inhibitor drugs against DSB repair proteins such as BRCA1 can effectively enhance the efficacy of current cancer treatment. Recently, Dr. Matthew Hartman's lab has identified a small nonphosphorylated peptide inhibitor of the BRCA1 BRCT, so we are interested in further investigate this inhibitor structural and function to obtain information for further refinement of therapeutic drug compound.

Method

We have verified the specificity of this inhibitor against BRCA1 BRCT using fluorescence polarization (FP) and obtained a crystal structural of it in complex with BRCA1 BRCT using X-ray crystallography. Then we carried out mutagenesis on BRCA1 BRCT to modify its key residues involved in inhibitor interaction and examined their importance through direct affinity measurement using FP. The inhibitor treatment is then applied in vivo and its effect on DNA damage response is examined by foci formation assay.

Result

Our structure reveals an interesting Glu-x-x-Phe(ExxF) motif replacing the conserved pSxxF motif required for phosphorylation dependent recognition at BRCT binding site. In addition, the hydrophobic residues at N-terminus of the peptide also form interactions with hydrophobic pocket at P-1 position of pSxxF binding site. All these key interactions are verified in vitro and the effectiveness of the inhibitor is also confirmed in vivo because cell treated with this inhibitor are clearly more sensitive to DNA damaging therapy.

Conclusions

We have presented here the first non-phosphopeptide inhibitor of BRCA1 and its crystal structure in complex with BRCA1 BRCT. Our study has not only provides a basis for developing other high affinity BRCA1 BRCT inhibitors, but may also reveal a new mechanism for possible phosphorylation-independent recognition of BRCA1 BRCT.

women & children's health research institute

Abstract #: 32
Presenter: Ganesh Venkatraman
Supervisor: David Brindley

Title: Inhibition of Autotaxin/LPA signaling sensitizes breast cancer to chemotherapy

Authors: Ganesh Venkatraman, Matthew Benesch, Xiaoyun Tang, Jay Dewald, Todd McMullen, David Brindley
Affiliations: University of Alberta

Research Activity: Women's Health : Oncology
Investigation Type: Quantitative Research

Introduction

Overcoming resistance to chemotherapy represents a major obstacle in the treatment of most cancers. The tumor microenvironment, which includes cytokines, chemokines and growth factors, is an important component of resistance to therapies. Targeting the microenvironment is an attractive strategy in overcoming resistance by providing increased specificity, decreased toxicity and preventing metastasis.

Autotaxin (ATX) is a secreted enzyme, which is primarily involved in wound-healing and tissue remodelling in response to local inflammation. It does this by stimulating the production of lysophosphatidate (LPA), which activates at least six G-protein receptors. These cause the migration of leukocytes, fibroblasts and keratinocytes to the injured area. ATX activity is also increased in chronic inflammatory disorders including metastatic cancers, which has been likened to “a wound that does not heal”. LPA promotes resistance to chemotherapy and radiotherapy, but the exact mechanism remains unclear. There are currently no accepted therapies, which block LPA signaling in cancers.

Methods

We used pharmacological and molecular biological approaches with human cancer cell lines to study the mechanism of LPA-induced chemoresistance. We also inhibited ATX activity and LPA synthesis in Balb/c mice injected orthotopically with syngeneic 4T1 breast cancer cells with an oral autotaxin inhibitor (ONO-8430506). This decreased tumor growth and metastases by 60% (1).

Results

We discovered that LPA through LPA_1 receptors increase the stability and nuclear translocation of the transcription factor, Nrf2. This increases the expression of multidrug-resistant transporters and anti-oxidant genes, resulting in decreased doxorubicin accumulation and protection against cell death. Autotaxin inhibition *in vivo* decreased the expression of Nrf2, multidrug resistant transporters and antioxidant genes in breast tumours. Further, we observed a synergistic effect of ONO-8430506 with doxorubicin in decreasing breast tumour growth and metastasis. Nrf2 expression was also higher among patients with recurrent breast tumours compared to non-recurring cancer.

Conclusion

Our results establish for the first time that LPA causes chemo-resistance by stabilizing Nrf2 expression and increasing the expression of anti-oxidant proteins and multidrug resistant transporters. We demonstrated in a mouse model that blocking LPA formation with an autotaxin inhibitor provides a completely novel adjuvant treatment for improving the efficacy of existing chemotherapeutic agents. We hope to introduce ONO-8430506 shortly into Phase 1 clinical trial in Edmonton for cancer treatment.

1) Benesch, M. G., Tang, X., Maeda, T., Ohhata, A., Zhao, Y. Y., Kok, B. P., Dewald, J., Hitt, M., Curtis, J. M., McMullen, T. P., and Brindley, D. N. (2014) Inhibition of autotaxin delays breast tumor growth and lung metastasis in mice, *FASEB J*.

(Funded By: Graduate Studentship)

women & children's health research institute

Abstract #:	33
Presenter:	Yue Yuen
Supervisor:	Lesley Mitchell
Title:	Polymorphisms in the genes coding for coagulation factor V and factor II are risk factors for deep vein thrombosis in pediatric cancer patients
Authors:	Yue Yuen, Lesley Mitchell, Kevin Dietrich
Affiliations:	University of Alberta
Research Activity:	Child and Youth Development : Oncology
Investigation Type:	Mixed Methods

Introduction

The two most common mutations associated with deep vein thrombosis (DVT) in the adult Caucasian populations are the Leiden mutation and prothrombin G20210A mutation found in the coagulation factor V and II genes respectively. The factor V Leiden and the prothrombin G20210A mutations are found infrequently; approximately 5% of the population carries the Leiden mutation and 2% carry the prothrombin G20210A mutation. There is an increased risk of DVT in adults 5 fold for factor V Leiden and 3 fold for prothrombin G20210A. Both mutations result in increased thrombin production, leading to a pro-coagulant state, emphasizing the biological importance of these genes in development of DVT. We hypothesised that there are may be other mutations in the Factor V and Factor II genes that are associated with DVT risk in pediatric oncology patients.

Methods

We performed a multicentre cross-Canada case control study. Survivors of childhood cancer who experienced DVT while undergoing treatment for their cancer (cases) were matched with survivors of childhood cancer who did not experience DVT (controls). We recruited 235 patients (75 patients with DVT and 160 controls without DVT) who were genotyped by tagging single nucleotide polymorphisms (SNPs) in the factor V and factor II genes. An r^2 of 0.8 for linkage disequilibrium and a MAF > 5% were used as threshold values for SNP selection while the chromosome region screened included 5000 base-pair regions flanking each gene. SNP selection identified 25 tagging SNPs for factor V and 6 tagging SNPs for factor II. Analysis of genetic polymorphisms was done by allele specific primer extension.

Results

Two SNPs were identified as risk factors for DVT in pediatric oncology patients: rs9332653 in the factor V gene (Odds Ratio: 0.44: 95% CI: 0.24-0.82 (p=0.01)) and rs3136516 in the factor II gene (OR: 2.73: 95% CI: 1.5-4.9 (p=0.0008)).

Conclusions

We have identified two novel polymorphisms associated with DVT in childhood cancer. Identifying child patients at increased risk of thrombosis would allow increased monitoring and potentially prophylactic anticoagulation. Future research will be aimed towards confirming these results in a validation cohort.

Funded By: AIHS

women & children's health research institute

Abstract #: 34
Presenter: Kirby A. Ziegler
Supervisor: D. Alan Underhill

Title: Defining PAX3 target gene networks and their dysregulation in birth defects and pediatric cancer

Authors: Kirby A. Ziegler, D. Alan Underhill
Affiliations: University of Alberta

Research Activity: Child and Youth Development : Oncology
Investigation Type: Quantitative Research

Introduction

The PAX3 transcription factor contributes to birth defects and pediatric cancer. Specifically, loss-of-function mutations in PAX3 cause Waardenburg syndrome types 1 and 3 (WS1 and WS3). These congenital conditions exhibit a range of neurocristopathies and can also be associated with musculoskeletal deformities in WS3. Moreover, PAX3 and the related PAX7 protein undergo chromosomal translocations with the gene encoding the forkhead transcription factor (FKHR) to produce oncogenic fusion proteins (PAX3 or PAX7-FKHR) in ~80% of pediatric alveolar rhabdomyosarcomas (ARMS). The normal and pathogenic effects of PAX3 are determined by the target genes it regulates. PAX3 contains two sequence-specific DNA-binding domains, the paired domain and homeodomain, and can interact with a range of target sites through differential use. We have established that a combination of alternative splicing and post-translational modification influences mode of binding, which is further modulated by the ARMS-associated translocation. We therefore hypothesize that PAX3 exists as a population of structural variants with distinct DNA-binding properties and target gene preferences.

Methods

DNA-binding profiles for human and mouse PAX3 as well as the oncogenic fusion protein PAX3-FKHR were derived from previously published sequence datasets. Complementary motif discovery (MD) methods, including the Weeder enumerative and exhaustive search algorithm and the Motif Discovery Scan (MDScan) alignment algorithm, were used to identify DNA-binding patterns for each protein. MD was subsequently validated using a discriminative support vector machine, kmer-SVM. Pattern frequencies from each computational experiment were aligned and aggregated into log-odds matrices called position weight matrices (PWM), each representing a single PAX3 probabilistic DNA-binding model. Regularized matrices were used to quantify the enrichment and distribution of PAX3 DNA-binding sites across different tissues and disease states.

Results

The resultant PAX3 DNA-binding libraries represent the first sets of optimal motifs described for full-length PAX3 variants. Furthermore, the results of this computational analysis have elucidated key differences between the binding specificity of normal PAX3 and pathogenic PAX3-FKHR proteins, which were previously undefined. Our ongoing work leverages PAX3 PWMs to query the distribution of target sites across genome-wide regulatory element datasets with the goal of defining specific target gene networks and how they may be altered in WS and ARMS.

Conclusion

Significantly, differential binding specificity described for PAX3-FKHR yielding an altered target gene network could underlie pathogenesis. Further validation of identified targets will give key insight into how PAX3 governs cell fate decisions and reveal strategies for manipulating PAX3 activity to therapeutic benefit.

Funded By: Graduate Studentship

women & children's health research institute

Abstract #:	35
Presenter:	Mohamed Eldeeb
Supervisor:	Richard Fahlman
Title:	The anti-apoptotic form of tyrosine kinase Lyn that is generated by proteolysis is degraded by the N-end rule pathway in Chronic myelogenous leukemia
Authors:	Mohamed Eldeeb, Richard Fahlman
Affiliations:	University of Alberta
Research Activity:	Child and Youth Development : Oncology
Investigation Type:	Mixed Methods

Introduction

Chronic myelogenous leukemia (CML), also known as chronic myeloid leukemia, is a myeloproliferative disorder characterized by increased proliferation of the granulocytic cell line due to the expression of p210 BCR-ABL, a fusion protein endowed with constitutive tyrosine kinase activity. While the development of imatinib (Gleevac), a tyrosine kinase inhibitor targeting the Bcr-Abl fusion protein for the treatment of chronic myeloid leukemia (CML), has greatly improved the control of CML a significant number of patient eventually develop imatinib resistance. While the most common resistance mechanism is the sporadic mutations to Bcr-Abl other mechanisms occurring at significant frequency include the overexpression of Src family kinases like Lyn. The activation of apoptotic pathways results in the caspase cleavage of the Lyn tyrosine kinase to generate the N-terminal truncated LynΔN. This LynΔN fragment has been demonstrated to exert negative feedback on imatinib induced apoptosis in chronic myelogenous leukemia (CML) K562 cells. Our investigations focus on LynΔN stability and how reduced stability reduces imatinib resistance. As the proteolytically generated LynΔN has a leucine as an N-terminal amino acid, we hypothesized that LynΔN would be degraded by the N-end rule pathway and thus contribute to the cancer killing activity of imatinib.

Methods

We used Cycloheximide Chase assay to monitor protein stability of LynΔN in CML cells. Western blot was used to determine protein quantity (as normalized to actin). We used flow cytometry to monitor apoptotic cell death. We used Fluorescence immunostaining and imaging to investigate the localization of LynΔN in cells.

Results

We recently published (Eldeeb MA and Fahlman RP. Oncotarget. 2014) reporting that LynΔN is a physiological substrate of the N-end rule pathway in chronic myelogenous leukemia (CML) K562 cells. We demonstrated that LynΔN is unstable and that its stability is dependent on the identity of its N-terminus. Additionally we established that LynΔN degradation could be inhibited by inhibiting either the proteasome or knocking down the UBR1 and UBR2 ubiquitin E3 ligases. Importantly, we also demonstrate that LynΔN degradation by the N-end rule counters the imatinib resistance of K562 cells provided by LynΔN expression.

Conclusion

Our data suggest a possible mechanism for the N-end rule pathway having a link to imatinib resistance in CML. With LynΔN being an N-end rule substrate, it provides the first example that this pathway can also provide a pro-apoptotic function as previous reports have currently only demonstrated anti-apoptotic roles for the N-end rule pathway.

women & children's health research institute

Abstract #: 36
Presenter: Raheem Suleman
Supervisor: Sunita Vohra
Title: Prevalence of pain, nausea/vomiting, and anxiety among pediatric oncology inpatients
Authors: Raheem Suleman, Denise Adams, Sunita Vohra
Affiliations: University of Alberta
Research Activity: Other
Investigation Type: Quantitative Research

Introduction

Although the inpatient pediatric oncology population has been well studied with regards to cancer treatment, less is known about the degree to which these patients experience symptoms such as pain, nausea/vomiting, and anxiety (PNVA).

Methods

As part of a cluster controlled clinical trial, we conducted daily assessments of PNVA symptom severity in consenting pediatric oncology inpatients. Over a six month period, we prospectively collected data on 106 inpatient stays in pediatric oncology, which represents 40 unique patients.

Results

Patients were 65% male, with a mean age of 8.0 ± 5.2 years and a median weight of 23.7 kg. They had received their cancer diagnosis a median of 5.6 months earlier and had a variety of primary diagnoses including leukemia (50.0%) and sarcoma (12.5%). They were treated primarily with chemotherapy (76.5%), and all patients survived to discharge or trial conclusion. The median length of stay in hospital was 4.6 days, with 78.1% of patients staying less than 10 days and 90.5% staying less than 20 days. Many patients described PNVA symptoms over the course of their stay and analysis of these data is ongoing. As an example, we provide data collected from the first day of measurement, when 29.2% of patients experienced pain, 29.6% nausea, and 45.6% anxiety. Nausea was generally mild for most patients: of those who reported nausea, 20.8% rated its severity as 4/10 of greater; 9.6% of patients had vomited within the past 24 hours. In contrast, pain and anxiety were less adequately controlled: of those patients with pain, 38.7% had pain of 4/10 or greater, and of those with anxiety, 41.7% reported anxiety of 4/10 or greater. At discharge, 91.0% of parents rated their child's quality of care as 8/10 or greater.

Conclusion

Our results suggest that there may be room for improvement in the assessment and treatment of PNVA symptoms in pediatric oncology inpatients.

Funded By: Support services

women & children's health research institute

Abstract #:	37
Presenter:	Yusuke Echigoya
Supervisor:	Toshifumi Yokota
Title:	Exons 45-55 skipping of the human dystrophin gene in vitro with antisense oligonucleotide cocktails
Authors:	Yusuke Echigoya, Joshua Lee, Toshifumi Yokota
Affiliations:	University of Alberta
Research Activity:	Child Health/Congenital Abnormalities
Investigation Type:	Quantitative Research

Introduction

Duchenne muscular dystrophy (DMD) is the most prevalent lethal genetic disorder in children and is caused by mutations in the *dystrophin* (*DMD*) gene. Dystrophin protein is essential for maintaining muscle fibre integrity. Exon skipping is a potential therapeutic strategy for treating DMD. Exon skipping uses short, synthetic DNA-like molecules called antisense oligonucleotides (AOs) to interfere with pre-mRNA splicing machinery. By removing exon(s) that disrupt the open reading frame, exon skipping can induce production of a functional protein, potentially ameliorating disease pathology. Current clinical trials have yielded encouraging results. Remaining challenges include limited applicability and unknown protein stability/function. The majority of DMD patients harbor deletion mutations within the region of exons 45-55 of the *DMD* gene. Multiple exon skipping of exons 45-55 in the *DMD* gene could provide a single therapeutic treatment for a large proportion of DMD patients. Additionally, a natural deletion mutation of the entire exons 45-55 is associated with exceptionally mild symptoms or asymptomatic individuals. The purpose of the present study is to test the feasibility of multiple exon skipping of exons 45-55 in the human *DMD* gene *in vitro*.

Methods

We designed cocktails of AOs called phosphorodiamidate morpholino oligomers (PMOs) for exons 45-55 skipping using our new prediction algorithms. Fibroblasts (skin cells) derived from two DMD patients with exons 45-50 and 46-50 deletion mutations (Coriell institute) were transformed to skeletal muscle cells with a retroviral vector containing the myogenic regulatory factor MyoD. Three immortalized DMD skeletal muscle cell lines with exons 45-52, 48-50 and 52 deletion mutations were obtained from our collaborators. These DMD cells were differentiated to myotubes (mature muscle cells) and transfected with PMO cocktails. The skipping efficacy was examined in RT-PCR. Immunocytochemistry was performed to confirm rescued dystrophin protein.

Results

RT-PCR results from DMD cells treated with the cocktail of 3, 5, 6, 8 or 10 PMOs showed the expected band size of an exons 45-55-skipped product. Sequencing analysis confirmed the removal of exons 45-55. We observed the restoration of dystrophin protein in the PMO cocktail-treated DMD cells by means of immunocytochemistry.

Conclusion

Based on the observation of exons 45-55 skipped mRNA and dystrophin protein in AO cocktail-treated DMD cells, we conclude that multiple exon skipping of exons 45-55 in the *DMD* gene is feasible *in vitro*. This is the first demonstration of successful exons 45-55 skipping in the human *DMD* gene.

Funded By: Graduate Studentship

women & children's health research institute

Abstract #:	38
Presenter:	Cadence Moorhouse
Supervisor:	Oana Caluseriu
Title:	Molecular characterization Of Al-Awadi/Raas-Rothschild/Schinzel/Fuhrmann-like Syndrome
Authors:	Cadence Moorhouse, FORGE Canada, Gaby Loots, Oana Caluseriu
Affiliations:	University of Alberta
Research Activity:	Child and Youth Development : Congenital Abnormalities
Investigation Type:	Quantitative Research

Introduction

Al-Awadi/Raas-Rothschild/Schinzel (AARRS) syndrome (OMIM 276820) is an autosomal recessive condition characterized by severe limb malformations in the three axes of limb development and other congenital anomalies due to mutations in wingless-type member 7A (WNT7A). Two siblings with an AARRSF-like condition born to healthy, consanguineous parents have been identified and mutational analysis of WNT7A was negative. The aim of this study was to molecularly characterize the clinically described phenotype. The affected children, two girls of two and four years of age respectively, presented with limb malformations in the three axes of limb development, absent uterus and developmental delay. One patient had a Dandy-Walker variant.

Methods

Due to the assumed recessive nature of the condition and based on the pedigree, homozygosity mapping was performed to identify the autozygous regions in the two affected individuals. There was no obvious causative gene identified by in silico analysis in these regions. Whole exome sequencing (WES) was conducted and variants in the autozygous regions were filtered, from which a short list of candidate genes remained.

Results

One homozygous variant, on chromosome 19, was identified in both patients. This variant was a frameshift insertion in exon 11 of heterogeneous nuclear ribonucleoprotein U-like 1 (HNRNPUL1) of the hnRNP family of proteins. Sanger sequencing was then used to confirm the mutation and the suspected segregation in the family. HNRNPUL1 interacts with bromodomain-containing protein 7, and the latter enhances the activity of the Dishevelled protein in the WNT signaling pathway. This observation is in keeping with our finding that transfecting wild type HNRNPUL1 into mouse cells decreases WNT receptor activity.

Conclusion

In this study, we were able to identify a novel candidate gene to support the molecular basis of a rare genetic disorder involving severe limb malformations. Future studies will evaluate the pathogenicity of this variant and the involvement of HNRNPUL1 in limb development.

Funded By: Innovation Grant

women & children's health research institute

Abstract #:	39
Presenter:	Maryam Hejazi
Supervisor:	David Eisenstat
Title:	Genetic regulation of photoreceptor cell differentiation in developing retina
Authors:	Maryam Hejazi, Vanessa Pinto, Jamie Zagozewoski, David Eisenstat
Affiliations:	University of Alberta
Research Activity:	Child and Youth Development : Congenital Abnormalities
Investigation Type:	Mixed Methods

Objective

Dlx homeobox genes are critical for development of the vertebrate retina. We are interested in identifying and characterizing DLX transcriptional targets. The *Crx* (Cone-Rod homeobox gene) is required for differentiation and maintenance of cone and rod photoreceptors. *Otx2* (Orthodenticle homeobox 2 gene) is required for specification of photoreceptors and bipolar cells. *Dlx1/Dlx2* double knock-out (DKO) mice have a significantly reduced ganglion cell layers and increased and ectopic expression of *Crx.* We hypothesized that DLX transcription factors repress *Crx* and *Otx2* expression during development.

Methods

Chromatin immunoprecipitation (ChIP) was performed to identify DLX2 occupancy at the *Otx2* and *Crx* promoters *in situ*. To identify specific DLX2 binding sites at the *Otx2* and *Crx* promoters, electrophoretic mobility shift assay (EMSA) was carried out. Quantitative real-time PCR (qRT-PCR) and immunofluorescence was performed on *Dlx1/Dlx2* DKO retinas to examine changes in *Otx2* and *Crx* expression in the absence of Dlx gene function. Luciferase reporter assays examined transcriptional activity of DLX2 on *Otx2* and *Crx* expression *in vitro.*

Results

ChIP demonstrates DLX2 binds to specific regions of *Crx* and *Otx2* promoters *in vivo*. EMSA demonstrates specificity of DLX2 binding to *Crx and Otx2* promoters *in vitro*. Additionally luciferase reporter assays demonstrate that DLX2 represses the expression of *Crx in vitro*. *Dlx1/Dlx2* DKO retinas demonstrate increased expression of *Crx* and *Otx2*.

Conclusion

Our data supports a regulatory role for DLX2 on *Crx* and *Otx2* expression during retinal development. Future directions include crossing our Dlx null mice to both *Otx2* and *Crx* reporter mice to verify the biological significance of DLX2 regulation of *Otx2* and *Crx* expression *in vivo.* Since OTX2 gene over-expression has been associated with poor prognosis in the childhood brain tumour medulloblastoma (Group 3), repressing its expression may be a novel therapeutic strategy.

women & children's health research institute

Abstract #:	40
Presenter:	Katrina Labonte
Supervisor:	Dr. Lori West
Title:	Investigation of A-Antigen specific tolerance following ABO-incompatible heart transplantation using a novel blood group a transgenic mouse model
Authors:	Katrina Labonte, Jean Pearcey, KeSheng Tao, Stephanie Tollenaar, Michael Mengel, Banu Sis, Peter Cowan, Bruce Motyka, Lori West
Affiliations:	University of Alberta
Research Activity:	Child and Youth Development : Transplant
Investigation Type:	Quantitative Research

Introduction

ABO-incompatible organ transplantation is associated with a high risk of antibody-mediated rejection (AMR), however, graft accommodation or immune tolerance can also occur. In infants, ABO-incompatible heart transplantation (ABOi HTx) can be performed safely as anti-blood group antibody (Ab) levels are low or absent. Following ABOi HTx, immune tolerance develops to the donor A/B antigen(s), by mechanisms not well understood. We generated transgenic mice (A-Tg, C57BL/6 [B6] background) that express blood group A-antigen on vascular endothelium and used these as donors and B6 wild-type (WT) mice as recipients to model 'A into O' Tx. We previously showed that A-Tg heart grafts undergo AMR in adult WT recipients with anti-A Ab. We hypothesized that young WT mice without anti-A Ab will not reject A-Tg heart grafts and will develop tolerance to A-antigen.

Methods

WT mice were transplanted at 4 weeks of age with A-Tg hearts (n=7). 13 weeks later, transplanted mice and non-transplanted littermates (n=8) were sensitized by injection of human A erythrocytes. Serum anti-A Ab titres were measured by hemagglutination assay and graft survival evaluated by palpation. Grafts were harvested 21 weeks post-transplant and assessed for morphological and immunophenotypical features of AMR.

Results

Prior to sensitization, 1 of 7 transplanted mice and 3 of 8 non-transplanted littermates had detectable anti-A Ab. Following sensitization, anti-A Ab were detected in 5 of 7 transplanted mice (median titre 1:128) and in all non-transplanted littermates (median titre 1:512). All grafts survived and none showed morphological features of AMR. One graft showed immunophenotypic evidence of AMR with moderate C4d deposition.

Conclusion

A-Tg hearts did not undergo AMR following Tx into young WT recipients, even after sensitization. That some recipients (2 of 7) did not produce anti-A Ab following sensitization is suggestive of A-antigen-specific tolerance. Generation of anti-A Ab following sensitization in the majority of recipients (although at lower titres than non-Tx littermates) but in the absence of graft damage may indicate graft accommodation.

Funded By: Support services

women & children's health research institute

Abstract #:	41
Presenter:	Shine Hariharan
Supervisor:	Ian Adatia
Title:	Cardiovascular associations and complications in pediatric patients listed for liver transplantation
Authors:	Shine Hariharan, Shreepal Jain, Prashant Bobhate, Long Guo, Jason Yap, Norman Knetman, James Shapiro, David Ross, Ian Adatia
Affiliations:	University of Alberta
Research Activity:	Child and Youth Development : Cardiology
Investigation Type:	Mixed Methods

Introduction

Portopulmonary hypertension (PoPH), Hepatopulmonary syndrome (HPS) and cirrhotic cardiomyopathy (CCM) are risk factors for adverse outcomes after liver transplantation in adults. We sought to determine the incidence of PoPH, HPS and cardiomyopathy in children referred for liver transplantation.

Methods

All children referred for liver transplant underwent clinical examination, upright and supine pulse oximetry, electrocardiogram (EKG), 2D, Doppler and contrast echocardiogram. Nuclear lung perfusion scan was done in children with a positive bubble contrast study.

Results

Between January 2010-July 2014, 51 patients were evaluated (median age 7 months, range 1-156; 27 males). Indications for liver transplantation were biliary atresia (n=23; 45%) metabolic disease (n=10; 20%), total parental nutrition induced cholestasis (n=7; 12%) and miscellaneous liver disease (n=11; 22%). None of the patients had PoPH by echocardiography. Contrast echocardiography revealed HPS in 4 cases (8%) (right to left shunt confirmed by radionuclide scan in 3/4) but only 2 patients (age 7 and 11 years) had severe cyanosis (right to left shunt quantified at 17-20%). Congenital cardiac anomalies were seen in 8 (16%) including patent ductus arteriosus (n=2), muscular ventricular septal defect, interrupted inferior vena cava with azygous continuation and left ventricular non-compaction, bicuspid aortic valve, supra valvar pulmonary stenosis and mitral valve prolapse with moderate mitral regurgitation and multiple atrial septal defects (ASDs). Septal or left ventricular hypertrophy was diagnosed by EKG (n=21/51, 41%) or echocardiography (n=12/51, 24%) and was significantly more common in patients with biliary atresia (p=0.03). All the patients had normal left ventricular systolic function. 29/51 (57%) underwent liver transplantation with 4 postoperative deaths including one with pulmonary arteriovenous malformations. Median post-operative ICU and hospital stay were 24.5 days (range 5-123 days) and 72 days (range 6-180 days) respectively and did not correlate with presence of septal hypertrophy. Post liver transplantation resolution of septal hypertrophy was confirmed in 2/11 and right to left shunt in 3/4. Two patients underwent cardiac surgery without adverse events (ASD closure and mitral valve replacement).

Conclusion

In our series of young children undergoing evaluation for liver transplantation 18% had structural cardiac anomalies and two patients required cardiac surgery prior to liver transplant justifying routine pre transplant cardiac evaluation. HPS was found in 8% and regressed after liver transplantation. Left ventricular or septal hypertrophy was more common in patients with biliary atresia and did not affect postoperative recovery. Porto pulmonary hypertension is rare in young children undergoing liver transplant.

Funded By: Start-up or Retention Funding

women & children's health research institute

Abstract #:	42
Presenter:	Awrad Nasralla
Supervisor:	Gina Rayat
Title:	Using manganese porphyrin to improve neonatal pig islet function in diabetic mice
Authors:	Awrad Nasralla, Jon Piganelli, Ray Rajotte, Gina Rayat
Affiliations:	University of Alberta
Research Activity:	Child and Youth Development : Transplant
Investigation Type:	Mixed Methods

Background:

Widespread application of islet transplantation is still limited to selected patients due to the shortage of human donors. Pig islets are being considered as an alternative source of islets due to several reasons including the similarity of insulin structure between human and pig. This provides unlimited source of islets that could be used for children with brittle type 1 diabetes. However, significant numbers of islets are lost during isolation and transplantation procedures due to oxidative stress. Synthetic antioxidants such as manganese (III) tetrakis (N-ethylpyridium-2-yl) porphyrin (MnP) was shown to protect islet from oxidative stress. In this study we speculate that pre-treatment of neonatal pig islets with MnP will protect them from oxidative stress and it will enhance their function after transplantation.

Methods

Neonatal pig islets were cultured with 0, 34, or 68 µM MnP for 24 hours at physiological conditions. They were then collected for q-PCR analysis to determine the level of the gene expression of antioxidant and antiapoptotic molecules such as heme-oxygenase-1 (HMOX-1), glutathione peroxidase-1 (GPx-1), superoxide dismutase-1 (SOD-1), B-cell lymphoma-2 (Bcl-2), and survivin, respectively. Islet viability was also determined using a two-color fluorescence assay. To examine whether pre-treatment of neonatal pig islets with MnP will improve their function *in vivo*, streptozotocin induced diabetic (≥20 mmol/L) NOD.SCID γ mice were transplanted with neonatal pig islets (2,000 IEQ) pre-treated with 0, 34 or 68µM MnP. Blood glucose levels of these mice were monitored once a week. When mice showed stable normal blood glucose levels, they were subjected to intraperitoneal glucose tolerance test (IPGTT). At the end of the study, the kidney bearing the islet transplant was surgically removed and was stained with hematoxylin & eosin, in addition to immunohistochemistry staining for insulin.

Results

We found a dose-dependent increase in SOD-1($p=0.04$), HMOX-1, and survivin ($p=0.03$) gene expression in islets pre-treated with MnP compared to untreated islets. The level of GPx-1 ($p=0.006$) and Bcl-2 gene expression was increased in islets pre-treated with 68 µM MnP compared to other groups. We also found that pre-treatment with MnP is not toxic to islets since the majority of islet cells were alive in all groups. NOD.SCID γ mice that received islets pre-treated with 34 µM MnP achieved normal blood glucose level earlier, and showed better response to high glucose when subjected to the intraperitoneal glucose tolerance test compared to other groups. Photomicrographs of islet-bearing kidney sections showed strong immunoreactivity to insulin.

Conclusion

Pre-treatment with MnP enhances the function of neonatal pig islets possibly through the antioxidant and antiapoptotic activities of MnP.

Funded By: CIHR, Saudi Ministry of Higher Education, ADI

women & children's health research institute

Abstract #:	43
Presenter:	Chantelle Champagne
Supervisor:	Dawna Gilchrist
Title:	Ought we to mend their broken hearts? The history of cardiac repairs in children with down syndrome
Authors:	Chantelle R Champagne, Melanie Lewis, Dawna M Gilchrist
Affiliations:	University of Alberta
Research Activity:	Child and Youth Development : Cardiology
Investigation Type:	Qualitative Research

Introduction

Advances in cardiac surgery for infants in the 1970s and early 1980s resulted in a series of ethical and social questions surrounding who should benefit from these procedures. Initial cardiac repair rates in children with Down syndrome were low; while these procedures are offered as standard of care today. The history of the treatment versus non-treatment of cardiac defects in children with Down syndrome has served as a test case for changes in the last fifty years in clinical decision making in persons with Down syndrome.

Methods

A broad literature search was conducted on Medline and Google Scholar with combinations of the following search terms: Down syndrome, trisomy 21, mongolism, cardiac defects, heart defects, cardiac surgery, cardiac repairs, atrioventricular septal defect, atrioventricular canal. Relevant articles were limited to those published in peer-reviewed journals, and their references were searched to find more articles. Historical sources were found through a combination of the above search strategy, searching for historical texts of cardiac surgery and Down syndrome in the University of Alberta Library Database, as well as acquiring bioethics and sociology sources suggested by mentors.

Results and Conclusions

This paper reviews the medical literature on the success of cardiac repairs in children with Down syndrome from the early 1970s – present and demonstrates increasing provision of cardiac repairs over time. A concurrent social history is also presented to place the clinical data in context of larger societal views of Down syndrome. During that time period, a complex social, ethical and legal evolution proved to play as important a role in cardiac interventions as rapidly advancing surgical techniques. The multifaceted question of providing cardiac surgery to children with Down syndrome illuminates the complex process of medical decision making in a variety of persons with underlying cognitive or medical conditions.

Funded By: Trainee Research Grant

women & children's health research institute

Abstract #:	44
Presenter:	Gordana Djordjevic
Supervisor:	Joan Robinson
Title:	Can one prescribe carbapenems to patients with IgE-mediated allergy to penicillins or cephalosporins?
Authors:	Gordana Djordjevic, Brittany Kula
Affiliations:	University of Alberta
Research Activity:	Other
Investigation Type:	Quantitative Research

Introduction

A drug allergy is defined as a specific immunologic reaction to a drug. Penicillins or cephalosporins are common causes of IgE-mediated allergic reactions. IgE-mediated reactions are of particular concern as they can be life threatening. Recurrence risk with re-exposure to the same drug is not known; subsequent reactions are often more severe than was the initial reaction. Patients with IgE-mediated allergy to penicillins or cephalosporins may react to the beta lactam ring structure that is common to all penicillins, cephalosporins, monobactams and carbapenems. The purpose of this review was to determine if carbapenems can be safely prescribed for patients who have had presumed IgE-mediated reactions to penicillins or cephalosporins. Patients with IgE-mediated reactions to one antibiotic are more likely to have allergies to other antibiotics. Our hypothesis was that although there would be some cross-reactivity, the rate of life-threatening events upon challenge with a carbapenem would be less than 1%.

Methods

A systematic review was conducted of published data on children and adults with a clinical history of IgE-mediated allergy to a penicillin and/or cephalosporin that were subsequently given a carbapenem. Reactions were classified as 1) proven IgE-mediated (hypotension, wheezing, angioedema, laryngeal edema, hospitalization or death with symptoms within 4 hours), 2) suspected IgE-mediated (pruritus, flushing, urticaria, or edema within 4 hours or 3) possible IgE-mediated (symptoms not described by authors or onset > 4 hours) and 4) non-IgE-mediated.

Results

Ten studies and 12 case reports fit the criteria, describing 854 participants. For patients with previous proven, suspected or possible IgE-mediated penicillin reactions (N=838), the incidence of any type of suspected allergic reaction to a carbapenem was 36/838 (4.3%; 95% confidence interval 3.1- 5.9%) and the incidence of proven (1/838), suspected (0/838) or possible (19/838) IgE-mediated reactions was 20/838 (2.4%; 95% confidence interval 1.6- 3.7%). Of the subset of patients with positive penicillin skin tests (N=295), only one had an allergic reaction (0.3%; 95% confidence interval 0.06- 1.9%) and this was a possible IgE-mediated reaction. For patients with previous proven, suspected or possible IgE-mediated cephalosporin reactions (N=12), the incidence of any type of allergic reaction to a carbapenem was 3/12 (25%) including two non-IgE-mediated reactions and one possible IgE-mediated reaction.

Conclusion

The cross-reactivity between penicillins and carbapenems for IgE-mediated reactions is very low but caution is still advised. Cross-reactivity rates may be higher between cephalosporins and carbapenems but minimal data is available.

Funded By: Trainee Research Grant

women & children's health research institute

Abstract #:	45
Presenter:	Alex Jackman
Supervisor:	Sunita Vohra
Title:	Perceptions of complementary and alternative medicine among undergraduate healthcare professional trainees in a Canadian university
Authors:	Alexandra Jackman, Anastasia Kutt, Sunita Vohra, Maria Mayan
Affiliations:	University of Alberta
Research Activity:	Other
Investigation Type:	Qualitative Research

Introduction

Complementary and alternative medicine (CAM), ex. Chiropractic, natural health products (NHPs), traditional Chinese medicine, etc. is widely used around the world. Future health care providers need training about CAM in order to safely and effectively guide patient choices. However, the incorporation of CAM into conventional education is variable among institutions, and often trainees obtain minimal exposure. Moreover, knowledge of trainee perceptions of CAM modalities and practitioners remains limited. This study aimed to investigate trainees' perceptions of the strengths and weaknesses of CAM therapies, and to explore perceptions that may be representative of specific disciplines.

Methods

Undergraduate health sciences trainees (medicine, nursing, pharmacy, occupational therapy, physical therapy, etc.) opted into a CAM stream of a mandatory interprofessional education course in a Canadian university. Trainees submitted reflective assignments regarding their perceptions of CAM after the first class. Data were qualitatively analyzed coding for trainees' perceptions of the strengths and weaknesses of CAM therapies, as well as their attitudes according to discipline.

Results

Trainee perspectives were generally positive across all disciplines. Trainees identified perceived CAM strengths as safety, efficacy, patient-centered-care, client empowerment, and improvement of client mental health. Trainees identified perceived CAM weaknesses as threats to safety, inaccessibility, and a lack of efficacy and empirical evidence, as well as sub-optimal understanding about CAM among conventional practitioners and clients. There was heterogeneity of opinion relating to the safety and efficacy of CAM. Trainees invoked their profession's lens in their perspectives of CAM, expressing the values inherent to their discipline early in their education.

Conclusion

The majority of trainees viewed CAM with a positive perspective, however differed considerably in their opinions of its safety and efficacy. Future curricula should therefore address trainee perceptions to optimize educational initiatives, as well as incorporate fundamental material to ensure adequate trainee knowledge and foster educated perceptions of CAM.

women & children's health research institute

Abstract #:	46
Presenter:	Abbeir Hussein
Supervisor:	Sarah Curtis
Title:	Acute physical injury and subsequent stress symptoms
Authors:	Abbeir Hussein, Sarah Curtis, Amanda Newton, Bill Sevcik , Cathy Falconer, Lindy Lindy Van Riper, Heidi Wilkes
Affiliations:	University of Alberta
Research Activity:	Child and Youth Development : Mental Health
Investigation Type:	Mixed Methods

Introduction

Injuries are the largest cause of morbidity and mortality among children in North America. Currently it is unknown how often children and families are affected by unhealthy stress after injury. Furthermore, healthcare providers lack information about how to identify which of these children and parents would most benefit from further education and care in the community. Our primary objective is to obtain data about the occurrence of posttraumatic stress symptoms in Canadian children and parents following physical injury. A secondary objective is to identify any child and parent characteristics that clinicians could use to predict children and parents at risk for the development of PTSS post-injury. Furthermore, we seek to evaluate whether acute care clinicians can accurately prognosticate which children may need psychological follow-up after acute physical injury without use of a screening tool.

Methods

Consecutive children presenting to the stollery ED over a six month period who have experienced physical injury and are being medically evaluated for such are eligible for the study. Severe injuries requiring immediate ICU or operative care, or those that impair consciousness are excluded. Information gathered includes demographics, injury characteristics, past injuries, and family functioning. Clinicians will rate PTSS likelihood at 1-month post-injury using a Likert 5-point scale. A brief screening questionnaire will be administered to parents and children to determine how many may be at high risk for stress following injury. Parents and children are then contacted one month later to fill out a stress symptom questionnaire to see if they have experienced post-trauma psychological distress. Mixed-model regression analyses will be conducted to investigate the potential longitudinal association between included predictor variables and PTSS symptoms. Univariate analysis will be used to determine the strength of association between each variable and the primary outcomes.

Results

Based on review of the published literature, we hypothesize that: 1) In the community, 10-30% of children will display persistent symptoms of PTSS 1 month after acute injury; 2) In the ED, 5-40% children will screen at risk for PTSS, and 20% mothers and <5 % fathers will screen positive for subsequent PTSS; 3) Several predictor variables for development of PTSS are identifiable at the acute care stage; and 4) Acute care clinicians will not accurately prognosticate which children may need psychological follow-up after acute physical injury without use of a screening tool.

Conclusion

Through this project we will: 1) learn the proportion, prognostic factors and degree to which children experiencing acute trauma (and their parents) will have psychological sequelae.

women & children's health research institute

Abstract #: 47
Presenter: Elizabeth (Beth) DeBruyne
Supervisor: Samina Ali

Title: Emergency medical services provider comfort with pre-hospital analgesia administration to children

Authors: Elizabeth DeBruyne, Amaly Rahman, Sarah Curtis, Sunil Sookram, Samina Ali
Affiliations: University of Alberta

Research Activity: Child and Youth Development : Pain Management
Investigation Type: Quantitative Research

Introduction

The under-treatment of pediatric pain is a significant concern among emergency clinicians and researchers. Although some have examined pre-hospital pain management, the deterrents to pediatric analgesia administration by Emergency Medical Services (EMS) have not yet been examined in Canada. This study was conducted to describe EMS pain management practices and provider comfort treating pediatric pain, describe differences in pain management between adults, adolescents and children, and to assess the potential barriers, misconceptions, difficulties and needs related to successful provision of pediatric analgesia.

Methods

A study-specific survey tool was created and distributed to all primary care paramedics (PCPs) and advanced care paramedics (ACPs) over four mandatory educational seminars in the city of Edmonton from September to December 2008.

Results

Ninety-four percent (191/202) of EMS personnel for the city of Edmonton completed the survey. The majority of respondents were male (73%, 139/191), aged 26-35 (42%, 80/191) and had been in practice less than 10 years (53%, 101/191). Seventy-four percent (141/191) of those surveyed were ACPs, while 26% (50/191) were PCPs. Although the majority of respondents reported using both pain scales and clinical judgement to assess pain for adults (85%, 162/191) and adolescents (86%, 165/191), children were 6 times more likely than adults (31%, 59/191 versus 5%, 10/191) to be assessed by clinical judgement alone. EMS personnel felt significantly more comfortable treating adults than children ($p<0.001$), and they were less likely to treat children even if they were experiencing identical types and intensities of pain as adults (all p values <0.05) and adolescents (all p values <0.05) Twenty-five percent of providers (37/147) assumed pediatric patients required less analgesia due to immature nervous systems. The major barriers to treating children's pain included limited clinical experience (34%, 37/110), difficulty in communication (24%, 26/110) and inability to assess children's pain accurately (21%, 23/110).

Conclusion

EMS personnel self-report that children's pain is less rigorously measured and treated than for adults. Educational initiatives aimed at increasing clinical exposure to children, as well as further education regarding simple pain measurement tools for use in the field may help to address identified barriers and discomfort with assessing and treating children.

Funded By: Trainee Research Grant

women & children's health research institute

Abstract #: 48
Presenter: Hannah Weinstangel
Supervisor: Irena Buka
Title: Environmental pediatrics: An introduction and an evidence-based online resource
Authors: Hannah Weinstangel, Irena Buka
Affiliations: University of Alberta
Research Activity: Other
Investigation Type: Qualitative Research

Introduction

The World Health Organization estimates that 3 million children under the age of five die annually from environmentally related disease[4]. In the United States, the cost of environmentally related public health concerns is estimated as greater than $55 billion[3]. Environmental exposure is among parents' top health concerns for children[2]. Yet the study of the effects of environmental exposures on health outcomes is a developing field, and clinicians feel inadequately prepared to address these concerns[3].

The Children's Environmental Health Clinic (ChEHC) is the first clinic of its kind in Canada. Their website includes a list of online resources on major topics related to child health and the environment. There has not yet been an objective evaluation of the comprehensiveness of the topics or scientific quality of the information on the website.

This study seeks to offer an accessible introduction to the field of environmental pediatrics, including an online resource for evidence-based information on key topics in the field. These resources assist in disease prevention, health promotion, education, and the increasing need to balance environmental health risks.

Methods and Results

A scoping review of scientific and grey literature in the field of environmental pediatrics was performed to inform a written introduction to the field of environmental pediatrics for publication and to identify gaps in the content of the ChEHC website. The content of the ChEHC website was then objectively evaluated using the National Network of Libraries of Medicine checklist for health websites[1]. The website was then updated, using the results of the study as a guide, to make it as relevant, complete, and evidence-based as possible.

Conclusion

Environmental pediatrics is an important, emerging topic. There is a need for accessible, evidence based pediatric environmental health resources for clinicians and the general public. The products of this study (a publication and website) respond to that need and thus assist in disease prevention and health promotion.

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Funded By: Trainee Research Grant

women & children's health research institute

Abstract #:	49
Presenter:	Arnaldo Perez
Supervisor:	Geoff Ball
Title:	Why do families initiate pediatric weight management? A multi-center, qualitative study of parents' reasons and facilitators
Authors:	Arnaldo Perez, Nicholas L Holt, Rebecca Gokiert, Jean-Pierre Chanoine, Laurent Legault, Katherine M Morrison, Arya M Sharma, Geoff DC Ball
Affiliations:	University of Alberta
Research Activity:	Child and Youth Development : Nutrition
Investigation Type:	Qualitative Research

Objective

To characterize enabling factors for treatment initiation among parents of children with obesity who were referred for multi-disciplinary, tertiary-level pediatric weight management.

Methods

One-on-one, semi-structured interviews were conducted with parents of children who were referred for pediatric weight management at one of four multidisciplinary clinics in Vancouver, Edmonton, Hamilton, and Montreal. Purposeful sampling was used to recruit parents by site and level of program involvement. Interviews were audio recorded and transcribed verbatim. Data were managed using *NVivo 10* and analyzed thematically.

Results

Most parents (n=65) were mothers, had completed some post-secondary education, and had a child with a BMI ≥95th percentile). Two main themes were identified regarding treatment initiation: Reasons and facilitators. Reasons related to losing weight (e.g., preventing further weight gain and health issues), perceived efficacy of the clinical program (e.g., obtaining compressive and reliable care), and family empowerment for weight management (e.g., enhancing child's self-management of overweight). Facilitators related to families (e.g., parental control over child's participation), referring physicians (e.g., child's need for weight management, benefits of the recommended care discussed with families), clinical programs (e.g., orientation session found useful), decision making process (e.g., decisions to initiate treatment made jointly by parents and children), and socio-environmental factors (e.g., short distance, significant others highlighting the need for weight management).

Conclusion

Parents initiated treatment when they perceived the need for pediatric weight management, found the recommended care more effective than alternative options, and did not face major barriers to engaging in care. Strategies to enhance initiation should address initiation barriers and capitalize on facilitating factors, especially those under the control of health care providers.

Funded By: Graduate Studentship

women & children's health research institute

Abstract #: 50
Presenter: Hasnain Raza
Supervisor: Tarek El-Bialy

Title: Effect of low intensity pulsed ultrasound on orthodontically induced tooth root resorption

Authors: Hasnain Raza
Affiliations: University of Alberta

Research Activity: Child and Youth Development: Nutrition
Investigation Type: Quantitative Research

Introduction

Previous studies reported that low intensity pulsed ultrasound (IPUS) can minimize orthodontically induced root resorption (OIRR) after simple tipping movement in human and in animals. The aim of this study was to evaluate the effect of IPUS on root resorption after buccal root torque in human premolars.

Methods

Twenty premolars were buccally torqued using 0.019 x 0.025 TMA wire that at a continuous torque 285 gm/mm. Torque was calibrated using an established torque machine. LIPUS was applied for twenty minutes per day for four weeks at 30mW/cm^2 of the transducer surface area. LIPUS devices were calibrated before and after treatment. CBCT was taken before treatment. After 4 weeks, all premolars were extracted for regular orthodontic treatment and root lengths were measured on initial CBCT and directly on the extracted teeth using a digital caliper. Comparison was performed using student t-test.

Results

There was significant decrease in root length in non LIPUS treated premolars (1.31 +/- 0.63 mm) compared to LIPUS treated premolars (0.22 +/- 0.27 mm) after treatment ($P<0.001$).

Conclusion

LIPUS application during buccal root torque in human premolars minimizes root shortening compared to non LIPUS treated premolars.

Funded By: Trainee Travel Grant

women & children's health research institute

Abstract #:	51
Presenter:	Abeer Alzaben
Supervisor:	Diana Mager
Title:	Quality of life in children and adolescents with Celiac Disease on gluten free diet
Authors:	Seema Rajani, Leanne Shirton, Rabin Persad, Justine Turner, Diana Mager
Affiliations:	University of Alberta
Research Activity:	Child and Youth Development : Nutrition
Investigation Type:	Quantitative Research

Introduction

Celiac disease (CD) is a life long autoimmune disease. Little is known regarding parental and child perceptions of quality of life in children with CD and other gastrointestinal disorders (GI) in Canada. The study objective was to compare parent and child perceptions of quality of life in children with CD and chronic GI disorders.

Methods

A prospective study was conducted in children and adolescents with biopsy proven CD (n=40; 9.6 ± 3.2 yrs; 11M, 29F) and in children with chronic GI diseases (GI-controls; n=20; 9.9 ± 4.5 yrs; 11 M, 9F). QoL was measured using the parent-proxy and child-reports for PEDSQL 4.0 and the CDDUX. Parent-child differences (*d*) in perceptions of QoL were determined by dividing the absolute differences by the standard deviation of each QoL domain (psychosocial, school, emotion, physical functioning, average) reported by the child. Weight and height-z scores were calculated using CDC Epi Info Software. A positive value > 0.2 indicates a parent ranked the child QoL lower than the child; -0.2 the parent ranked the QoL higher than the child.

Results

Weight-for-age z-scores were significantly different between CD-children (-0.43± 1.27) and GI-control (0.50 ± 0.94; p=0.01). CD-children had higher average QoL (81 ± 10 vs 73 ± 9; p<0.01); and higher physical functioning scores (91± 9 vs 81 ± 11; p<0.01) than GI-control. Parents of children with CD perceived the child to have a lower QoL than the CD child when compared to parents of children with other GI disorders (1.3 ± 3.1 (CD) vs -2.2 ± 6.7 (GI controls); p=0.02). Higher QoL scores were reported by CD-children without GI symptoms for school functioning (86 ± 9 (-) vs 71 ± 17 (+); p<0.01)), psychosocial (88 ± 7 (-) vs 75 ± 15 (+); p<0.01), and average QoL score (86 ± 5 (-) vs 77 ± 11 (+); p=0.01) than those CD children without GI symptoms.

Conclusion

In general, CD-children report better QoL then children with undifferentiated gastrointestinal complaints. Parents of CD-children perceived their child's QoL more adversely than the child's perception, even in the absence of GI symptoms.

women & children's health research institute

Abstract #:	52
Presenter:	Jillian Avis
Supervisor:	Geoff Ball
Title:	Attrition and the management of pediatric obesity: An Integrative Review
Authors:	Jillian Avis, Jasmine Dhaliwal, Nicole Nosworthy, Nicholas Holt, Lonnie Zwaigenbaum, Allison Rasquinha, Geoff Ball
Affiliations:	University of Alberta
Research Activity:	Child Nutrition
Investigation Type:	Mixed Methods

Introduction

Challenges exist in providing effective services for pediatric obesity management. Chief among these is a high degree of attrition, which can reduce therapeutic benefits and contribute to inefficient health services delivery. The objective of this study was to document and characterize predictors of and reasons for program attrition in the management of pediatric obesity.

Methods

We searched literature published up to January 2014 in five electronic databases, including CINAHL, EMBASE, MEDLINE, PsycINFO, and Scopus. Papers were included if they were published in English, included 0 – 18 year olds, had a primary focus on pediatric weight management, incorporated lifestyle and behavioral changes without the use of pharmacotherapy, provided attrition data, and reported information about predictors and/or reasons for attrition from a family-based intervention provided in a research or clinical setting. Twenty-three papers (n=20 quantitative; n=2 qualitative; n=1 mixed methods) met our inclusion criteria. Clarity of study aims, objectives, methods, and data analysis were appraised using Bowling's checklist.

Results

Attrition varied study-to-study according to definition (min – max: 4 – 83%; median: 37%). There were few consistent predictors of attrition between studies, although drop out was higher among US-based families receiving public health insurance. Older boys and girls were also more likely to discontinue care, but children's sex and baseline weight status did not predict attrition. The most commonly reported reasons for attrition were logistical barriers and programs not meeting families' needs.

Conclusion

Attrition is a common phenomenon. Developing and evaluating strategies that are designed to minimize the risk of attrition, especially among families who receive public health insurance and older boys and girls, are needed to optimize the effectiveness of pediatric obesity management.

Funded By: Graduate Studentship

women & children's health research institute

Abstract #:	53
Presenter:	Elise Watkins
Supervisor:	Eric Parent
Title:	Predictors to identify Adolescents with Idiopathic Scoliosis who will benefit from Schroth exercises within a randomized control trial
Authors:	Elise Watkins, Eric Parent, Sanja Schreiber, Doug Hill, Doug Hedden, Marc Moreau, Sarah Southon, Alain Moreau
Affiliations:	University of Alberta
Research Activity:	Other
Investigation Type:	Quantitative Research

Introduction

Adolescent Idiopathic Scoliosis (AIS) is a 3D spinal deformity affecting 1-3% of the population and is most common in females. AIS can result in chronic pain, decreased function, external deformity, and poor self-image. Most patients have a good prognosis and will not require brace or surgical treatment. Others have a higher risk of worsening. Among those at risk of worsening it is not clear who benefits from exercises. Identifying predictors of success with treatment will help therapists offer exercises only to patients likely to benefit.

Methods

Patients with AIS (n=50), with spinal curves 10° to 50°, were randomized to a standard care group or a Schroth exercise added to standard care group. Standard care consisted of observation or bracing for six months. In addition to standard care, the Schroth group participated in supervised exercises combined with a home program for six months. At baseline, the following potential predictors of success were assessed using questionnaires and a physical exam: curve severity at baseline (Cobb angle), Schroth curve type, Risser sign, self-efficacy score, and prognostic blood marker results (sCD44 and OPN). Subjects were categorized as successful if showing ≤5° curvature progression at six months.

Continuous variables were dichotomized using ROC curve analyses. Association of the dichotomized variable with the outcome was tested using Chi-square. Variables with Chi-Square p <0.20 were entered in a logistic regression analysis to determine the significance of the predictor and "predictor by treatment" interaction terms for predicting success.

Results

A baseline spinal curve severity ≥24° was a significant prognostic variable (ie. predict success in both groups). The interaction between curve severity and treatment was not a predictor of success (ie. does not predict success specifically when treated)(p=0.99). Self-efficacy and curve types did not contribute to predict success (p>0.20) and also did not specifically predict response to exercises. A Risser sign of ≥1 (p=0.089), sCD44 concentration of ≤547 (p=0.078) and OPN levels of ≤532 (p=0.184) did not reach significance as prognostic variables and were also not retained in the logistic regression models as treatment modifiers.

Conclusion

Baseline spinal curve severity was the only variable predicting ≤5° curvature progression at the end of treatment but it was not specifically associated with response to Schroth treatment. The power for this preliminary analysis is low. With more subjects, baseline Cobb angle, Risser sign, and blood test results show promise as pronostic factors but other factors should be examined as treatment modifiers.

Funded By: Graduate Studentship

women & children's health research institute

Abstract #:	54
Presenter:	Harmanpreet Kaur
Supervisor:	Tarek El-Bialy
Title:	Effect of functional appliance and ultrasound on the mandibular growth.
Authors:	Harmanpreet Kaur, Hasan Uludag, Douglas Dederich, Tarek El-Bialy
Affiliations:	University of Alberta
Research Activity:	Other
Investigation Type:	Quantitative Research

Objective

Previous studies have shown that both functional appliance (FA) and low intensity pulsed ultrasound (LIPUS) can enhance mandibular growth. The aim was to study the possible synergetic effect of functional appliance (FA) and low intensity pulsed ultrasound (LIPUS) on the mandibular condylar growth.

Methods

54 Sprague Dawley growing rats were divided into 6 groups (n = 9) namely; 1. Control – with no FA or LIPUS 2. FA group 3. LIPUS 20 min 4. LIPUS 40 min 5. FA + LIPUS 20 min 6. FA + LIPUS 40 min. Custom made FA was constructed for each rat and was placed on the upper and lower anterior teeth when the rats were 28 days old. LIPUS was applied on the right side of the mandible for 20 min or 40 min per day for four weeks. MicroCT analysis was performed using Micro CT imager, Skyscan 1076, Skyscan NV, Belgium, with resolution of 18 µm. The parameters evaluated from the scans were: bone volume fraction (BV/TV), trabecular thickness (Tb.Th), and trabecular number (Tb.N), trabecular separation (Tb.Sp) and bone mineral density (BMD).

Results

FA groups showed lower weight as compared to the control and LIPUS treated group. Micro CT analysis showed statistically significant results in all the parameters: BVTV (p=0.00), Tb.Th (p=0.00), Tb.Sp (p=0.008), Tb.N (p=0.00) and BMD (p=0.00). BVTV and Tb.Sp were higher for the LIPUS 20 min application while Tb.Th, Tb.N and BMD were higher for LIPUS 40 min. BVTV, Tb.N and BMD were higher for the combination therapy with 20 min while Tb.Th was equal and Tb.Sp was higher in 40 min combination therapy.

Conclusion

Both treatments i.e. LIPUS and the combination therapy have positive effect on the condylar growth as compared to the control and FA groups. But LIPUS treatment shows enhanced mandibular growth as compared to the combination treatment.

Funded By: Trainee Travel Grant

women & children's health research institute

Abstract #:	55
Presenter:	Cassandra Janetzki-Flatt
Supervisor:	Oana Caluseriu
Title:	Investigating the genetic cause of a Congenital Myasthenic- like Syndrome
Authors:	Cassandra Janetzki-Flatt, Hanna Kolski, Joe Watt, Atilano Lacson, Norma Leonard, Georg Schmolzer, Ainsley Kerr, Stacey Hume, Oana Caluseriu
Affiliations:	University of Alberta
Research Activity:	Child and Youth Development : Congenital Abnormalities
Investigation Type:	Quantitative Research

Introduction

Congenital Myasthenic Syndromes (CMS) are a group of rare clinically and genetically heterogeneous disorders characterized by impaired neuromuscular transmission. Patients experience progressive muscle weakness involving ocular, limb, and bulbar muscles. Mutations in the 18 CMS genes known to date are estimated to explain approximately 50% of clinically diagnosed CMS. The exact diagnosis in these disorders is extremely important to provide answers to families, customize management including the start of early and appropriate therapy, prevent life-threatening events, improve clinical outcomes overall, and provide information for family planning. This study is an interdisciplinary investigation of a Canadian consanguineous family with two affected children initially suspected to have a CMS-like disorder (also based on neurophysiological studies). The male sibling, with the more severe findings, was subsequently diagnosed with a severe giant axonopathy on sural nerve biopsy.

Methods

Extensive clinical diagnostic testing failed to identify a cause for this condition to date. Based on our family history, an autosomal recessive pattern of inheritance was assumed for the trait studied. Homozygosity mapping by SNP array was performed and four possible candidate genes were identified. Exome studies were completed and analysis of variants focused on previously identified autozygous regions.

Results

A homozygous variant in a gene encoding the high-affinity choline transporter was identified and segregated with the phenotype in this family. In-silico analysis using multiple software programs supported the pathogenicity of this mutation. This candidate gene is essential in the transport of choline for adequate acetylcholine production, and a knockout mouse model reproduces the lethal phenotype identified in our patients. Future directions include studies to further support the pathogenicity of the mutation.

Conclusion

This study describes a novel CMS-like phenotype and molecularly characterizes this condition employing the use of Next Generation Sequencing technology. Our work contributes to improving clinical care in a family with a rare genetic disorder, and opens the opportunity for exploring new therapies for this group of debilitating neurotransmitter conditions.

Funded By: Innovation Grant

women & children's health research institute

Abstract #:	56
Presenter:	Sue Rene Soon
Supervisor:	Hamdy El-Hakim
Title:	A systematic review of the evidence on spontaneous resolution of laryngomalacia and its symptoms
Authors:	Sue Rene Soon, Vruta Patel, Hamdy El-Hakim
Affiliations:	University of Alberta
Research Activity:	Child and Youth Development : Congenital Abnormalities
Investigation Type:	Qualitative Research

Purpose

Systematic review of the existing literature on spontaneous resolution of laryngomalacia (LM) or its symptoms in otherwise healthy newborns.

Methods

Electronic search of English language articles reporting on the natural resolution of congenital LM (in search engines, Pubmed, Medline and Embase) in healthy newborns till date. We included prospective or retrospective studies that documented endoscopic diagnosis of LM in children, with sufficient follow up, and assessment of resolution by subjective and objective end points. We excluded case reports, narrative reviews, surgical literature and studies which included patients with associated co-morbidities affecting the airway without subgroup analysis.

Results

Of the 831 articles identified by the search, only two studies met our inclusion criteria (n=321 patients). Both were retrospective and one had an additional prospective arm. Stridor resolution was the main end point and it resolved in 88% (283/321). The level of evidence was low. The rate of resolution varied from 83% at 1 year to 93% at 9 months. It occurred at a mean of 8.3 months (range 4-9 months). Patient recruitment, and follow up were not clearly reported. Swallowing and sleep end points were not reported in many instances, and endoscopic resolution never assessed.

Conclusion

There is no evidence that LM resolves endoscopically. Low level of evidence supports that stridor and respiratory distress resolve spontaneously, and caution has to be exercised upon counseling the parents. Other clinical manifestations have not been studied. Prospective longitudinal trials are required to better understand the natural history.

women & children's health research institute

Abstract #:	57
Presenter:	Carolina Araujo
Supervisor:	Daniela Costa
Title:	Effects of fluid extract of mulberry (Morus Nigra) on antioxidant enzyme activity in experimental model of type 1 diabetes Mellitus
Authors:	Carolina Araujo, Joamyr Rossoni Jr, Karine Lúcio, Marcelo Silva, Richard Schulz
Affiliations:	Other
Research Activity:	Other
Investigation Type:	Quantitative Research

Introduction

Diabetes mellitus (DM) is a growing epidemic affecting both women and children's health. It is estimated that over 150 million people have diabetes and the World Health Organization expects that number to reach 285 million by 2025. DM (Type I and Type II) is associated with increased oxidative stress and decreased antioxidant capacity, resulting in the oxidative damage of cellular components. Oxidative stress plays a role in the pathogenesis of diabetes and is most often triggered by hyperglycemia. New antioxidant therapies are essential to reduce the complications of diabetes-induced oxidative stress. Fruit with antioxidant properties such as mulberry (*Morus nigra*) may prove to be an effective supplement in DM treatment.

Methods

The aim of this study is to evaluate the antioxidant potential of mulberry pulp in type 1 diabetic rats. Experimental diabetes was induced by 135 mg/kg alloxan (i.p.). There were 3 experimental groups (n=8): control, diabetic, diabetic-treated rats. Diabetic-treated rats were given 1 mL/day of mulberry pulp three days after administration of alloxan. Control and untreated diabetic rats were given water. Animals were sacrificed after 30 days of treatment. Oxidative stress and antioxidant capacity was evaluated by measuring superoxide dismutase (SOD) and catalase activity in the liver.

Results

Diabetic rats had increased SOD activity compared to control. In contrast, catalase activity was significantly decreased in diabetic rats compared to control. Our study found that 30 day treatment with mulberry pulp (1 mL/day) restored SOD and catalase activity in the liver compared to control.

Conclusion

Our results support the hypothesis that mulberry increases catalase and decreases SOD activity in type 1 diabetic rats. Mulberry-induced inhibition of SOD may reduce levels of hydrogen peroxide and other reactive oxygen species, resulting in a decrease in oxidative stress. Our results suggest mulberry's antioxidant properties may make it a beneficial supplement in the treatment of diabetes mellitus.

women & children's health research institute

Abstract #:	58
Presenter:	Sarah Aziz
Supervisor:	Greg Tyrrell
Title:	Increased incidence of pertactin-deficient Bordetella pertussis infections in Alberta 2012-2013
Authors:	Sarah Aziz, Greg Tyrrell
Affiliations:	University of Alberta
Research Activity:	Child and Youth Development : Infection, Inflammation, Immunology
Investigation Type:	Quantitative Research

Introduction

Pertussis (whooping cough) is a contagious respiratory infection caused by *Bordetella pertussis* bacteria that most severely affects young children. Despite high vaccine coverage since the 1940s, the number of laboratory-confirmed pertussis cases at Alberta's Provincial Laboratory for Public Health more than tripled from 71 in 2011 to 225 in 2012. Similar resurgences of pertussis in vaccinated populations have been partially attributed to genetic changes in the *B. pertussis* bacterium--changes that make the bacteria circulating in the population less similar to the bacteria used as models in vaccine development. For example, after the introduction of the pertussis vaccine in the United States, Japan and France, researchers found that more and more *B. pertussis* strains no longer expressed pertactin, a *B. pertussis* protein used in the vaccine. Resurgences have also been attributed to waning vaccine efficacy after the fifth vaccine dose given at 4-6 years of age. In this study, we determined how many *B. pertussis* isolates from clinical cases of pertussis in Alberta in 2012-2013 expressed pertactin and correlated these results with patient age to determine what role these factors may have played in the 2012 outbreak.

Methods

We tested *B. pertussis* isolates from whooping cough patients in our 2012-2013 collection for pertactin production by immunoblot after 3 days' incubation on Regan-Lowe agar. Pertactin-negative isolates were screened for a common 1kb insertion element (IS481) by polymerase chain reaction amplification of the pertactin gene. We also investigated whether the proportion of isolates expressing pertactin varied across age groups.

Results

The proportion of isolates not producing pertactin more than doubled from 19% in 2012 to 46% in 2013. At least half of these pertactin-negative strains could not make pertactin because of an IS481 insertion in the pertactin gene. Patients aged 5-15 years were more likely than other age groups to be infected with pertactin-negative *B. pertussis*.

Conclusion

These data show that pertactin-negative *Bordetella pertussis* is on the rise in Alberta and that children aged 5-15 years may be more vulnerable to these altered strains compared to other age groups. Therefore, genetic divergence between circulating and vaccine strains as well as waning vaccine efficacy after the fifth dose may have contributed to Alberta's 2012 pertussis outbreak. Further studies on changes in vaccine antigens and patterns of susceptibility in immunized populations may lead to vaccination policies that better control whooping cough and other vaccine-preventable diseases.

Funded By: Summer Studentship

women & children's health research institute

Abstract #:	59
Presenter:	Vívian Figueiredo
Supervisor:	André Talvani
Title:	The affect of high fat diet in acute Trypanossoma Cruzi Infection
Authors:	Vívian Figueiredo, Evandro Lopes, Richard Schulz, André Talvani
Affiliations:	Other
Research Activity:	Child and Youth Development : Infection, Inflammation, Immunology
Investigation Type:	Quantitative Research

Introduction

Nutritional status plays an important role in both normal physiology and the immune response. The qualitative and quantitative aspects of diet are decisive in the development of malnourishment, obesity or other co-morbidities. In particular, a high fat (HF) diet seems to interfere in the pathogenesis of certain parasitic infections by altering the immune response, dependent on nutritional status. Thus, the aim of this study is to evaluate the inflammatory interferences of a HF diet in mice during acute infection with *Trypanosoma cruzi*, the causative agent of Chagasic cardiomyopathy which is an important cause of heart failure in women and children In South America.

Methods

C57BL/6 mice (n=40) were divided into groups 4 groups, to be infected or not with *T. cruzi* and fed with (i) conventional diet (AIN 93M) or (ii) a HF diet (60% lipids). The diet regimen began 8 weeks before infection, upon which mice were kept 4 weeks before euthanasia.

Results

The HF diet was able to increase the body weight and the amount of adipose tissue in all groups. In parallel, in the infected group subjected to the HF diet the quantity of parasites was higher, with higher circulating levels of total cholesterol and LDL. In infected animals, there were elevations in plasma IL-10 and TNF-α, and lower levels of leptin independent of diet. In the heart, more inflammatory cells were present with *T. cruzi* infection, but were not affected by diet.

Conclusion

These preliminary data suggest that a HF diet affects lipids profile and increases the parasite load of mice with *T. cruzi*. The proposed diet resembles one where people have inadequate nutritional intake, but while consuming foods high in fat content. Thus this study implies that a high-fat diet may further worsen health in individuals infected with *T. cruzi.*

Funded By: UFOP, FAPEMIG, CAPES, CNPq

women & children's health research institute

Abstract #:	60
Presenter:	Iyla So
Supervisor:	Catherine Field
Title:	Effect of feeding a mixed choline diet on immune development during suckling
Authors:	Iyla So, Erin Lewis, Susan Goruk, Caroline Richard, Catherine Field
Affiliations:	University of Alberta
Research Activity:	Child and Youth Development: Infection, Inflammation, Immunology
Investigation Type:	Quantitative Research

Introduction

The major forms of dietary choline are phosphatidylcholine (PC), free choline (FC) and glycerophosphocholine (GPC). Research in rodents found these forms are absorbed and metabolized differently. Total choline requirements of women during pregnancy and lactation increase, reflecting the increased need for choline by the fetus and infant. Lactation is a critical period for immune system development during which choline is required; however, limited research exists on maternal choline intake on immunity. The objective of this study was to examine the effect of feeding different amounts of the major forms of choline on immune system function and development during the suckling.

Methods

At birth, Sprague-Dawley rat dams were randomized to one of three isocaloric diets with the same fat (20% w/w) and choline (1.0g/kg diet) content, differing only in forms of choline: a) Control (100% FC), b) Dairy (50% PC, 25% GPC, 25% FC), c) High GPC (75% GPC, 12.5% PC, 12.5% FC). At 3 weeks, dams (n=6 per diet) and two pups from each litter were euthanized and spleen immune cells were isolated and subjected to two separate methods: 1) flow cytometry to identify immune cell populations, 2) T cell stimulation by Concanavalin A (Con A, polyclonal T cell mitogen) to quantify cytokine production *ex vivo* via ELISA. After confirming normality, differences between groups were determined by ANOVA.

Results

There was no difference in body weight of dams among diets. Body weight, spleen and liver weights of Dairy and High GPC pups was higher than Control ($P<0.05$). Flow cytometry revealed no significant differences in relative % of total CD3+, helper (CD3+CD4+) and cytotoxic T cells (CD3+CD8+) in spleen among diets for either pups or dams. With ConA stimulation, there was no difference in IL-2 production among diets for pups and dam splenocytes. Dairy dam splenocytes produced less IFN-γ and IL-6 than Control ($P<0.05$). High GPC dams produced less IFN-γ, IL-10 and IL-6 than Control ($P<0.05$). TNF-α production did not differ among Control, Dairy and High GPC dams. Dairy pups produced less cytokines (IFN-γ, TNF-α, IL-6, IL-10) than Control ($P<0.05$) whereas High GPC pups produced less TNF-α than Control ($P<0.05$).

Conclusion

Overall, feeding a mixture of choline forms to lactating dams improved offspring growth. Additionally, the forms of choline in the maternal diet appear to modify the cytokine response to a T cell mitogen by dams and offspring.

Funded By: Summer Studentship

women & children's health research institute

Abstract #: 61
Presenter: Melissa Wood
Supervisor: Sarah Forgie

Title: Using photography-based social media in microbiology and infectious diseases education

Authors: Melissa Wood, Sarah Forgie
Affiliations: University of Alberta

Research Activity: Child and Youth Development : Infection, Inflammation, Immunology
Investigation Type: Mixed Methods

Introduction

Many undergraduate students use social media as portfolios of personal current events. However, these platforms may also be used as learning tools, offering students the flexibility of accessing information anytime, anyplace, and in any space. We examined Instagram, a photography based online social networking platform, as a tool to reinforce learning related to microbiology and infectious diseases.

Methods

An Instagram account (iiimemoryhangers) was created during the infection, inflammation, and immunity block. Memory Hangers (visual mnemonics with accompanying explanations, representing specific concepts discussed in lectures) were uploaded in a synchronous fashion to the account. After reviewing ground rules, students were able to access the Instagram Memory Hangers, comment on them or like them. The tool was evaluated with usage analysis and student surveys.

Results

Usage analysis identified that 58/199 students (29%) followed the iiimemoryhangers account. Thirty-five memory hangers were uploaded over the 7-week block and 85 likes were posted by 26 different students. Of the 199, 125 students responded to the survey (63%) and among respondents 43/125 (34%) stated that they used the Instagram Memory Hangers. Of those 43 students, the majority looked at them at least weekly (N=21), at home (N=31), during the evening (N=27), but students also reported use at school, on public transit, and at all hours of the day and night. Thirty-one students reported the most useful aspect of the Instagram Memory Hangers to be both the visual component and the explanation. In addition, 35 students identified the importance of easy accessibility. Overall, 36/43 (84%) of students that used Instagram Memory Hangers, stated that they were useful for studying course content.

Conclusion

The Instagram Memory Hangers were a useful study aid, allowing students to easily access and review essential microbiology and infectious diseases concepts using visual mnemonics and brief explanations.

women & children's health research institute

Abstract #:	62
Presenter:	Han Zhang
Supervisor:	Hamdy El-Hakim
Title:	Variables associated with repeat ventilation tube insertion in healthy non-syndromic children
Authors:	Han Zhang, Yaser Alrajhi, Hamdy El-Hakim
Affiliations:	University of Alberta
Research Activity:	Child and Youth Development : Infection, Inflammation, Immunology
Investigation Type:	Quantitative Research

Objectives

To determine the variables associated with repeated ventilation tube (rVT) insertions for recurrent acute otitis media (RAOM) and or otitis media with effusion (OME) in otherwise healthy children.

Methods

This was designed as a retrospectively controlled nested cohort study at a tertiary pediatric centre. They were identified from a prospectively collected surgical database. Eligible subjects were those who had undergone rVT and a consecutive concurrent control group who received only one ventilation tube insertion. Exclusion criteria included craniofacial abnormalities, syndromes, and conditions increasing the risk for RAOM and or OME, and other indications for VT. Demographics, tympanic membrane characteristics, associated chronic rhinitis, parental smoking breast-feeding history, large day care attendance, and soother use was collected. Univariable analysis was done. I thought we did multivariable analysis as well.

Results

Over a period of 10 years, 59 patients underwent rVT (5.6%). 180 children who underwent one VT were included in the control group. There was no difference in gender distribution (p=1, 1.73:1 versus 1.76:1), mean age (p=0.69, 4.7 ±3.33 versus 4.4±3.17) or chronic rhinitis (P=0.36, OR 1.376, 95% CI: 0.69-2.74). However, rVT group was significantly more associated with a smoking parent (P=0, OR 61.8, 95% CI 21.26-176.07), large day care attendance (P=0, OR 23.39, 95% CI: 8.637-57.54), breast feeding <3months (P=0, OR 0.074, 95% CI: 0.028-0.331), soother use (p=0, OR 21.49, 95% CI: 7.81-55.87), and tympanic membrane atelectasis (P<0.0005). The same factors were also found to be significant upon multiple regression analysis (p<0.05).

Conclusion

Otherwise healthy children with RAOM and/or OME are at a greater risk of rVT if they attend large day cares, were not breast fed for ≥3months, if their tympanic membranes were atelectatic or if their parents smoke. Counseling regarding these modifiable risk factors appear very important and may affect profoundly health care utilization.

women & children's health research institute

Abstract #:	63
Presenter:	Joe Ou
Supervisor:	Eytan Wine
Title:	Breaking the barrier: Host-microbial interactions in pediatric inflammatory bowel diseases
Authors:	Joe Ou, Deenaz Zaidi, Eytan Wine
Affiliations:	University of Alberta
Research Activity:	Child and Youth Development : Infection, Inflammation, Immunology
Investigation Type:	Quantitative Research

Introduction

Inflammatory bowel diseases (IBD), which include ulcerative colitis and Crohn disease (CD), are immune-mediated chronic conditions affecting primarily the small and large intestines with increasing incidence in Canada, especially among the pediatric population. While the etiology of these diseases is unclear, gut microbiota are altered in IBD patients and may contribute to gut injury. Differences in the prevalence of adherent-invasive *Escherichia coli* (AIEC) strains have been noted between non-IBD controls and CD patients. Furthermore, some *E. coli* strains can cause severe intestinal infection. Thus, differences in *E. coli* strain composition could be involved in IBD pathogenesis. In particular, we aimed to compare the *in vitro* invasion potential of *E. coli* strains isolated from non-IBD controls and IBD patients.

Methods

E. coli strains previously isolated during endoscopy from pediatric non-IBD controls and CD patients were cultured in DMEM/F12 to establish growth curves and OD vs. CFU/mL standard curves. Invasion potential of patient *E. coli* isolates were then compared by infecting T84 colorectal carcinoma cells using gentamicin protection assays.

Results

Standard curves for clinical isolates were successfully established. Preliminary results with 3 isolates from each group showed that while invasion varied with each *E. coli* isolate, there was no significant difference in invasion capacity between the non-IBD (2046±367 CFU/mL) and CD (1914±459 CFU/mL) *E. coli* isolate groups, $t(24) = 0.22$, $p = 0.83$.

Conclusion

These results suggest that other factors besides differences in *E. coli* invasion account for gut injury in IBD. However, only a few isolates were used, and more isolates need to be tested before final conclusions can be drawn.

Funded By: Summer Studentship

women & children's health research institute

Abstract #:	64
Presenter:	Allen Fu
Supervisor:	Eytan Wine
Title:	Characterizing pathobionts and their interaction with the intestinal epithelial lining: contributions to inflammatory bowel diseases
Authors:	Allen Fu, Misagh Alipour, Eytan Wine
Affiliations:	University of Alberta
Research Activity:	Child and Youth Development : Infection, Inflammation, Immunology
Investigation Type:	Quantitative Research

Background

Inflammatory bowel diseases (IBD) are disorders of the intestinal tract involving dysfunction of the epithelial lining and an overactive inflammatory response. The human gut may contain over 10^{14} bacteria but healthy individuals are able to prevent bacteria from penetrating the intestinal tract by a complex system of immune and epithelial cells, including secretion of mucins and antibacterial molecules as a method of defense. However, some bacteria in the gut are more appropriately termed pathobionts, a term describing resident bacteria with pathogenic potential. The goal of the study is to characterize the interactions of pathobionts with intestinal epithelial cells in order to better understand the pathophysiology of IBD. The aims are to 1) compare binding of bacteria isolated from pediatric patients with or without IBD to a mucus layer *in vitro* and to 2) establish a method to visualize the interactions of bacteria isolates from pediatric IBD patients with intestinal epithelial cells *in vitro*.

Methods

For the first aim, we incubated bacteria from IBD and non-IBD patients with crude porcine mucin or mucin produced from human colon adenocarcinoma cells (HT29) and performed bacterial binding assays. For the second aim, we incubated bacteria from IBD and non-IBD patients with HT29 cells grown on Transwell filters and developed a method to visualize bacterial penetration into the cell layer.

Results

Bacteria from non-IBD patients show little binding to crude mucin, suggesting that mucin alone may play a protective role in warding against bacterial binding. Interestingly, while both IBD and non-IBD bacteria show greater binding to mucin producing HT29 cells over non-mucin producing HT29 cells, there is overall less binding of IBD bacteria to mucin.

Conclusion

Taken together, our data suggest that IBD bacteria may require other cellular factors to achieve stronger binding to mucin and that the act of binding to mucin alone may not be enough to cause damage to the host. Future studies of IBD pathogenesis will involve further investigation of non-IBD and IBD bacteria penetration into the epithelial layer.

Funded By: AIHS, NASPGHAN

women & children's health research institute

Abstract #: 65
Presenter: Deenaz Zaidi
Supervisor: Eytan Wine

Title: Broken fences; epithelial gaps and microbes in inflammatory bowel disease.

Authors: Deenaz Zaidi, Michael Bording-Jorgensen, Hien Huynh, Carroll Matthew, Eytan Wine
Affiliations: University of Alberta

Research Activity: Child and Youth Development : Infection, Inflammation, Immunology
Investigation Type: Mixed Methods

Introduction

Inflammatory Bowel Diseases (IBD), encompassing Crohn Disease and Ulcerative Colitis are highly prevalent in children in Canada with unknown etiology. Multiple factors including alterations in microbial composition, increased intestinal permeability and immune dysregulation contribute to IBD pathogenesis. Increased epithelial cell extrusion, as measured by counting gaps between epithelial cells, has not been assessed in children. Our hypothesis is that epithelial gap density is elevated in pediatric IBD patients and correlates with microbial virulence, barrier disruption and inflammation. Our objective was to study the correlation between epithelial gaps, microbial virulence and gut inflammation.

Methods

In a prospective, blinded, cohort study, epithelial gap density of the duodenum in pediatric IBD patients and non-IBD controls was evaluated using probe-based confocal laser endomicroscopy (pCLE) after injecting florescein. Epithelial gap density was defined as the number of gaps normalized to epithelial cells counted. Epithelial gaps were related to serum inflammatory markers and disease scoring indices. Intestinal aspirates were analyzed for cytokine levels, microbial quantification via qPCR, and bacterial culture. Effects of luminal factors on microbial invasion potential were assessed by Gentamicin protection assays on T84 cells. Fluorescein levels were quantified to assess permeability.

Results

86 participants have been recruited. Epithelial gap density was significantly higher in IBD patients, whereas, anaerobic bacteria and florescein levels were marginally higher in IBD patients compared to non-IBD controls. C-reactive protein and ESR levels as well as disease activity was higher in a subset of IBD patients who had higher epithelial gaps. Aspirates from patients incubated with cells altered invasion of bacteria *in vitro.* PCR of bacterial isolates showed prevalence of *E. coli* from various phylotypes and presence of diverse virulence factors.

Conclusion

Results indicate that epithelial gaps, pathogens, and host factors likely play integrated roles in IBD pathogenesis. Effects of luminal aspirates on microbial invasion potential suggests that host factors can affect microbial behaviour. Analysis of bacterial virulence and association with barrier disruption will provide further insight into the complex pathogenesis of IBD. Evaluating epithelial gap density and its relation with clinical parameters might be helpful in better defining treatment options.

Funded By: Trainee Travel Grant

women & children's health research institute

Abstract #:	66
Presenter:	Misagh Alipour
Supervisor:	Eytan Wine
Title:	Mucus attenuation in the terminal ileum of children with ulcerative colitis promotes bacterial interaction with the mucosal surface
Authors:	Misagh Alipour, Deenaz Zaidi, Consolato Sergi, Hien Huyhn, Eytan Wine
Affiliations:	University of Alberta
Research Activity:	Child and Youth Development : Infection, Inflammation, Immunology
Investigation Type:	Quantitative Research

Introduction

The partitioning of bacteria and the intestinal epithelial lining forms an integral barrier for gut homeostasis. In patients with Inflammatory Bowel Diseases (IBD), a breakdown of this barrier correlates with increased inflammation and bacteria-cell interaction. We aimed to examine the interaction between bacteria and the ileal mucosa in pediatric IBD.

Methods

Mucosal biopsies from the terminal ileum of children with IBD (n=20) [Crohn Disease (CD) and Ulcerative Colitis (UC)] and non-IBD (n=11) were collected during colonoscopy/ileoscopy. Methacarn-fixed paraffin-embedded sections were histologically graded, and quantitatively assessed for goblet cell and mucus production with Alcian blue/Periodic acid-Schiff staining. Biopsies were also assessed for bacteria (EUB338) by FISH, mucin (MUC2) and immunoglobulin-A and -G by immunofluorescence.

Results

In UC patients, goblet cells were depleted and mucus secretion was significantly lower. Co-staining for mucin and bacteria showed infiltration of bacteria into the ileum mucus layer, and bacteria were found in close proximity to the epithelial lining in children with CD and UC compared to non-IBD (no bacteria found in mucosal layer). The production of IgA and IgG in the lamina propria and secretion into the lumen was increased in CD and UC patients.

Conclusion

Here we show that the ileum of UC patients confer to mucus and goblet cell depletion, with an increase in bacteria in contact with the epithelial layer and elevated immunoglobulin response in both CD and UC. Characterizing these specific bacteria, may lead to novel diagnostic tools and microbe-based treatments.

Funded By: Innovation Grant

women & children's health research institute

Abstract #:	67
Presenter:	Tamara Germani
Supervisor:	Lonnie Zwaigenbaum
Title:	Prevalence of overweight and obese children and adolescents with autism spectrum disorder in Edmonton, Alberta
Authors:	Tamara Germani, Jeffery Bennett, Lori-Ann R. Sacrey, Lonnie Zwaigenbaum
Affiliations:	University of Alberta
Research Activity:	Child and Youth Development : Neuro-cognitive Development
Investigation Type:	Quantitative Research

Introduction

In Canada, it is estimated that nearly one in 3 children are overweight or obese (Roberts et al., 2012). With a myriad of contributing factors and potential for serious long-term health consequences, overweight/obesity status constitutes an urgent and complex public health issue (Avis et al., 2014). Moreover, recent reports suggest that approximately 35-38% in American children with ASD are overweight or obese, higher than the general population (Sharp et al., 2014; Zuckerman et al., 2014). To date, no studies have looked at weight status among children with Autism Spectrum Disorder (ASD) in a Canadian population.

Research Question

What is the prevalence of overweight or obesity in a clinical sample of children with ASD in Edmonton?

Methods

Participants were recruited in Edmonton, Alberta within the 12 months since receiving their diagnosis of ASD (as defined by the DSM-IV-TR) as part of an international registry, Autism Treatment Network. Primary health care provider (i.e. nurse practitioner, developmental pediatrician, etc.) completed several baseline measures, including age, gender, height, and weight. BMI was calculated for each participant using date of birth, date assessed, gender, height and weight, using the recommended BMI calculations by the Centre for Disease Control (2000) and terminology provided by Barlow et al (2007).

Results

Complete information was available for 130 children with ASD (males = 108). Median age of participants was 5 years, 9 months (range: 2 years, 2 months – 17 years, 4 months; standard deviation: 3 years, 5 months). In total, 2% of children had BMI under the 5^{th} percentile (underweight), 55% of children had BMI within the 5^{th} to 85^{th} percentile (normal weight), 41% of children were over or equal to the 85^{th} percentile (overweight or obese) and 21% of children were over or equal to the 95^{th} percentile (obese).

Conclusions

These findings are similar, if not slightly higher, to the prevalence of overweight and obese status in children with ASD but different from typically developing Canadian children. Further monitoring is needed longitudinally to monitor the prevalence of overweight and obesity in children and adolescents with ASD, and to provide appropriate intervention.

Funded By: Graduate Studentship

women & children's health research institute

Abstract #: 68
Presenter: Chloe Luck
Supervisor: Rachel Wevrick
Title: Hedonic feeding in a mouse model of Prader-Willi Syndrome
Authors: Chloe Luck
Affiliations:
Research Activity: Child and Youth Development : Neuro-cognitive Development
Investigation Type:

Introduction

Prader-Willi Syndrome (PWS) is a genetic disorder characterized by an initial failure to thrive followed by extreme hyperphagia. Food intake is controlled through two different neural pathways, homeostatic feeding and hedonic feeding. Homeostatic feeding is controlled by the hypothalamus and modifies feeding based on physiological need. Hedonic feeding is based on the reward value of the specific food item and is centered around neurons in the ventral tegmental area (VTA) that project to other brains areas to learn the reward value of the food source and drive subsequent food seeking behaviour. The abnormal motivation to eat observed in PWS suggests a disruption in the hedonic feeding pathway. *Magel2* is one of the genes inactivated in PWS, and mice lacking *Magel2* have a PWS-like phenotype. The aim of this research project is to characterize how the dopamine reward circuitry is disrupted using a mouse model lacking *Magel2*.

Methods

Immunohistochemistry (IHC) was used to quantify the number of dopaminergic cells of nuclei within the neural feeding circuitry, including the paraventricular nucleus, the arcuate nucleus, the substantia nigra and the VTA. To assess the adaptive responses to changes in diet, *Magel2*-null and wildtype animals were exposed to and withdrawn from high-fat diet. Molecular changes including activation of ERK, AKT and CREB proteins through phosphorylation will be quantified to assess the response to withdrawal of HF diet. The accumulation of ΔFosB will be used to compare the adaptive response to exposure to high-fat diet. High-performance liquid chromatography was used to measure the levels of biogenic amines in the nuclei of the reward pathway. Further experiments will include using IHC to measure leptin signaling in the VTA of *Magel2*-null and wildtype animals.

Results

An increased number of dopaminergic neurons was observed in the paraventricular nucleus of *Magel2*-null animals compare to wildtype littermates, however there was no difference observed in any of the other nuclei measured. Using tyrosine hydroxylase IHC, it was determined that there was no significant difference in the area measurements of any of the dopaminergic nuclei.

Conclusion

Understanding how hedonic feeding is disrupted in a mouse model of PWS could help pinpoint where in the neural feeding circuitry Magel2 acts and how the deletion of this gene contributes to the pathology of PWS and other eating disorders.

Funding for this research was provided by the Department of Medical Genetics, University of Alberta, and the Women and Children's Health Research Institute.

Funded By: Graduate Studentship

women & children's health research institute

Abstract #: 69
Presenter: Qaasim Mian
Supervisor: Georg M. Schmölzer
Title: Excessive tidal volumes administered through Positive Pressure Ventilation in preterm infants may cause brain injury
Authors: Qaasim Mian, Po-Yin Cheung, Khalid Aziz, Megan O'Reilly, Gerhard Pichler, Georg M. Schmölzer
Affiliations: University of Alberta
Research Activity:
Investigation Type:

Introduction

International resuscitation guidelines recommend positive pressure ventilation (PPV) if infants fail to initiate spontaneous breathing. The purpose of PPV is to deliver an adequate tidal volume (V_T), establish functional residual capacity, achieve gas exchange, and initiate spontaneous breathing, while minimizing lung injury. High V_T delivery during PPV in the delivery room (DR) is common and has been associated with brain injury in animal models. The aim of the study was to examine if high V_T delivery during PPV cause brain injury in preterm infants.

Methods

Infants $\leq$29 weeks gestational age receiving PPV through facemasks were included. At the Royal Alexandra Hospital physiological parameters including V_T are routinely monitored during the initial stabilization in the DR. A breath-to-breath analysis for V_T was performed during mask PPV. The median values of V_T delivery were compared with recently described reference ranges for V_T in spontaneously breathing preterm infants at birth (Mian et al, 2014). Infants were divided into two groups according to V_T delivery $\leq$ or > 5.8 mL/kg (low and high V_T, respectively). Significant brain injury with major intraventricular hemorrhage (IVH) was assessed based on routine ultrasound imaging within the first week of life.

Results

From January 2013 to June 2014, 63 preterm infants were included. Infants receiving high V_T had a mean (SD) gestational age of 26.2 (1.9) weeks and a birth weight of 854 (247) grams. For infants receiving low V_T, gestational age was 27.6 (1.4) weeks and birth weight 1133 (268) grams. Of 50 infants with high V_T, 26 (52%) developed IVH (10 grade IV, 1 grade III, 3 grade II, and 12 grade I). Of 13 infants with low V_T, only one had signs of brain injury with grade II IVH.

Conclusion

High V_T delivery in preterm infants during mask PPV at birth potentially causes brain injury.

Funded By: Summer Studentship

women & children's health research institute

Abstract #:	70
Presenter:	Supraja Rengan
Supervisor:	Jennifer Toye
Title:	Influence of socioeconomic status on neurodevelopmental outcomes in very preterm infants, in the Canadian context
Authors:	Supraja Rengan, Jennifer Toye, Linda Carroll, Amber Reichert, Mossarat Quereshi
Affiliations:	University of Alberta
Research Activity:	Child and Youth Development : Neuro-cognitive Development
Investigation Type:	Quantitative Research

Introduction

Premature birth is an ongoing and multifactorial public health concern in Canada, and Alberta continues to be the province with the highest rate of preterm birth (8.8 per 100 live births). In addition to the ongoing physical health problems associated with preterm birth, these babies are more prone to delays in multiple domains of child development including cognitive, behavioral, and language development. Further aggravating the issue is that preterm birth is more common, and increasing rapidly in low socioeconomic (SES) populations – a group already disadvantaged in the same domains of development. The combined risk from prematurity and SES in the premature infant population has been coined as a "double jeopardy" referring to the cumulative effect biological and social factors have on infant development. In our study, we looked for an association between SES and early development in preterm infants within our community

Methods

We used the deprivation index from CPHI for Edmonton to classify our population at the time of birth using their postal code at admission. Infants born less than 29 weeks gestation born from 2008 – 2011 and residing in the city of Edmonton at the time of birth are included in this study. Any infants with major congenital anomalies and/or death prior to 18 months were excluded. Neurodevelopmental impairment assessed at 18 and 36 months were used in this study (i.e. moderate or severe disability). Birth postal code information and maternal/neonatal characteristics were obtained from the Edmonton Neonatal Database. Follow-up information was obtained from the Glenrose Neonatal Follow up Clinic Database.

Results

In comparison to the high/average SES groups, the low SES infants had lower average gestational age and birth weight. In addition, preliminary analysis found that the low SES infants also had poorer neurodevelopmental outcomes in comparison to the average/high SES groups.

Conclusion

Our results are similar to other studies conducted elsewhere, where infants of a low SES background face greater neurodevelopmental delays in comparison to their average and high SES counterparts. However, further analysis is needed. Information gathered from this research will provide baseline information regarding the impact area based social and material factors have on the early childhood development of very preterm infants in Edmonton. It will provide direction and support for further prospective research to identify modifiable factors to mitigate negative influences and enhance positive influences on neurodevelopment in very preterm infants.

Funded By: Department of Pediatrics

women & children's health research institute

Abstract #: 71
Presenter: Rachel Skow
Supervisor: Craig Steinback
Title: Sex differences in the neurovascular responses following exposure to low oxygen
Authors: Rachel Skow, Christina MacKay, Margie Davenport, Craig Steinback
Affiliations: University of Alberta
Research Activity: Other
Investigation Type:

Introduction

Evidence suggests that females exhibit a cardio-protective effect prior to menopause. That is to say, that cardiovascular morbidity and mortality is lower in females. This may be due to the differences in circulating hormone levels between males and females. Recent evidence has shown that there are sex related differences in the vascular responses chemoreflex stress (i.e. low oxygen). The mechanisms behind these differences are not fully understood, but may include variations in sympathetic nerve activity.Sympathetic nerve activity, a potent regulator of vascular function, increases during, and remains elevated following exposure to hypoxia (reduced oxygen). However, it remains unclear if and how sex may affect sympathetic nerve activityand resultant vascular function during and following hypoxia. We tested the hypothesis that the increase in sympathetic nerve activity during following hypoxia would leadto differences in vascular function (e.g. mean arterial pressure, total peripheral and femoral vascular resistance) between sexes.

Methods

Participants (n=16; females=7; 24±3yrs; mean ± SD) were instrumented to measure heart rate, mean arterial blood pressure and cardiac output (Finometer), and femoral artery blood flow (Doppler ultrasonography). Total peripheral resistance was calculated form mean arterial blood pressure and cardiac output. Similarly, femoral vascular resistance was calculated from femoral blood flow and mean arterial blood pressure. Data were collected continuously during 10-minutes of baseline, 10-minutes of hypoxia (~80% SpO2), and 20-minutes of recovery. Averages (1-min) taken during baseline, the end of hypoxia, and every 5-minutes during recovery, were compared using two-way repeated measures ANOVA (sex by time comparisons).

Results

Both total peripheral and femoral vascular resistance were decreased during hypoxia ($p<0.05$), however, no significant differences were observed between sexes. Furthermore, both total peripheral and femoral vascular resistance were not different during recovery compared to baseline ($p>0.05$). However, females exhibited blunted heart rate and mean arterial blood pressure responses ($p<0.05$) responses during hypoxia.

Conclusion

These data suggest that females exhibit a blunted pressor response to exposure to low oxygen, but these differences were absent following low oxygen exposure; this may be one mechanism why females exhibit a cardio-protective effect prior to menopause. Further work investigating the sympathetic nerve activity response to hypoxia and neurotransmitter release in males and females will be necessary to confirm this claim.

Funded By: NSERC

women & children's health research institute

Abstract #: 72
Presenter: Charlotte Usselman
Supervisor: Margie Davenport

Title: Longitudinal cerebrovascular function during pregnancy: A case study

Authors: Charlotte Usselman, Emily King, Craig Steinback, Margie Davenport
Affiliations: University of Alberta

Research Activity: Other
Investigation Type: Quantitative Research

Introduction

Pregnancy is associated with profound cardiovascular adaptations including a rapid 50% increase in blood volume, 40% increase in cardiac output and 15% increase in heart rate. However, the longitudinal adaptations of the cerebrovascular circulation during gestation remain poorly understood.

Methods

To further understand the influence of pregnancy on cerebrovascular function, we conducted a longitudinal assessment of basal middle cerebral artery blood flow and blood flow reactivity to a hyperoxic, CO2 rebreathing protocol in a 36 year old woman during her second pregnancy. Pre-pregnant values were assessed during the early follicular phase of the menstrual cycle in the month prior to conception and on 24 subsequent occasions up until delivery (40 weeks gestation). Beat-by-beat mean arterial pressure (MAP) was derived using photoplethysmography (Finometer), middle cerebral artery blood flow velocity (MCAVP) was measured using transcranial Doppler ultrasound (Multigon), End-tidal PCO2 and PO2 were derived using real-time gas analysis (ADInstruments).

Results

From conception to 40 weeks of gestation, there was a progressive, chronic, respiratory alkalosis and decrease in resting end-tidal PCO_2 (35 Torr to 28 Torr) despite no appreciable change in resting MCAVP (62 vs. 65 cm/s). Throughout gestation MAP also remained stable. Conversely, cerebral reactivity to CO_2 increased 116% from pre-pregnancy to the 40th week of gestation (0.9 cm/s/Torr to 1.9 cm/s/Torr respectively).

Conclusion

These longitudinal data suggest that while resting blood flow in the middle cerebral artery is unchanged, cerebrovascular reactivity to CO_2 increases with gestation during healthy pregnancy. Such changes may serve to buffer and protect the cerebral circulation to chronic decreases in PCO_2 during gestation.

women & children's health research institute

Abstract #: 73
Presenter: Jenny Yoon
Supervisor: Sujata Persad

Title: Neuroprotective effects of sulforaphane on Hypoxic-Ischemic Neurons

Authors: Jenny Yoon
Affiliations: University of Alberta

Research Activity: Child and Youth Development : Perinatel Stroke
Investigation Type: Quantitative Research

Introduction

Cerebral Palsy (CP) constitutes the primary outcome of premature nerve injury. Impairment of oxygen and glucose supply during pregnancy to the fetus can induce neuron damage and death. Mental retardation, seizures, learning disabilities, and other mental diseases can occur as a result of this insufficient nutrient delivery to the fetus. Cell death occurs through overstimulation of excitatory amino acid receptors, calcium influx, and formation of free radicals and inflammatory cytokines. Therapeutic interventions that are efficacious for the injured newborn are limited mainly because the majority of insults (90%) resulting in CP occur *during pregnancy and* current therapies only address those injuries that occur during labor and delivery or after birth, therefore addressing only 10% of the injured newborns.

Natural health products are known to contain metabolites that prevent brain injury following hypoxia/ischemia. Sulforaphane is an isothiocyanate found in vegetables such as broccoli sprouts, and cabbage that has anti-inflammatory, anti-oxidant, anti-apoptotic effects. Sulforaphane has demonstrated potential to protect against acute brain injury in cases of stroke and oedema. It has also been shown to exhibit neuroprotective properties in hypoxic-ischemic brain injuries.

Hypothesis Sulforaphane will differentially prevent injury in neuronal cells exposed to oxygen glucose deprivation (OGD).

Methods

To investigate the rescue effects of sulforaphane on neurons exposed OGD, cortical neurons of P2 Long Evans rats were examined. Verification of a neuron-rich cell culture was done by using anti-Neuron Specific Enolase antibody and Western Blot analysis. To determine the optimal OGD time to achieve LD50, the neurons were cultured for 7 days and exposed to 1, 4, 8, 12, 18, or 24 hours of OGD at 5% oxygen, 5% carbon dioxide, and 90% nitrogen in glucose free media. OGD was followed by reoxygenation for 24 hours at 5% carbon dioxide and 95% air. To determine the neuroprotective effects of sulforaphane, 0.5, 1, 2, 2.5, 5, 10, 25, or 50µmol/L of sulforaphane was added to the culture during OGD and reoxygenation. We determined the percentage of cell death under all conditions by using Trypan Blue exclusion and Lactate Dehydrogenase (LDH) assays.

Results

LD50 was achieved with 1 hour of OGD then 24 hours of reoxygenation. SFN did not affect cell viability in normoxic conditions. However, 10µmol/L of SFN decreased cell death caused by OGD compared to the OGD-treated cells in the absence of SFN. Interestingly, treatment of cells with 50 µmol/L SFN resulted in significant increase cell death.

women & children's health research institute

Abstract #:	74
Presenter:	Ann-Marie Przyslupski
Supervisor:	Jerome Yager
Title:	Hypoxic-ischemic neuroprotection by sulforaphane is concentration-dependent and not influenced by hypothermia
Authors:	Ann-Marie Przyslupski, Edward Armstrong, Ke Qin Shen, Jerome Y. Yager
Affiliations:	University of Alberta
Research Activity:	Child and Youth Development : Perinatel Stroke
Investigation Type:	Quantitative Research

Introduction

When newborns are deprived of oxygenation and blood flow, this may result in hypoxic-ischemic brain damage (HIBD). Neonates affected by HIBD endure lifelong neurological disabilities. These are characterized by a spectrum of cognitive and motor impairments and may also manifest as epilepsy, academic delay, and undeveloped motor co-ordination. Post-ischemic hypothermia (33.5±0.5°C) is currently the only protective intervention and standard of care for HIBD, but it does not completely prevent brain damage and is ineffective against severe HIBD. We hypothesized that combining hypothermia with sulforaphane (SFN), a potent anti-inflammatory/anti-oxidant metabolite derived from cruciferous vegetables, would improve the neuroprotection afforded by hypothermia alone, on moderate HIBD. In addition, we sought to determine whether this combination therapy was dose-dependent.

Methods

We experimentally-induced unilateral HIBD in 7-day-old Long-Evans rats via right carotid artery ligation and subjecting them to hypoxia [8% O_2, 90min]. Post-hypoxia, pups were exposed to normothermic or hypothermic environmental conditions for 24h, yielding core body temperatures of 37°C and 31°C, respectively. Subcutaneous injections of SFN (1 or 5mg/kg) or saline (Control) were administered at the onset of hypothermia/normothermia and continued every 24h for 7 days. On postnatal-day-30, pathology was characterized by calculating the percent of the right hemisphere that was damaged, using the left hemisphere as a control (%RHD).

Results

Assessment of %RHD showed that, compared to normothermic saline control, sulforaphane (5mg/kg; $p<0.01$) and hypothermia ($p<0.001$) both significantly reduced %RHD when administered independently. However, combining hypothermia and SFN unfortunately did not show an additive effect in reducing HIBD. No differences regarding sex and body weight were observed between groups at any time point. No mortality occurred as a result of hypothermia/normothermia or SFN/saline administration.

Conclusions and Discussion

Our results demonstrate that SFN (5mg/kg) and hypothermia were equally effective at reducing HIBD. However, the two treatments did not act synergistically when used in combination. Several previous studies by our group and others have found similarly that combining therapies with hypothermia is not additive in nature. As a result, out future direction will involve mechanistically analyzing the pathways for hypothermic neuroprotection, to best determine the timing for combination therapy.

Funded By: Branch Out Neurological Foundation, NeuroDevNet, NCE

women & children's health research institute

Abstract #:	75
Presenter:	Brittany Lissinna
Supervisor:	Jaynie Yang
Title:	Motor learning on a split-belt treadmill in children
Authors:	Brittany Lissinna, Roseleen John, Jaynie Yang
Affiliations:	University of Alberta
Research Activity:	Child and Youth Development : Perinatel Stroke
Investigation Type:	Quantitative Research

Introduction

We continuously adapt well-learned motor skills to accommodate short-term changes in our environment, such as walking on sand or ice. Children acquire these motor skills as they explore new environments and experience dramatic changes in body dimensions. Previous research has shown that motor adaption occurs differently in typically developing children compared to adults, but little is known about children with early brain injury (1), which was the purpose of this study. Motor learning was studied on a treadmill with two belts, which can be run at different speeds (split-belt), a task that is novel to children and adults alike.

Methods

Data were collected from 5 healthy children, 2 children with perinatal stroke and 4 healthy adults while walking on a split belt treadmill (2:1 speed ratio). Adaptation and retention of motor learning was assessed on two consecutive days. On Day 1 participants first walked with the belt speeds the same (tied-belt) to determine baseline symmetry of walking, followed by 15 minutes of split-belt walking to quantify the initial asymmetry (error) and later symmetry of walking after practice (late adaptation). When the participants returned on Day 2 they began walking the with the belt speeds split as in Day 1, to measure retention of motor learning. Finally, they returned to tied-belt walking to measure the aftereffect, asymmetry in the opposite direction from the initial error, a signature of the learning.

Results

Initial asymmetries in step length induced by split-belt walking were rectified by practice in all three groups. Return to tied-belt walking on Day 2 showed an aftereffect of similar size for all 3 groups, with adults displaying the fastest recovery of symmetry and little difference between healthy children and children with perinatal stroke. All three groups displayed similar retention of walking patterns on Day 2.

Conclusion

These preliminary results confirm previous research indicating that children take longer to learn motor patterns than adults (1). Children with perinatal stroke learned equally well as uninjured children, and showed comparable retention; suggesting therapy to improve their walking will be retained. More data is required to verify these preliminary findings.

1) Vasudevan et al. (2011) Journal of Neuroscience 31(8):3055-3065

2) Musselman (2011) Journal of Neurophysiology

Funded By: Summer Studentship

women & children's health research institute

Abstract #:	76
Presenter:	Jennifer Gyoba
Supervisor:	Francois Bolduc
Title:	A drosophila melanogaster fragile X syndrome model of sensory processing
Authors:	Jennifer Gyoba, Alaura Androschuk, Steven Langer, Francois Bolduc
Affiliations:	University of Alberta
Research Activity:	Child and Youth Development : Neuro-cognitive Development
Investigation Type:	Quantitative Research

Introduction

Fragile X syndrome (FXS) is the most common cause of intellectual disability (ID) in males and represents a significant portion of patients with autism spectrum disorder (ASD). A common feature in FXS and ID in general is sensory processing defects. For instance, a high threshold to pain but a high sensitivity to sound is common in FXS but poorly understood. The cause of FXS is due to transcriptional silencing via hypermethylation of the Fragile X gene (FMR1) resulting in a loss of Fragile X Mental Retardation Protein (FMRP). dfmr1 is the Drosophila melanogaster homolog of FMR1 and is highly conserved in comparison to humans. We have shown that FX flies have memory and social interaction defects similar to what is observed in humans. Here, we show that FX flies are defective in processing of stress cues.

Methods

We used Drosophila between 2-3 days old in groups of 50 and submitted to mechanical stress via vortex. Naïve flies were tested for their response to either a stress environment (tube with previously vortexed flies) or a neutral environment (tube with no flies). Flies were given 1 minute to choose and then counted. Statistical analysis with Student T test was performed in PRISM.

Results

We observed that wild-type flies avoided the stress environment whereas the FX flies had a significant defect (N=6 experiments per genotype, $p<0.001$, Student t test). We obtained similar results for 2 different dmfr1 mutant alleles, suggesting a gene specific defect.

Conclusion

Sensory processing is known to be abnormal in patients with FXS but also in ID and ASD in general. Our model shows that dfmr1 mutant flies have problem responding in a stressful environment. Further work is ongoing to uncover the molecular basis of this defect.

Funded By: CIHR

women & children's health research institute

Abstract #:	77
Presenter:	Rebecca Long
Supervisor:	Lawrence Richer
Title:	Autonomic responses in children with persistent post-concussion symptoms
Authors:	Rebecca Long, Heather Edgell, Heather Edgell, Ryan Forster, Lawrence Richer
Affiliations:	University of Alberta
Research Activity:	Other
Investigation Type:	Quantitative Research

Introduction

Concussions are a common condition in children that may cause persistent symptoms which last for longer than a month after the injury. These symptoms are called persistent post-concussive symptoms (PCS). There is clinical evidence that many patients with PCS report orthostatic intolerance, which can be measured by an increase in heart rate (HR) of ≥30bpm, with an associated decrease in systolic blood pressure (SBP) of ≥20mmHg. These responses are indicative of autonomic dysfunction. We hypothesized that PCS in children is associated with autonomic dysfunction.

Methods

This was a sub-study of the 5P Concussion study (Zemek et al, 2013, BMJ Open 3(8), 1-10), from which participants were recruited from the Stollery Pediatric Emergency Department. Participants rated their symptoms before and after the injury using a Post Concussion Symptom Inventory (PCSI). We recruited participants from this population and measured continuous HR and SBP responses to 15 minutes of 70^{o} head-up tilt (i.e. orthostatic stress). Children (aged 8-17) who reported PCS in their PCSI 4-weeks after a concussion were placed in the symptomatic group (n=4), and children who did not report PCS in their PCSI 4-weeks after a concussion were placed in the control group (n=4). We took measurements at 4 weeks and 12 weeks post injury.

Results

Individual changes in HR and SBP due to tilt were averaged within groups. The control group showed a HR increase of +47.9±5.5 bpm and a SBP change of -54.1±5.0mmHg at 4 weeks, and +48.9±6.2bpm with -40.8±4.2 mmHg at 12 weeks. The symptomatic group showed a HR increase of +58.6±5.3 bpm and SBP change of -49.6±8.4 mmHg at 4 weeks, and +51.6±7.9 bpm and -60.9±8.6mmHg at 12 weeks.

Conclusion

We cannot make statistical conclusions from this data, as we do not have sufficient power (n=4 in each group). However, we did observe trends for a recovery in heart rate response to tilt in the symptomatic group bringing them to similar levels as the control group at 12 weeks. We also noticed that both groups have a HR increase ≥30bpm as well as a SBP reduction of ≥20mmHg, suggesting that all post-concussion children display abnormal autonomic responses to tilt regardless of PCS. Further research should be done looking at a control group of children who do not have a concussion in order to determine a pediatric normal response range.

women & children's health research institute

Abstract #: 78
Presenter: Jamie Zagozewski
Supervisor: David Eisenstat

Title: Dlx homeobox genes and epigenetic regulation of retinal cell fate

Authors: Jamie Zagozewski, Qi Zhang
Affiliations: University of Alberta

Research Activity: Other
Investigation Type: Quantitative Research

Introduction

Understanding the genetic pathways that govern retinal cell fate specification and differentiation is critical for both the development of cell-based therapies for treatment of blindness as well as identifying the retinoblastoma cell of origin. The homeodomain transcription factor family is known play critical roles in retinal progenitor cell differentiation and development while the role of epigenetics in this process is only beginning to be understood. Our goal is to examine coordination between *Dlx* homeobox genes and chromatin modifiers in regulation of retinal progenitor differentiation. We hypothesize DLX2 promotes progenitors to adopt retinal ganglion cell (RGC) fates while concomitantly repressing photoreceptor cell fate. We expect DLX2 and H3K27me3 to co-localize at photoreceptor specific promoters while, DLX2 and H3K4me3 localize at promoters for RGC specific genes.

Methods

Chromatin immunoprecipitation (ChIP) was utilized to identify DLX2 localization at specific gene targets in the developing murine retina. A modified ChIP experiment (ChIP-reChIP) identifies co-localization of DLX2 and histone modifications specific for transcriptionally repressed chromatin. Immunohistochemistry was carried out on *Dlx1/Dlx2* double knockout tissue to examine expression of both RGC and photoreceptor gene expression in the absence of *Dlx* regulation. *In utero* retinal electroporation was use to examine the consequence of *Dlx2* gain-of-function during embryonic retinal development.

Results

H3K27me3 and DLX2 were identified at the promoter of *Otx2* in the developing retina *in situ*. H3K27me3 was excluded from promoters of RGC markers, *TrkB* and *Brn3b*, which are bound by DLX2 during retinal development *in vivo*. ChIP-reChIP confirmed co-localization of DLX2 and H3K27me3 at photoreceptor specific targets and while co-localization is not observed at RGC specific genes. Retinas lacking *Dlx1/Dlx2* have increased and ectopic expression of CRX and reduction of BRN3A and BRN3B expression. Gain-of-function experiments showed that retinal cells ectopically expressing DLX2 also ectopically expressed BRN3B, whereas CRX and OTX2 expression was excluded from these cells.

Conclusion

Our findings suggest that *Dlx* cooperates with chromatin modifiers to promote retinal progenitors to adopt RGC fate while repressing photoreceptor cell fate. Future directions will include ChIP of the H3K4me3, which demarcates active promoters as well as ChIP-reChIP with H3K4me3 and DLX2. ChIP using *Dlx1/Dlx2* knockout embryonic retinas and co-immunoprecipitation experiments with chromatin modifying machinery will determine if DLX2 directly recruits this machinery as a mechanism to regulate retinal cell fate.

Funded By: Graduate Studentship

women & children's health research institute

Abstract #:	79
Presenter:	Deena Hamza
Supervisor:	Peter Silverstone
Title:	The importance of early screening in primary care to identify substance use in youth, and the most versatile and brief tool available to date
Authors:	Deena Hamza, Peter Silverstone
Affiliations:	University of Alberta
Research Activity:	Child and Youth Development : Mental Health
Investigation Type:	Mixed Methods

Introduction

The rate of substance misuse has increased, with nearly 6 million Canadians aged 15 or older meeting criteria for substance use disorder. Of these, youth between the ages of 15 and 24 exhibit the highest rate of substance misuse. This underscores the need for early prevention and intervention measures.

This review focuses on the importance of early screening for youth, and the potential benefits of screening in the primary care setting in this age group using one screening tool designed for this purpose, the CRAFFT Screening Tool for Substance Use (CRAFFT).

Methods

Multiple databases were searched for appropriate publications, including: PsycINFO; PubMed; Health Sciences: A SAGE Full-Text Collection; JSTOR; Journals@Ovid Full Text; SAGE Journals Online and Psychology. The search was limited to articles published from 1992 to December 2013, particularly focusing on treatment in North American populations, and those focusing on adolescent substance misuse. Additionally, further manual searches of publications having the words “Substance Use” or “Addictions” in the title was performed. Additional keywords were “youth addictions”, “screening”, “primary care”, “screening tools”, “addiction prevention”, “addiction intervention”, “prevalence of substance misuse”.

Results

Primary care screening continues to be a potential means to identify at-risk youth. The ease of accessibility is acknowledged by researchers and physicians; however, concerns regarding time-commitment and knowledge of treatment pathways are prominent obstacles plaguing the implementation of physician-based screening. From the review, consistent evidence suggested the CRAFFT appears to be a versatile and reliable brief screening tool.

Conclusion

Physician-led screening of adolescent patients may allow for early detection substance use. The potential for early intervention may limit harm associated with substance use in youth, and preventing more serious substance use disorders and mental health issues. Although limited time and knowledge are prominent barriers preventing implementation of primary care screening, use of the CRAFFT may enable recognition of illicit and licit substance misuse. Additionally, training for physicians and providing a treatment algorithm may supplement knowledge regarding the best addiction care pathways.

women & children's health research institute

Abstract #:	80
Presenter:	Tristan Robinson
Supervisor:	Rebecca Gokiert
Title:	Supporting early child development through the co-creation of knowledge in a CBR partnership
Authors:	Tristan Robinson, Rebecca Gokiert, Rebecca Georgis
Affiliations:	University of Alberta
Research Activity:	Child and Youth Development : Mental Health
Investigation Type:	Mixed Methods

Introduction

A community-based research (CBR) partnership between the University of Alberta, the Yellowhead Tribal College, and four First Nation communities has identified and incorporated community strengths, language, and cultural values into understanding healthy early child development (ECD) from a First Nation perspective. The partnership used information gathered through the First Nation Child Development (FNCD) project to develop a supplemental questionnaire to the Early Development Instrument (EDI; Janus & Offord, 2007). The EDI is a population-based tool for measuring development in kindergarten children. Each community participated, over three years, in gathering data through focus groups, the EDI, and the newly created supplements that both family members and teachers completed to identify areas of strength and needed support for community action planning. This poster will highlight the process of engaging with communities to translate the knowledge co-created through the project into meaningful activities and tools that would be useful for developing community supports. The creation of a community calendar and final report will be used as case examples.

Methods and results

Community-based research (CBR) values the equitable involvement of all partners throughout the research process (Israel, Schulz, Parker, & Becker, 1998). Given the historical and negative experiences some First Nation communities have with research, CBR is seen as a desired approach to facilitate ownership and control over research (First Nations Centre, 2007). The FNCD project brought community research committees together, facilitated communication meetings and engaged in an iterative process of data collection, analysis and findings to ensure that community members were involved throughout the research process. The information shared back with the communities was accomplished through a final report which utilized visual representation of the data, and community members' voices alongside the quantitative data from the EDI and FNCD questionnaires. Furthermore, a calendar was created and given to community members as a resource to share healthy ECD ideas and artwork of the children in each community.

Conclusion

The CBR method of research brought the four First Nation communities, the YTC College and researchers from the UofA together to understand healthy ECD from a community perspective. All partners participated in creating a final report and the community calendar, which can be used as foundational documents in future community planning and development.

Funded By: Trainee Travel Grant

women & children's health research institute

Abstract #: 81
Presenter: Alaura Androschuk
Supervisor: Francois Bolduc

Title: Energetic requirement of memory formation

Authors: Alaura Androschuk, Cory Rosenfelt, Francois Bolduc
Affiliations: University of Alberta

Research Activity: Child and Youth Development : Neuro-cognitive Development
Investigation Type: Quantitative Research

Introduction

Learning and memory are core necessities for the brain of the developing child. Nonetheless, little is known about the energetic requirement related to memory formation and its function in neurodevelopmental disorders. The fruit fly Drosophila has been used extensively to study learning and memory as well as feeding. Memory formation can be seen following various training paradigms. Flies require repeated training to form memory but only training blocks separated by rest intervals, known as spaced training, allows for formation of long-term memory. This form of memory is protein synthesis dependent. Massed training on the other hand, consists of repeated training without rest intervals, resulting in a protein synthesis independent form of memory, which does not last as long. We have shown that fly mutants for many neurodevelopmental genes have defect in spaced training memory. The caloric intake related to each training paradigm (spaced vs. massed) has not been previously studied.

Methods

To determine the caloric requirement of flies following spaced and massed training, we utilized a modified version of the capillary feeder assay (CAFE) to monitor the consumption of a 5% sucrose solution over a 24-hour period following a mock training, spaced and massed training. We used a digital camera to record the consumption every 30 minutes after training. Levels of the feeding solution were analyzed using ImageJ. Statistical analysis was completed in PRISM using repeated measure one-way ANOVA.

Results

5% sucrose consumption is greater for massed trained flies as compared to spaced trained flies ($p < 0.0001$, $N=4$). 5% sucrose consumption is greater for untrained flies as compared to spaced trained flies ($p < 0.0001$, $N=4$). 5% sucrose consumption is not significantly different between massed trained flies and the untrained control flies ($N=4$).

Conclusion

Contrary to initial expectations these results are surprising since it was anticipated that the protein synthesis dependent formation of memory (formed after spaced training) would have a higher energetic requirement than protein synthesis independent formation of memory (formed after massed training). Further experiments are required to assess if the duration of the training or other factors are affecting our recording of the fly consumption.

Funded By: CIHR

women & children's health research institute

Abstract #: 82
Presenter: Mohamed Elboraee
Supervisor: Kalid Aziz
Title: Umbilical lines are an independent risk factor for adverse outcomes in very preterm babies
Authors: Mohamed Elboraee, Kumar Kumaran, Jennifer Toye, Khalid Aziz
Affiliations: University Of Alberta
Research Activity: NICU
Investigation Type: A retrospective study with secondary database analysis

Background:
Placement of umbilical arterial and/or venous (UA or UV) lines is a common practice in the care of preterm babies. It is not, however, clear whether routine placement improves neonatal outcomes.

Introduction:
Although umbilical catheters are a standard component of the neonatal intensive care, they have significant complications, including: blood-borne catheter-related infection, air embolism, a substantial blood loss, thromboembolic complications, disorders of cardiac rhythm, and pericardial or pleural effusion.

Objective: To explore the effect of umbilical lines on mortality and morbidities in extremely preterm babies in Canada after adjustment for confounders such as gestation and acuity.

Methods:
Data were abstracted from the Canadian Neonatal Network database for babies born at <29 weeks gestational age (GA) from January 2010 to December 2012 (excluding babies who were moribund on admission or with major congenital anomalies). Four groups were identified: Gp0 with no umbilical lines; Gp1 with umbilical venous (UV) lines only; Gp2 with umbilical artery (UA) lines only; and Gp3 with both UA and UV lines. Data fields included patient demographics, peripartum factors, major inpatient morbidities [nosocomial infection (NI), necrotizing enterocolitis (NEC), bronchopulmonary dysplasia (BPD), brain injury (BI) and retinopathy of prematurity (ROP)], and mortality. Univariate and multivariable regression analyses compared the outcomes of 4 groups.

Results:
Of 4623 babies 820 (17.7%) were in Gp0, 1032 (22.3%) in Gp1, 120 (2.6%) in Gp2, and 2651 (57.3%) in Gp3. With increasing number of lines babies were smaller, had lower Apgar scores, were more likely to have high SNAPII scores, and were more likely to be born by Cesarean section. Univariate analysis showed that babies with no umbilical lines (Gp0) had the lowest mortality and lowest rates of NI, NEC, BPD, BI, and ROP. Increasing from one to two lines also increased rates. After adjustment for risk factors (see table and footnote) babies with no lines had significantly lower rates of a composite outcome of death or major inpatient morbidity - there was no difference in mortality between groups. Similar results were obtained when the model was adjusted for SNAPII instead of Apgar score.
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Conclusions:
Most very preterm babies in Canada get UA and/or UV lines (usually both). Umbilical lines are more likely to be inserted into smaller, sicker babies. However, after adjustment for risk factors and acuity, babies with no lines are more likely to survive without major morbidity. Adding a second umbilical line appears to increase risk further. Clinical strategies should take into account the inherent risks of UA and/or UV lines. Alternative practices, such as early placement of peripherally inserted central catheters, or avoidance of umbilical lines altogether, require further evaluation.

Acknowledgement:
Canadian Institutes of Health Research team in Maternal-Infant Care (MiCare) for providing organizational support to the Canadian Neonatal NetworkTM; and the Ontario Ministry of Health and Long-Term Care for providing financial support to the Maternal-Infant Care Research Centre at Mount Sinai Hospital, Toronto, Ontario. We also acknowledge the 29 sites and site investigators, too many to list here, who contributed their time, resources, and data to this study.

women & children's health research institute

Abstract #:	83
Presenter:	Christy-Lynn Cooke
Supervisor:	Sandra Davidge
Title:	Fetal growth restriction and increased susceptibility to cardiovascular disease in offspring born from dams of advanced maternal age
Authors:	Christy-Lynn Cooke, Alison Care, Jude Morton, Amin Shah, Laura Reyes, Sandra Davidge
Affiliations:	University of Alberta
Research Activity:	Maternal Research : Fetal Origins of Adult Disease
Investigation Type:	Quantitative Research

Introduction

The age at which women deliver their first child has increased steadily in recent years, particularly in Western societies. Advanced maternal age is associated with increased maternal and perinatal morbidity and mortality. However, little is known about the effect of advanced maternal age on pregnancy adaptations. Further, the long-term impact on adult offspring from aged mothers and whether they are at an increased risk of cardiovascular disease in unknown.

Methods and Results

Aged female Sprague Dawley rats (9 months; approximately equivalent to a 35 year old woman) and young controls (4 months) were mated with young males. Cardiac function and vascular reactivity were studies in 4 month old male and female offspring from aged and young dams (n = 3 per group). Systolic blood pressure was increased on GD19 in aged rats compared to young rats (young=108.8±5.1 mmHg vs. aged=131.4±5.8 mmHg, $P<0.05$). Aged dams had a reduced capacity to carry viable pregnancies (young=90% vs. aged=50%), and had reduced litter sizes (young=15.0±0.57 pups vs. aged=8.5±1.6 pups, $P<0.01$). Fetuses from aged dams had a reduced body weight at GD20 compared to young dams (3.78±0.1g vs. 3.19±0.2g, $P<0.05$). Using the isolated working heart system, adult male offspring (4 months) from aged dams had impaired cardiac recovery following 10 minutes of ischemia. Using wire myography, male but not female offspring from aged dams demonstrated impaired endothelial relaxation in systemic arteries (EC_{50} = $4.5x10^{-8}$ vs $5.9x10^{-8}$ M methacholine). However, female offspring from aged dams had an increased vasoconstrictor response compared to those from young dams (Max constriction 81 ± 9 versus 96 ± 6 mN/mm).

Conclusion

In a rat model of advanced maternal age, pregnancy outcome is impaired and offspring demonstrate adult onset cardiovascular dysfunction via sex-specific mechanisms. Determining the pathophysiologic pathways by which advanced maternal age affects pregnancy adaptations may help improve both short term pregnancy outcomes as well as long term cardiovascular consequences for the offspring.

Funded By: Start-up or Retention Funding

women & children's health research institute

Abstract #:	84
Presenter:	Taher Al Jishi
Supervisor:	Consolato Sergi
Title:	Factor V Leiden mutation in women with early recurrent pregnancy loss: a meta-analysis and systematic review of the causal association
Authors:	Taher Al Jishi, Consolato Sergi, Mark Walker
Affiliations:	University of Alberta
Research Activity:	Maternal Research : Fetal Origins of Adult Disease
Investigation Type:	Quantitative Research

Background

Recently, the interest has focused on the increased prevalence of thrombophilic defects in women with gestational complications.

Objective

To explore whether women with early recurrent pregnancy loss (RPL) are at increased risk of being carriers of the Factor V Leiden (FVL) mutation compared to those who have a normal reproductive history.

Methods

A manual and electronic literature search was undertaken to identify studies with a case–control population of women with two or more first trimester RPLs of undetermined origin and age- and ethnicity-matched control group with normal reproductive history and at least one full-term delivery. Both groups were screened for FVL mutation. A quality assessment was performed according to the pre-established validity criteria and using the Cochrane handbook guidelines for observational studies. The combinability of studies was assessed by clinical and statistical methods (Breslow–Day's test of homogeneity). Quantitative data were abstracted with regard to the prevalence of FVL mutation in the case and control group, and 2 × 2 tables were created. The ratio comparing the odds of FVL mutation in women with early RPL with the odds of FVL mutation in women with normal reproductive outcome was calculated with its 95 % confidence interval (CI) by Mantel–Haenszel method.

Results

Nine studies met the inclusion criteria and were selected for review. A total of 2,147 women were screened for the FVL mutation, 1305 women with early RPL and 842 women with no gestational complications. Women with early RPL had indeed a statistically significantly increased carrier frequency of FVL mutation, the common OR being 1.68 (95% Cl: 1.16 – 2.44).

Conclusion

FVL carrier state may increase the susceptibility for early RPL. Testing for FVL mutation should be considered in women with unexplained early RPL and thrombophylaxis has been suggested in women with unexplained RPL associated with FVL mutation.

women & children's health research institute

Abstract #:	85
Presenter:	Sarah Bridgman
Supervisor:	Anita Kozyrskyj
Title:	Association between early life fecal immune and metabolic biomarkers and overweight status at 3 years of age: Study overview
Authors:	Sarah Bridgman, Meghan Azad, Catherine Field, Andrea Haqq, Allan Becker, Stuart Turvey, Piush Mandhane, Malcolm Sears, David Wishart, Anita Kozyrskyj, Padmaja Subbarao
Affiliations:	University of Alberta
Research Activity:	Maternal Research : Fetal Origins of Adult Disease
Investigation Type:	Quantitative Research

Introduction

Obesity is currently of public health concern and factors that contribute to its development are multifactorial. Recently, attention has turned towards our commensal gut bacteria (known as "gut microbiota") and their metabolites as a potential causative factor in the development of obesity and associated metabolic disorders.

Through leverage of two existing studies, Synergy in Microbiota Research (SyMBIOTA) and the Canadian Healthy Infant Longitudinal Development (CHILD) cohort, the overall aim is to examine the association between fecal biomarkers of infant gut metabolism (short chain fatty acids) and immunity (fecal immunoglobulin A) at 3 months of age with overweight status at 3 years in 673 infants.

Methods

Fecal immunoglobulin A (IgA) in stool samples taken from infants at 3 months of age will be quantified using Human IgA enzyme linked immunosorbant assay (ELISA) kits. Short chain fatty acids (SCFA) will be extracted from fecal samples and analyzed using gas chromatography mass spectrometry (GC-MS). Anthropometric measurements taken at age 3 years will be used to classify children as normal weight or overweight according to BMI-for-age z-scores. Associations between fecal biomarkers and later child overweight will be tested, adjusting for breastfeeding status at 3 months of age and other relevant covariates.

Results

In a pilot sample of 48 infants, median fecal IgA at 3 months was 14.9µg per gram of protein (IQR 7.1-30.2). Fecal IgA concentration increased with increasing exposure to breastfeeding at 3 months (p trend = 0.01); IgA was lower in breastfed infants who were at risk for overweight at age 3. In infants not breastfed at 3 months, median IgA was significantly higher in children at later risk of overweight (Mann Whitney Test p=0.039). In data collected so far, 11.3% of CHILD infants (N=568) are classified as overweight at 3 years. The proportion of children who were overweight at 3 years was significantly increased with decreasing breastfeeding exposure at 3 months (p trend <0.001).

Conclusion

In our preliminary unadjusted analysis, breastfeeding exposure at age 3 months was positively associated with fecal IgA and negatively associated with overweight status at 3 years of age. Pilot analysis suggests an association between fecal IgA and later child overweight according to breastfeeding status at 3 months. Future analysis will provide data on SCFA concentrations, and associations between fecal IgA and SCFA at 3 months of age and overweight status at 3 years adjusted for potential confounding factors including breastfeeding exposure.

Funded By: Innovation Grant

women & children's health research institute

Abstract #:	86
Presenter:	Vanessa Marensi
Supervisor:	Elaine Leslie
Title:	Characterizing the post translational modification of placental glutathione S-Transferase P1 (Gstp1) By Fatty Acids.
Authors:	Vanessa Marensi, Megan Yap, Luc Berthiaume, Elaine Leslie
Affiliations:	University of Alberta
Research Activity:	Maternal Research : Fetal Origins of Adult Disease
Investigation Type:	Mixed Methods

Glutathione *S*-transferase P1 (GSTP1) is major phase II enzyme which protects the developing baby from toxic compounds through conjugation with the tripeptide glutathione (g-Glu-Cys-Gly). GSTP1 is described as a cytosolic enzyme; however, we have reported the strong association of GSTP1 with the plasma membrane. The location of a protein such as GSTP1 within a cell can have a significant effect on its function. GSTP1 is not removed from the plasma membrane under harsh stripping conditions [e.g., alkaline treatment], known to remove proteins peripherally associated with membranes. GSTP1 is very hydrophilic and we hypothesize that the addition of a hydrophobic component is required to allow its strong interaction with membranes. Palmitoylation is the post-translational addition of a 16-C saturated fatty acid to proteins, most commonly on Cys residues through a thioester bond. This addition can be catalyzed by palmitoyl transferases (PAT) and allows the protein to anchor to cellular membranes. In the current study, we found that GSTP1 is modified by palmitate. GSTP1 has four Cys residues (Cys15, Cys48, Cys102 and Cys170), and a 4X Cys-less (CysàAla) mutant ectopically expressed in MCF7 cells surprisingly retained labelling with palmitate. N-ethylmaleimide (NEM) is known to block Cys residues at neutral pH and amines such as Lys side chains at alkali pH. In vitro palmitoylation with purified GSTP1 demonstrated that a palmitoyl acyl transferase (PAT) is not required for palmitoylation and NEM pre-treatment prevented labelling of purified GSTP1. Together, these results indicate that GSTP1 is modified by palmitate but it is not clear yet whether it is a Cys, Ser and/or an amino acid with an amine side chain that are/is modified by palmitate. We are currently working on the identification of the modified amino acid(s) to further characterize the function of this post-translational modification of GSTP1. Supported by Canadian Institutes of Health Research, Alberta Cancer Foundation and Alberta Innovates Health Solutions.

Funded By: Support services

women & children's health research institute

Abstract #:	87
Presenter:	Juliana Monteiro
Supervisor:	Solina Richter
Title:	Early Breastfeeding in a Brazilian Baby Friendly Hospital according to the health professionals' concept
Authors:	Monise Martins Silva, Juliana Monteiro, Ana Marcia Nakano, Solina Richter
Affiliations:	University of Alberta
Research Activity:	Maternal Research : Nutrution
Investigation Type:	Qualitative Research

Introduction

In order to promote, protect and support breastfeeding, institutions which adhere to the Baby Friendly Hospital Initiative (BFHI), adopted the so-called "Ten steps for the breastfeeding success". The fourth step of the BFHI consists in helping mothers initiate breastfeeding within half an hour after birth. The objective of this study was to analyze the health professionals' practices regarding the assistance of mothers and newborn babies with initiating breastfeeding in half an hour of birth within the reality of Baby Friendly Hospitals.

Methods

It was a qualitative approach study, which allowed the subjective voices of the participants to be heard. The study was conducted at a hospital in Passos, Brazil. Twenty-one health professionals (doctors, nurses, and a psychologist) who worked at the Obstetric Center at the hospital agreed to participate after signing the Informed Consent Form. The data were collected from July to October, 2013. Observation during the intrapartum and early postpartum periods and semi-structured interviews with the health professionals were used to collect data. The data were analyzed using the Meaning Interpretation Method.

Results

According the data analysis, four categories were identified: the conception and the practice provided by the health professional; the mother's contribution during the breastfeeding according to the professionals' point of view; elements that are relevant the breastfeeding; and the health assistance model in the process of breastfeeding in the delivery room. Participants were aware of the practices related to initiating breastfeeding within half an hour of birth; however, the completion of this practice was not verified. Participants considered mothers as passive during the implementation conduction of this practice. They reported easy and difficult elements related to breastfeeding, but they did not use strategies that could improve the easy practices. The health assistance model focus on technical and biological issues. Assistance during the intrapartum period happens in a fragmented and mechanical way.

Conclusion

This study reveal that health professionals need to reflect on the "Ten steps for the breastfeeding success" practices in order to reorganize their practices and fulfill the actions advocated by the breastfeeding within half an hour of birth, favoring the rate improvement of breastfeeding and as a result, the improvement of the maternal and child health.

women & children's health research institute

Abstract #:	88
Presenter:	Ginger Sullivan
Supervisor:	Beverley O'Brien
Title:	Support for women experiencing obstetrical fistula in Northern Ghana
Authors:	Ginger Sullivan , Beverley O'Brien, Prudence Mwinituo, Solina Richter , Zubia Mumtaz
Affiliations:	University of Alberta
Research Activity:	Other
Investigation Type:	Qualitative Research

Introduction

For every woman who dies during pregnancy or childbirth, 23 will suffer from a related morbidity; one of the most severe is obstetric fistula (WHO, 2010). Ghana, a low-income country in sub-Saharan Africa reports high maternal morbidity rates with an estimated 500 to 1000 new cases of obstetric fistula every year.

Methods

A focused ethnographic study was conducted to explore the perception of support experienced by women who have or have had an obstetric fistula, and those close to these women. Data were collected utilizing in-depth interviews (n=14), participant observation and scrutiny of relevant records.

Results

Presentation of obstetric fistula information was not in a format that was readily understandable for women and their families. Food and other basic requirements for daily living were not necessarily available in the fistula centre. Travelling for care was costly and frequently distance from their communities. Fistula repair surgery was available at unpredictable times and only for a few days every one to two months.

Conclusion

Findings revealed perceptions of support reported by affected women as well as spousal, familial, community and formal sources; perceptions of support were particularly focused on access to information and economic support. Recommendations to improve access to treatment for women living with obstetric fistula and reduce maternal morbidity include: directing resources and creating a dedicated specialist fistula centre in Tamale and provide education to front line workers such as nurses, midwives, and public health workers to prevent obstetric fistula and promote safe motherhood practices.

women & children's health research institute

Abstract #:	89
Presenter:	Jasmin Bal
Supervisor:	Richard Fedorak
Title:	C-Reactive Protein is elevated with clinical disease activity during pregnancy in women with Inflammatory Bowel Disease
Authors:	Jasmin Bal, Vivian Huang, Karen Kroeker, Brendan Halloran, Levinus Dieleman, Richard Fedorak
Affiliations:	University of Alberta
Research Activity:	Women's Health : Infection, Inflammation, Immunology
Investigation Type:	Quantitative Research

Introduction

Women with inflammatory bowel disease (IBD) have a risk of flaring their IBD during pregnancy. C-reactive protein (CRP) is an inflammatory serum marker that is often elevated with flares of IBD. CRP can also be elevated during healthy pregnancies. In other words, it is unclear whether CRP can be used as a non-invasive biomarker of clinical disease activity in pregnant women with IBD. The aim of this study is to determine if an elevated CRP is associated with clinical disease activity during pregnancy among women with IBD.

Methods

Female IBD patients (18 to 45 yrs) were enrolled pre-conception (PC) or at each trimester of pregnancy (Tx). At each clinic visit, women were grouped by clinical disease activity, using the Modified Harvey Bradshaw Index for Crohn's disease patients and Partial Mayo Score for ulcerative colitis patients. CRP was also measured at each visit (only patients who had previously documented CRP elevations with flares of their IBD were included for analysis).

Results

Twenty-one patients (median age 29.0 years) seen over 45 clinic visits were included for analysis. To examine the association of CRP with clinical disease activity, we compared CRP in women with clinically active and non-active disease. The median CRP trended higher in women with clinically active disease compared to those with clinically non-active disease at PC (6.95 vs 2.35 mg/L; p=0.154), T1 (24.75 vs 1.70 mg/L; p=0.164), T2 (7.30 vs 4.50 mg/L; p=0.537), and T3 (5.45 vs 2.00 mg/L; p=0.792), respectively.

Conclusion

Women with IBD who had clinically active disease during preconception and pregnancy had higher CRP levels than women who had clinically non-active disease. This suggests that CRP remains a valid tool for assessing clinical IBD activity during pregnancy.

Funded By: Summer Studentship

women & children's health research institute

Abstract #:	90
Presenter:	Nanlin Yin
Supervisor:	David Olson
Title:	A novel in vitro model for understanding the regulation of uterine chemotactic factor for labour initiation
Authors:	Nanlin Yin, Jun Takeda, Xin Fang, Hongbo Qi, David M Olson
Affiliations:	University of Alberta
Research Activity:	Women's Health : Infection, Inflammation, Immunology
Investigation Type:	Mixed Methods

Introduction

Each delivery whether at term or preterm is preceded by an invasion of circulating leukoctyes into the uterine myometrium and decidua. They are attracted by a chemotactic factor that we have identified in the fetal membranes (amnion, chorion) and decidua. However, the regulation of expression for this factor is unknown. Therefore we have developed an *in vitro* human tissue culture model to study the regulation of its experssion. Our aim is to describe the model and characteristics of the chemotactic factor.

Methods

Tissue cultures: Fetal membranes with attached decidua vera from term, not in labour placentas delivered by elective cesarean section at the Royal Alexandra Hospital were used. The protocol was approved by the AHS/UA REB and consent granted in each case. Intact tissues were cut into 12mm pieces (100mg) by a punch. Following washing, the pieces were placed into the wells of 6 well culture plates (6.9 cm^2) and incubated for 24h at 37°C in HEPES-buffered Dulbecco's Minimum Essential Medium (DMEM) maintained at pH 7.4. Following 48h the media were discarded and new DMEM containing either agonists or vehicle was added for 24-94h. The medium was collected and stored at -80°C for subsequent leukocyte migration activity (LMA).

LMA: Peripheral blood (5mL) was obtained from women immediately following term spontaneous vaginal delivery. The leukocytes were separated by Hetasep™ and gentle centrifugation. Leukocytes (10^5) were inserted into the upper compartment of a modified Boyden Champber and approximately 25mL (125µg protein) of medium containing chemoattractant was placed into the lower compartment. The two compartments were separated by a filter containing 3 µm pores. The chambers were incubated for 90 min at 37°C. At the end of this time, the number of cells that migrated to the lower chamber were quantified by FACS analysis.

Results

Tissue DNA and RNA remained steady over 96h suggesting the minced tissues remained viable. There was a time-dependent increase in the release of chemoattractant activity into the media from 24h to 96h when it reached a plateau. Upwards of 45,000 cells migrated when chemoattractant was present. Blanks were negligible.

Conclusion

We have successfully developed a new model for studying the regulation of the uterine cheomoattractant. Future studies will assess the responsiveness of human fetal membranes in this model system to a number of inflammatory and non-inflammatory agonists that mediate the processes of parturition and preterm birth.

Acknowledgements: Chongqing Medical University, GAPPS, CIHR, and WCHRI

Funded By: Innovation Grant

women & children's health research institute

Abstract #:	91
Presenter:	Ariane Thaise Frello Roque
Supervisor:	Gerri Lasiuk
Title:	The experience of high risk puerperium women: vital power influence
Authors:	Ariane Thaise Frello Roque, Telma Elisa Carraro, Vera Radünz, Gerri Lasiuk, Kathleen Hegadoren
Affiliations:	University of Alberta
Research Activity:	Maternal Research : Perinatal Mental Health
Investigation Type:	Qualitative Research

Background

Within the Brazilian health care context, women are considered to have a high-risk puerperium when she is discharged but her newborn child remains hospitalized in the Neonatal Intensive Care Unit (NICU). This separation can lead women to distance themselves from family while attempting to manage household responsibilities and being with their babies in hospital. The uncertainty involved in the newborns' health, as well as women's divided loyalties and energies can have a negative impact on breastfeeding and puerperal healing.

According to the Carraro Care Model, an existential transition occurs during the postpartum period. During this transition, the baby transforms form an idealized ethereal being to a real and separate human whose needs are different from and take precedence over those of the mother. For this transition to occur, women and their families need support to strengthen their vital power - a life force innate to human beings.

Purpose

To understand the experiences of high-risk puerperal women whose newborns were admitted to the neonatal unit in Florianópolis, Santa Catarina, Brazil.

Method

This narrative inquiry is theoretically informed by the writings of Florence Nightingale, the Carraro Care Model, and the tenets of narrative inquiry. Following ethics from Federal University of Santa Catarina Ethics Committee, puerperal women were recruited to the study if they were 18 years or older, had newborn infants in the NICU, and provided informed consent. Seven women who met inclusion criteria participated in individual interviews, which were audio-recorded and analyzed. Data analysis followed the six-phase method described by Fritz Schütze.

Findings

The women's narratives focused on their feelings that were highly contextualized within the hospital environment during this particular phase of their lives. Participants reflected on the challenges of interacting in an unknown environment for an indeterminate period and entrusting their children to professionals. The women sought personal connection and support among the other mothers on the unit and the nursing staff was seen as positive factors to manage the day-to-day experiences between their two worlds.

Implication

This study increases our understanding of the experiences of woman whose newborns remained in one Brazilian NICU and of how these experiences influenced the women's health and well-being in the early puerperium. Targeted nursing interventions within the hospital environment are significant and powerful supports for mothers during this period.

Funded By: CAPES - Brazil

women & children's health research institute

Abstract #:	92
Presenter:	Mais Aljunaidy
Supervisor:	Sandra Davidge
Title:	Mechanisms of vascular dysfunction in a rat model of preeclampsia and fetal growth restriction.
Authors:	Mais Aljunaidy, Jude Morton, Sandra Davidge
Affiliations:	University of Alberta
Research Activity:	Maternal Research : Preeclampsia
Investigation Type:	Quantitative Research

Introduction

Preeclampsia is a pregnancy complication diagnosed by hypertension and proteinuria after the 20th week of gestation and is a leading cause of maternal and fetal morbidity and mortality. In order to investigate therapeutic strategies for prevention and/or treatment of preeclampsia, a robust animal model is required. A recent study has shown that a low oxygen environment during pregnancy leads to signs of preeclampsia. However, the impact on uterine artery function/blood flow, and ultimately fetal outcomes, in this model has not been explored. We assessed the pregnancy outcomes of this model in order to obtain a model in which to test various potential treatment regimes.

Methods

Sprague Dawley rats were housed either in normal atmospheric conditions or exposed to hypoxia (10.5%) during pregnancy(gestational day (GD) 6-20; term=22 days. Uterine vascular function was assessed using both *in vivo* (ultrasound biomicroscopy at GD 20) and *ex vivo* (wire myography at GD 21) techniques. After euthanasia on GD 21, fetal and placental biometrics were measured.

Results

In the hypoxic model, the maximum velocity of uterine artery blood flow (normoxia: 828.39±79.20 mm/s vs. hypoxia: 513.84±53.44 mm/s, P<0.01) and the uterine artery resistance index (normoxia: 0.63±0.04 vs. hypoxia: 0.52±0.01, P<0.01) were both decreased. The maximum velocity of the umbilical artery blood flow, however, increased (normoxia: 189.31±15.12 mm/s vs. hypoxia: 233.13±10.56 mm/s, P<0.05) along with fetal heart rate (normoxia: 237.49±4.55 bpm vs. hypoxia: 269.83±10.46 bpm, P<0.01). Moreover, in the hypoxic group, fetal body weight (normoxia: 5.50±0.15 g vs. hypoxia: 4.60±0.19 g, P<0.01), crown-rump length (normoxia: 4.50±0.09 cm vs. hypoxia: 4.10±0.08 cm, P<0.01), abdominal girth (normoxia: 4.60±0.15 cm vs. hypoxia: 4.00±0.09 cm, P<0.01) and litter size (normoxia: 15.4±0.5 vs. hypoxia: 13.0±1.7, P<0.01) were all reduced. There were no differences in uterine artery responses to the vasoconstrictor phenylephrine, however, vascular sensitivity to the endothelium-dependent vasodilator methacholine (MCh) decreased (pEC_{50} normoxia: 6.43±0.30 vs. hypoxia: 5.57±0.20, P<0.01).

Conclusion

Dams exposed to hypoxia demonstrated a maternal vascular phenotype characterized by altered maternal/fetal blood flow and intrauterine growth restricted offspring. Our future studies will address a possible intervention strategy using a mitochondrial antioxidant with nanoparticle delivery for targeted distribution to the placenta.

Funded By: CIHR

women & children's health research institute

Abstract #:	93
Presenter:	Shieva Auch
Supervisor:	Gerri Lasiuk
Title:	Associations among lifetime interpersonal violence and selected perinatal outcomes: Preliminary findings from the TIPS
Authors:	Shieva Auch, Gerri Lasiuk, Thierry Lacaze-Masmonteil, Leonora Hendson, Radha Chari, Colleen Norris, Kathy Hegadoren
Affiliations:	University of Alberta
Research Activity:	Maternal Research : Perinatal Mental Health
Investigation Type:	Quantitative Research

Introduction

The Trauma in Pregnancy Study (TIPS) is a longitudinal prospective cohort study of the effects of trauma (e.g. motor vehicle crash, falls, work-related injury, or interpersonal violence) during pregnancy on pregnancy outcomes, maternal health, and child development. The primary objective of the larger study was to examine associations among trauma during pregnancy, perinatal complications, and cognitive, motor and social developmental delays in childhood. A secondary objective was to examine the relationship between trauma during pregnancy and a wide range on maternal and infant health outcomes. Purpose: To examine the impact of lifetime interpersonal violence (IPV) on selected demographic, antepartum, and intrapartum variables for women in the TIPS.

Methods

In this preliminary analysis, women (N=140) were assigned to groups based on their report of lifetime IPV (childhood maltreatment, intimate partner violence or sexual or physical assault). Women were included in this analysis if a delivery record was present and they had a singleton pregnancy. Using SPSS, independent t-tests were used to examine between-group differences of demographics, antepartum, and labour and delivery variables.

Results

Significant differences ($p \leq 0.05$) between the two groups were found for the following demographic variables at entry: maternal age; experiencing a trauma during pregnancy; perceptions of emotional health in the last 6 months; health problems during pregnancy; past history of depression; smoking status; relationship status and whether the pregnancy was planned. As expected, scores on the Adverse Childhood Experiences survey differed. Selected intrapartum variables found to be significantly different ($p \leq 0.05$) between groups include stage of labour duration; rates of caesarean section; and the use of narcotics (but not epidural) for intraprtum pain management.

Conclusion

For these preliminary analyses it is clear that these two groups of women are distinctly different. Women who have experienced interpersonal violence at any time reported more risk factors associated with postpartum depression. Assessment of past violence experiences in the pregnancy would identify women who may require more intrapartum and postpartum supports. Further multivariate analyses are needed to delineate relationships among these differing variables and the implications for maternal and child health outcomes.

Funded By: RAH Foundation and ACCFCR

women & children's health research institute

Abstract #: 94
Presenter: Devishree Krishnan
Supervisor: Todd Alexander
Title: Effect of sodium ingestion on urinary calcium excretion
Authors: Devishree Krishnan
Affiliations: University of Alberta
Research Activity: Other
Investigation Type: Quantitative Research

Introduction

Kidney stones are becoming increasingly prevalent in childhood. The major risk factor for kidney stone formation is the production of urine with increased calcium content, called hypercalciuria. Children and adults with hypercalciuria are also at an increased risk of decreased bone mineral density, or osteoporosis, likely due to a persistently negative calcium balance. Pan et al., recently identified the sodium proton exchanger isoform 3, which is expressed in the renal proximal tubule, as a link between renal sodium and calcium reabsorption. However, the mechanisms linking sodium ingestion to calcium excretion are poorly delineated.

Hypothesis

We therefore hypothesize that increased sodium ingestion decreases NHE3 activity thereby increasing urinary calcium excretion.

Methods and Results

Experiments were carried out on humans, consuming a control diet or a high salt diet for 7 days. Urine samples were collected at the end of the diets. Urine analysis revealed significantly increased Na^{+} and Ca^{2+} excretion in the humans consuming a high salt diet. Similar experiments were performed on wild-type mice, fed a control diet (0.8% NaCl) or a high salt (8% NaCl) diet for 7 days. Urine, serum and tissues samples were collected. Urine analysis, revealed significantly increased Na^{+} and Ca^{2+} excretion in the WT mice with a high salt diet. No significant difference in protein or mRNA expression of NHE3 was observed. Renin expression was significantly decreased in high salt fed mice, a hormone known to effect NHE3 activity. Whether angiotensin II mediated increase in NHE3 activity also increases transepithelial calcium flux, in response to altered sodium ingestion is not known (although angiotensin II administration does cause calciuria). To test whether this is the case we will employ an *in vitro* cell culture model, opossum kidney cells, a proximal tubular cell culture model known to express NHE3 that is regulated by a number of hormones, including Angiotensin II. We will treat OK cells with angiotensin II and then measure calcium flux across confluent monolayers of cells.

Conclusion

Together these studies will provide support for our hypothesis that angiontensin II mediated regulation of NHE3 is the link between dietary sodium ingestion and urinary calcium excretion. By delineating the molecular link between sodium ingestion and calcium excretion we will uncover novel therapeutic targets for kidney stone disease.

Funded By: Graduate Studentship

women & children's health research institute

Abstract #:	95
Presenter:	Nicholas Kuzik
Supervisor:	Valerie Carson
Title:	Physical activity and sedentary behaviour of toddlers and preschoolers in child care centres in Alberta, Canada
Authors:	Nicholas Kuzik, Dawne Clark, Nancy Ogden, Vicki Harber, Valerie Carson
Affiliations:	University of Alberta
Research Activity:	Other
Investigation Type:	Quantitative Research

Introduction

The early years (≤4 years) provides an important window of opportunity to establish healthy habits of regular physical activity and minimal sedentary behaviour for healthy growth and development and chronic disease prevention. In Canada, just over half of children aged 0 to 5 years attend non-parental child care, making it a suitable setting to promote these healthy habits. To date, no study has objectively measured physical activity and sedentary time of toddlers (19-35 months of age) attending child care centres or reported on how sedentary time is accumulated among toddlers or preschoolers (e.g., short sedentary bouts or longer sedentary bouts). Additionally, demographic differences of physical activity and sedentary behaviour during child care centres are unclear. Therefore, the objectives of this study were to describe levels of physical activity and levels and bouts of sedentary time during child care in a sample of toddlers and preschoolers (19-60 months) from Alberta, Canada, and to examine if levels and bouts differed between age, sex, and parental immigration status.

Methods

Results are based on 106 children, aged 19-60 months from eight participating child care centres throughout Alberta, Canada. Data were collected at baseline of a study examining revised Alberta Child Care Accreditation Program Quality Standards. Levels of physical activity (light (LPA), moderate-to-vigorous (MVPA)) and levels and bouts (1-4, 5-9, 10-14, and >15 minutes) of sedentary time during child care were derived with a motion sensor called an accelerometer using 15-second intervals during October/November, 2013. Median [Interquartile ranges] and ANCOVAs, accounting for the clustered nature of the data, were calculated.

Results

Minutes/hour spent in sedentary time, LPA, and MVPA were 32.0 [28.2, 34.3], 22.8 [20.8, 24.6], and 5.2 [3.2, 7.1], respectively. Frequency/hour of sedentary bouts lasting 1-4, 5-9, 10-15 and >15 minutes were 8.79 [7.71, 9.68], 0.72 [0.49, 0.96], 0.09 [0.05, 0.16], and 0.00 [0.00, 0.04], respectively. Preschoolers obtained more MVPA than toddlers, and girls had more sedentary bouts/hour lasting 5-9 minutes. No other significant differences in levels or bouts were observed.

Conclusion

This is the first Canadian study to report on the levels of physical activity and levels and bouts of sedentary time among toddlers and preschoolers attending child care centres. Children spent over half their time sedentary, mainly in shorter bouts, and the majority of their physical activity participation was of light-intensity. Future work could focus on interventions and initiatives to increase MVPA and decrease sedentary time, while reinforcing short sedentary bouts.

Funded By: Trainee Travel Grant

women & children's health research institute

Abstract #:	96
Presenter:	Lesley Brennan
Supervisor:	Stephane Bourque
Title:	Relationship between maternal iron level and birth outcome in Alberta women: an APrON cohort analysis
Authors:	Lesley Brennan, Mohammadreza Pakseresht, Catherine J. Field, Rhonda Bell, Fatheema Begum Sudhan, Donna Manca, Nalini Singhal, Maeve O'Beirne, Stephane Bourque
Affiliations:	University of Alberta
Research Activity:	Maternal Research : Nutrution
Investigation Type:	Quantitative Research

Introduction

Iron deficiency (ID) occurs when the body's iron demands exceed supply. It affects billions of people worldwide and is a common cause of anemia. ID is prevalent during pregnancy, when iron is required for fetal development, and is associated with negative birth outcomes[1]. The majority of pregnant women do not receive the recommended daily iron through diet, therefore supplementation is encouraged. While much research has focused on iron and pregnancy in developing nations, little is known about the status of Canadian women. Here we characterize maternal iron status and associated health consequences (birth outcome and infant health) in a cohort of women participating in the Alberta Pregnancy Outcomes and Nutrition (APrON) study. Ferritin is the most reliable indicator of iron status, though it may be influenced by inflammation, and was the primary measure used.

Methods

Maternal nutritional/supplemental intake, indicators of iron status and anemia, and birth/infant health data were obtained from APrON Cohort 1 participants (n=600). Descriptive statistics were conducted on participants' demographics, nutritional intake and iron status, in addition to measures of birth outcome (gestational age, birth weight), and infant health (APGAR scores, NICU admission). Inferential statistics included assessment of correlation (Spearman's rank correlation coefficient) between ferritin level at each trimester and indicators of birth outcome/infant health.

Results

Participants were predominantly married, Caucasian, and Canadian-born, with above-average education and income, and a mean age of 31.6 years. The mean gestational age was 39 weeks and birth weight was 3371 g. NICU admission was rare (7.2%) and mean APGAR scores were above 8. On average, women received the recommended daily iron throughout pregnancy. Median ferritin levels were within the normal range early in pregnancy but dropped in the third trimester. Correlation analysis revealed a weak positive correlation between first trimester ferritin and 5 minute APGAR score (r = 0.231, $p<0.013$), and a weak negative correlation (r = -0.188, $p<0.001$) between third trimester ferritin and birth weight.

Conclusion

The APrON cohort represents a healthy group of mothers and infants with access to quality health care, nutrition, and supplementation. Our findings agree with previous studies positively correlating iron intake with APGAR score[1]. In addition, we identified a negative correlation between ferritin level and birth weight, which is consistent with the literature and suggests excess iron intake during pregnancy, or the presence of inflammation[2].

(1) Rioux & LeBlanc (2007). *Appl. Physiol. Nutri. Metab. 32*:282 (2) Casanueva & Viteri (2003). *J. Nutri.*, *133*:1700S.

Funded By: Start-up or Retention Funding

women & children's health research institute

Abstract #:	97
Presenter:	Sydney Schmidt
Supervisor:	Margie Davenport
Title:	Exercise During Pregnancy: Current recommendations by Canadian maternity health care providers.
Authors:	Sydney Schmidt, Radha Chari, Margie Davenport
Affiliations:	University of Alberta
Research Activity:	Maternal Research : Preeclampsia
Investigation Type:	Quantitative Research

Objective

While the benefits of exercise throughout pregnancy have been widely studied, few have investigated the guidelines and tools used to prescribe exercise to pregnant women. The objective of our study was to examine the uptake and implementation of recommendations for exercise during pregnancy by Canadian practitioners.

Methods

Survey Monkey software was used to create a valid e-survey investigating Canadian maternity healthcare providers' beliefs and current practices and tools used for prescribing exercise during pregnancy. The survey was distributed by the Society of Obstetricians and Gynaecologists of Canada (SOGC) to members agreeing to accept surveys (n=1282)

Results

The survey was completed by 195 respondents (15.2%) with the majority of practitioners recommending healthy pregnant women (99.8%) and women at risk for developing preeclampsia (96.3%) exercise throughout gestation. 55.5% prescribe current SOGC/CSEP guidelines of 30 minutes of moderate intensity exercise 3-4 times a week, 26.3% recommend the current guidelines of the American College of Obstetricians and Gynecologist (30 minutes of moderate intensity exercise on most days of the week), while 12.3% continue to follow former ACOG guidelines that exercise should not exceed 140bpm. The PARmed-X for Pregnancy is used by 26.1% of practitioners with an additional 57.5% indicating that they were not familiar with this screening tool. Bed rest is no longer commonly recommended for women diagnosed with preeclampsia.

Conclusion

Exercise is widely recommended to pregnant women in Canada; however, the guidelines used vary considerably. Practitioners are not always aware of current best practice and tools being used when consulting with pregnant women.

Funded By: University of Alberta President's Grant for the Creative and Performing Arts - Human Performance Scholarship Fund

women & children's health research institute

Abstract #:	98
Presenter:	Kelycia Leimert
Supervisor:	David Olson
Title:	PGF2α promotes uterine transformation through positive feedback interactions and synergy with IL-1β in human myometrium smooth muscle cells (HMSMC)
Authors:	Kelycia Leimert, Barbara Verstraeten, Xin Fang, Carine Bourguet, William Lubell, Sylvain Chemtob, David Olson
Affiliations:	University of Alberta
Research Activity:	Maternal Research : Pre-term Birth
Investigation Type:	Quantitative Research

Introduction

Uterine transformation is essential to parturition, involving interactions between a series of 'birth cascade' pathways to transform the uterus of pregnancy into the contractile uterus of delivery. We have condensed the complex process of uterine transformation into three stages: positive feedback, synergy and amplification. PGF2α is a key signaling mediator in parturition; we have discovered that PGF2α not only induces uterine contraction but is also involved in the induction of uterine transformation through positive feedback and synergistic interactions. Previously we demonstrated that PGF2α stimulates COX-2 and IL-6 mRNA and protein abundance in HMSMC via its receptor, PTGFR, and that IL-1β stimulates PTGFR, COX-2 and IL-6 mRNA and protein abundance in HMSMC. We hypothesized that IL-1β elevation of PTGFR would correspondingly increase the ability of PGF2α to stimulate uterine transformation.

Methods

HMSMC were treated for 24h with DMEM only, followed by 6h PGF2α (10^{-5} M) and extracted for mRNA abundance determination by real-time RT-PCR. A second set of cells were treated for 24h with IL-1β (5 ng/mL) then washed and treated for another 6h with DMEM alone or with PGF2α (10^{-5} M). N=8 patients, statistical analysis was performed on Log10-transformed data: ANOVA followed by Tukey post hoc testing ($p \leq 0.05$).

Results

6h of PGF2α treatment (alone) increased relative mRNA abundance for COX-2 by 4.8-fold ($p<0.01$) and IL-6 by 8.2-fold ($p<0.001$). Cells treated with 24h IL-1β followed by 6h DMEM increased relative mRNA abundance for PTGFR by 3.6-fold, COX-2 by 19.4-fold ($p<10^{-5}$), and IL-6 by 36-fold ($p<10^{-5}$). In return, both PGF2α and IL-1β treatment increased mRNA expression of IL-1β receptor IL-1R1 ($p<0.001$). IL-1β treatment for 24h followed by 6h of PGF2α treatment increased COX-2 mRNA abundance synergistically 35-fold ($p<10^{-6}$) and increased IL-6 mRNA abundance by 104-fold ($p<10^{-6}$). CAR10 allosteric FP antagonists do not block this effect.

Conclusion

Positive feedback interactions involving PGF2α, IL-1β and other signaling intermediates contribute to the process of uterine transformation. Moreover, IL-1β treatment followed by subsequent PGF2α stimulates extremely large synergistic increases in COX-2 and IL-6 mRNA abundance. These data suggest that in vivo preconditioning with IL-1β increases myometrial responsiveness to PGF2α tremendously thereby promoting a feed-forward amplification that activates the uterus for labour.

Acknowledgements: March of Dimes, CIHR, Global Alliance for the Prevention of Prematurity and Stillbirth, an initiative of Seattle Children's.

Funded By: Trainee Travel Grant

women & children's health research institute

Abstract #:	99
Presenter:	Rose Sun
Supervisor:	Sandra T. Davidge
Title:	Mechanism of resveratrol action on improving cardiovascular function in growth restricted offspring on a high-fat diet
Authors:	Rose Sun, Sandra T. Davidge, Jude S. Morton, Dr. Amin Shah
Affiliations:	University of Alberta
Research Activity:	Maternal Research : Preeclampsia
Investigation Type:	Quantitative Research

Introduction

Children born from a suboptimal intrauterine environment have increased susceptibility to postnatal stressor such as high fat diets and aging. These secondary stressors in growth-restricted offspring can further exacerbate the risks of developing cardiovascular and metabolic diseases such as hypertension, coronary artery disease, and type 2 diabetes. It has been shown that intrauterine growth restricted (IUGR) male rat offspring exposed to a high-fat (HF) diet are more susceptible to develop cardiovascular pathologies as young adults; effects that can be offset by treatment with the polyphenol, resveratrol (Resv). The objective of the current study was to determine the effect of Resv supplementation to prevent cardiovascular dysfunction in female IUGR rat offspring on a HF diet. We hypothesized that Resv would revert the effects of IUGR and HF diet by reducing oxidative stress to improve nitric oxide mediated cardiovascular function.

Methods

Female control or IUGR rat offspring (created by exposing pregnant dams to hypoxia, 11.0±0.5% O_2, for the last third of pregnancy) were randomly assigned to receive a HF diet or a HF diet supplemented with Resv (4g/kg of diet) from 3-12 weeks of age. Vascular function was evaluated in isolated mesenteric arteries using wire myography. Superoxide and endothelial nitric oxide synthase (eNOS) in cardiac tissue were measured using DHE staining and western blot, respectively.

Results

In control offspring, inhibitors of NOS isoforms did not modify methocholine (MCh)-induced vascular relaxation. However, in IUGR offspring, the component of maximal MCh-mediated relaxation attributed to eNOS was enhanced (53% of relaxation in IUGR vs. 19% in control, $P<0.05$) and Resv treatment decreased this effect (8% in IUGR + Resv). In addition, Resv decreased vascular sensitivity to MCh in both control and IUGR offspring. In cardiac tissue, Resv significantly decreased superoxide production (mean intensity of staining: 3.69 AU ± 0.60 SEM, $P<0.01$), which was elevated in IUGR offspring only (6.50 AU ±0.05 SEM IUGR vs. 4.13 AU ±0.40 SEM Control, $P<0.05$). Furthermore, eNOS protein levels increased 2.5 fold in IUGR offspring with Resv intervention (protein expression in IUGR group 4.430 AU, vs. IUGR + Resv 11.075 AU, $P<0.05$).

Conclusion

In summary, Resv reduced cardiac oxidative stress in IUGR offspring. Interestingly, Resv decreased the enhanced eNOS-mediated vascular relaxation that was observed in only IUGR offspring. In conclusion, prenatal hypoxia-induced IUGR in combination with a HF diet leads to altered cardiovascular function in young female offspring, and postnatal Resv supplementation had differential mechanisms in cardiac and vascular tissue.

women & children's health research institute

Abstract #:	100
Presenter:	Priatharsini (Tharsini) Sivananthajothy
Supervisor:	Dr. Jane Springett
Title:	Understanding perceptions of community engagement held by stakeholders within the family care clinic planning process
Authors:	Priatharsini (Tharsini) Sivananthajothy, Yvonne Chiu, Dr. Jane Springett
Affiliations:	University of Alberta
Research Activity:	Other
Investigation Type:	Qualitative Research

Introduction and Objectives

The early childhood period is emphasized as the most important developmental stage. However, the effects of poverty, inadequate housing, and lack of appropriate support systems for parents and their children are only marginally considered when providing health care services. Recognizing the importance of health promotion, prevention and the social determinants of health, Family Care Clinics (FCCs) were designed by Alberta Health to provide integrated, community based, comprehensive primary health care. The objectives of this research project were to: a) understand how FCCs incorporated early childhood development (ECD) programs, and b) explore how the voices of the community were represented within the development of FCCs.

Methods

A descriptive qualitative inquiry was conducted to explore the research objectives. Snowball sampling was utilized to recruit participants critical to the planning process within phase 1 and phase 2 FCCs along with community organizations working in ECD. Nine in-depth interviews were conducted with participants from eight organizations either in person, or over the phone between the months of June - September 2014. A qualitative content analysis was conducted to inductively determine emerging themes.

Results

Community Engagement:

Two distinct phases of planning were identified as critical periods for community engagement: firstly the public forums held by Alberta Health to engage with interested community organizations to discuss the implementation of FCCs within the community; secondly, the community working groups formed to develop the proposal. However, discrepancies within the definition of community, who was invited as stakeholders and who was not, were identified as challenges in both phases of community engagement. Many participants acknowledged the lack of representation from grassroots organizations, and also cited the extremely short timeline given during the summer months as critical barriers for engaging with the community.

Women, Children and ECD:

Many FCCs did not have specific programming for ECD, as emphasis was placed on providing health services targeting specific populations, including chronic disease management. However, FCC proponents described an emphasis on the social determinants of health, providing vulnerable populations, including women and youth, opportunities to obtain health and social supports to prevent ill health.

Conclusion and Implications

Engagement was described as an opportunity to create trust and provide the “hand-holding” necessary to connect the unattached population to a primary health care provider. Further engagement with the local community and grassroots organizations is necessary to truly establish a trusting relationship necessary for uptake of FCC services by the vulnerable populations.

Funded By: Summer Studentship

women & children's health research institute

Abstract #:	101
Presenter:	Osnat Wine
Supervisor:	Alvaro Osornio-Vargas
Title:	DoMiNO Project: Data mining and newborn outcomes exploring environmental variables and health outcomes using an integrated KT approach
Authors:	Osnat Wine, Alvaro Osornio-Vargas
Affiliations:	University of Alberta
Research Activity:	Other
Investigation Type:	Qualitative Research

Introduction

This interdisciplinary research project includes 24 members who investigate chemical and socioeconomic environmental influences on maternal/infant birth outcomes (low birth weight, preterm births, stillbirths and perinatal mortality). Using publicly funded databases (National Pollutants Release Inventory, Stats Canada, Canadian Neonatal Network, and Alberta Perinatal Health Program), we investigate association patterns among adverse birth outcomes (ABO), multiple pollutants released by industry/traffic to air and maternal and socioeconomic variables, across Canada. The complexity of this project requires interdisciplinary expertize and collaboration, between academia and knowledge users, to obtain, analyze and interpret useful information from large sets of data to advance utilization of the research.

Methods

We employ *Geo-spatial distribution* of variables and *Newly developed Data mining methodologies* to explore multipollutant interactions, as well as potential interactions of these pollutants, with ABO and socioeconomic and maternal biological variables. The project design also reflects an *integrated knowledge translation* strategy, resulting from collaboration between knowledge users from government, data-provider agencies, NGO's, and interdisciplinary researchers. This collaborative researcher- knowledge user team oversees development of the end-of-project knowledge translation strategy and evaluation of the initiative.

Anticipated results and Conclusion

Project outcomes include

1) Identification of co-location/spatial association of ABO with multiple combinations of environmental and other known risk factors that can serve as foundation for future research focusing on identifying causal relationships.

2) Newly developed approach to data mining as a tool for exploring multi-factorial and multi-pollutant relationships to environmental health outcomes.

3) Evaluation of knowledge users and interdisciplinary researchers collaboration and its contribution to knowledge translation for environmental health research.

Funded By: CIHR/NSERC, TD Bank Financial Group Grant

women & children's health research institute

Abstract #: 102
Presenter: Irena Buka
Supervisor: Alvaro Osornio

Title: Children summer exposure to environmental tobacco smoke. Results from the first phase of a larger seasonal exposure study.

Authors: Irena Buka
Affiliations: University of Alberta

Research Activity: Other
Investigation Type: Quantitative Research

Introduction

Smoking rates in Alberta (21%) are among the lowest in Canada, but children's exposure to environmental tobacco smoke (ETS) is still a concern. Regulation of smoking in public places has shifted the burden to exposures in the home. Education measures promote outdoor versus indoor smoking when cessation is not possible. We are interested in assessing exposures in a city where extreme weather conditions could predispose children, especially in winter, to household ETS exposure. We present summer results of a study-evaluating child ETS seasonal exposure differences.

Methods

Children (1 to 5 years-old) were recruited in a general pediatrics clinic during the summers of 2012 and 2013. Consenting accompanying caregivers responded to a validated questionnaire exploring ETS exposure in their children's living environments. Children provided urine samples for cotinine/creatinine ratios (CCR in nmoles/mmoles per liter) for ETS exposure assessment.

Results

Questionnaires and urine samples were collected from 52 participants. According to questionnaires, only four children were declared ETS free (Group-1) and had a median CCR of 2.39, with none above the overall children's median of 5.0 (range: 0.53-231.68). Forty-eight children (92%) were identified to have some degree of ETS exposure. Sixteen had exclusive outdoor household exposure (Group-2) and had a median CCR of 6.16, with nine (56%) with CCR>5. Fourteen had clear indoor/outdoor ETS exposure in their households (Group-3), and the median CCR was 12.51, with eleven children (79%) with CCR>5. Four had some degree of indoor ETS exposure outside of their homes (Group-4) and a median CCR of 4.34, with two (50%) with CCR>5. Fourteen had exclusive outdoor ETS exposures in public places (Group-5) and a median CCR of 3.46 with four of the children (29%) with CCR>5.

Medians among groups were only significantly different between the ETS-free group (Group-1) and those exposed in their household (Groups 2+3 and Group-3 alone) ($p<0.05$). Although the proportion of children with CCR>5 in those exclusively exposed in public places (Group-5) is half of those exposed in their outdoor households environments (Group-2) (29 vs. 56%), the difference was marginally significant ($p=0.06$).

Conclusion

The number of responders reporting ETS exposures was unexpectedly high compared to smoking rates in Alberta. Urine CCR confirmed that a high number of children had ETS exposures, regardless of caregivers smoking indoors or outdoors. As self-imposed smoking bans may be more difficult to adhere to in cold weather, we anticipate even higher ETS exposures in samples collected during the winter.

Funded By: Covenant Health research Centre

women & children's health research institute

Abstract #:	103
Presenter:	Katelynn Crick
Supervisor:	Lisa Hartling
Title:	A descriptive and comparative analysis of child-relevant systematic reviews in the cochrane database of systematic reviews
Authors:	Katelynn Crick, Lisa Hartling, Brian Rowe
Affiliations:	University of Alberta
Research Activity:	Other
Investigation Type:	Qualitative Research

Introduction

Systematic reviews (SRs) identify and summarize all existing studies on a particular topic and are a key resource to support clinical decision-making. In 2009, a comprehensive description of published child-relevant SRs compiled. This study aims to identify all child-relevant SRs produced through the Cochrane Collaboration to date, and to describe these SRs according to their content and methodological approaches. An update and comparison of these child-relevant SRs to the findings in 2009 will help to: 1) identify the extent of child-relevant evidence available in SRs, 2) identify gaps in the evidence base that have been addressed since 2009, 3) identify remaining and new gaps, 4) identify methodological advancements, and 5) identify methodological limitations in SRs.

Methods

All child-relevant SRs produced through the Cochrane Collaboration (n=1347) were identified and described according to their content and methodological approaches. This step represented an update of the Child Health Field Review Register (CHFRR), which is a widely accessible database that supports therapeutic decision-making. The content of the updated CHFRR was compared to the 2009 CHFRR in terms of clinical and methodological content.

Results

Of 5,520 SRs Cochrane SRs were identified, 1,338 were child-relevant. Overall, these reviews included 16,804 primary studies involving over 38,346,913 participants. The most commonly represented clinical areas are Airways (11.5%), Cystic Fibrosis and Genetic Diseases (7.9%), Acute Respiratory Infections (7.8%), Developmental, Psychological and Learning Disorders (6.7%), and Infectious Diseases (6.2%). Corresponding authors were most often from Europe (51%), North America (15%), and Australia (15%). The majority of SRs examined pharmacological interventions (52%). Authors specified a primary outcome in 82% of the SRs. 56% of reviews used the Cochrane Risk of Bias tool to assess methodological quality. 25% of reviews used allocation concealment to assess risk of bias and 7% used the Jadad scale, even though these tools are considered outdated. Publication bias was formally assessed in only 14% of reviews. The majority of SRs conducted at least one meta-analysis (73%).

Conclusion

We described the content and methodological characteristics of child-relevant SRs in the Cochrane CHFRR. There have been advances in methodological methods since 2009 including the proportion of reviews specifying a primary outcome and the proportion of reviews using the Cochrane Risk of Bias tool to assess methodological quality. The CHFRR offers an important resource for clinical decision-making, synthesizing an extensive body of primary research. Further content analysis will allow us to identify clinical topics of priority for future SRs.

Funded By: Graduate Studentship

women & children's health research institute

Abstract #:	104
Presenter:	Maryam Elyasi
Supervisor:	Maryam Amin
Title:	Impact of sense of coherence on oral Health-related behaviors: A systematic review
Authors:	Maryam Elyasi, Lucas Guimarães Abreu, Parvaneh Badri, Humam Saltaji, Carlos Flores-Mir, Maryam Amin
Affiliations:	University of Alberta
Research Activity:	Other
Investigation Type:	Quantitative Research

Introduction

There is compelling evidence to support that positive health behaviors could be influenced by psycho-social factors. Sense of coherence (SOC) is a psychosocial determinant of people's health behavior. It appears that individuals with a strong SOC may be more predisposed to a healthy lifestyle and are more likely to respond to health-related advice as compared to their counterparts with a weak SOC. The aim of this review was to critically analyze the empirical evidence on the association between SOC and oral health behaviors through a systematic review of the published data.

Methods

A systematic search up to April 2014 was carried out using the following electronic bibliographic databases: PubMed, Ovid MEDLINE; ISI Web of Science; and Ovid PsychInfo. Studies were included if they evaluated the relationship between SOC and oral health behaviors (e.g., tooth brushing frequency, dietary habits, dental attendance, and smoking). We excluded studies that only assessed the relationship between oral health status and SOC without evaluating oral health behaviors. The Health Evidence Bulletins-Wales appraisal checklist was employed to evaluate the methodological quality of included studies.

Results

Thirty nine potential papers met the preliminary selection criteria and following a full-text review, 11 papers were finally selected for this systematic review. Results provided by the included studies indicated different levels of association between SOC and oral health behaviors. The most frequent behaviors investigated were tooth brushing and dental attendance pattern. The impact of SOC on performing positive oral health behaviors, to some extent, was related to demographic and socio-economic factors. In addition, mothers' SOC influenced children's oral health practices.

Conclusion

A more favorable oral health behavior was observed among those with a stronger SOC suggesting that the SOC can be a determinant of oral health-related behaviors including tooth brushing frequency, daily smoking, dental attendance and sugar-intake frequency.

women & children's health research institute

Abstract #:	105
Presenter:	Abul Kalam Azad
Supervisor:	YangXin Fu
Title:	RUNX3 plays an oncogenic role in ovarian granulosa cell tumor (GCT) cells
Authors:	Abul Kalam Azad, Nidhi Gupta, Samir Barghout, Nubia Zepeda, Zhihua Xu, Michael Weinfeld, YangXin Fu
Affiliations:	University of Alberta
Research Activity:	Women's Health : Oncology
Investigation Type:	Mixed Methods

Introduction

Granulosa cell tumors of the ovary (GCTs) are the rare form of ovarian cancers which arise from sex cord-stromal cells. GCTs account for approximately 5% of all ovarian malignancies. There are two distinct subtypes of GCTs: the rare juvenile and the more common adult form. Although the prognosis is more favorable compared to the epithelial ovarian cancer, the advanced or recurrent tumors show poor diagnosis. Surgery is the predominant form of treatment. However, the viable treatment options are still limited for patients with advanced and recurrent GCTs. The molecular pathogenesis of GCTs remains poorly understood. Therefore, a better understanding of the molecular pathogenesis of GCTs will help us to develop more effective therapeutic strategies. RUNX3, a member of the RUNX family of transcription factors, regulates gene expression in a tissue-specific manner and plays either a tumor suppressing or an oncogenic role in a cancer-specific manner. Published work has shown that RUNX3 is an oncogene in epithelial ovarian cancer. It has been shown that *RUNX3* gene promoter is hypermethylated and the expression of RUNX3 is lost GCT cells. The objective of this project is to investigate whether RUNX3 plays a role in GCTs.

Methods

SVOG (immortalized granulosa cell line), KGN (adult human GCT cell line) and COV434 (juvenile GCT cell line) are used for the study. KGN and COV434 cells retain many characteristics of primary GCT cells. RUNX3 expression in these cell lines was examined by Western blotting. We stably overexpressed RUNX3 in KGN cells which lack expression of the endogenous RUNX3. Because COV434 cells express a high level of RUNX3, we inactivate RUNX3 in COV434 cells by overexpressing a dominant negative form of RUNX3 (dnRUNX3). Overexpression of RUNX3 and dnRUNX3 was confirmed by Western blotting. Cell growth, colony formation, and migration were measured by the neutral red uptake assay, the soft agar assay and the scratch assay, respectively.

Results

Overexpression of RUNX3 significantly increases proliferation, anchorage-independent growth in soft agar and migration of KGN cells. By contrast, inactivation of RUNX3 by overexpression of the dnRUNX3 reduces COV434 cell growth.

Conclusion

Our results suggest an oncogenic role of RUNX3 in GCTs.Ongoing work focuses on the molecular mechanism underlying these effects of RUNX3. In the future, we will determine whether RUNX3 expression affects the tumorigenicity of GCT cells using mouse xenograft models.

Funded By: Start-up or Retention Funding

women & children's health research institute

Abstract #:	106
Presenter:	Preethi Krishnan
Supervisor:	Sambasivarao Damaraju
Title:	Identification of microRNAs as prognostic markers for Breast Cancer
Authors:	Preethi Krishnan, Sunita Ghosh, Ashok Narasimhan, John Mackey, Olga Kovalchuk, Sambasivarao Damaraju
Affiliations:	University of Alberta
Research Activity:	Women's Health : Oncology
Investigation Type:	Quantitative Research

Introduction

Identifying optimal biomarkers for a subset of early stage breast cancer (BC) patients who may be at potential risk for recurrence of the disease is of paramount importance to guide therapeutic decisions. Implementing aggressive therapies long before the disease recurs may improve outcomes. Although ER, PR and HER2 currently provide prognostic value, these alone are not sufficient to identify those at risk since tumor heterogeneity (molecular and histological) and inter-individual variations to treatment response also contribute to treatment failure, leading to poor clinical outcomes (Overall survival, OS and Relapse Free Survival, RFS). MicroRNAs (18-25nt) are small non-coding RNAs, which regulate gene expression by either mRNA degradation or by translational repression and have shown promise as potential prognostic markers. We hypothesize that differential expression levels of miRNAs in tumors contribute to inter-individual variations in response to treatment and eventually outcomes. The objectives of the study are to identify prognostic miRNAs using next generation sequencing (NGS) platform.

Methods

Total RNA extracted from Formalin fixed paraffin embedded tissues of 104 tumor (Luminal A, n=74 and Triple Negative Breast Cancer (TNBC), n=30) samples were subjected to NGS (Illumina Genome Analyzer IIx) and analyzed using Partek Genomics Suite software 6.6. RNAs were filtered for low read counts and only those with a minimum of 10 read counts in at least 90% of the samples were retained (149 miRNAs). Cox's proportional hazards regression model (SAS9.3) was performed for univariate and multivariate analyses (adjusting for confounders) to identify prognostic miRNAs associated with outcomes. $p<0.05$ was considered to be statistically significant for all the analyses.

Results

25 miRNAs and 23 miRNAs were significant in univariate analysis for OS and RFS. hsa-miR-151a-3p (Hazard ratio, HR = 2.68), hsa-miR-181d-5p (HR = 0.313), hsa-miR-27a-3p (HR = 3.229), hsa-miR-363-3p (HR = 0.430) and hsa-miR-99b-5p (HR = 2.664) were found as potential independent prognostic factors for OS. hsa-miR-148b-3p (HR = 0.366), hsa-miR-181d-5p (HR = 0.406), hsa-miR-203a (HR = 0.379), hsa-miR-98-5p (HR = 5.493) and hsa-miR-99b-5p (HR = 3.290) were found as potential independent prognostic markers for RFS.

Conclusion

Except hsa-miR-27a-3p and hsa-miR-203a, other identified miRNAs have not yet been reported for BC prognostication. However, these miRNAs require further validation to ascertain their role as biomarkers.

Funded By: Canadian Breast Cancer Foundation

women & children's health research institute

Abstract #:	107
Presenter:	Mahalakshmi Kumaran
Supervisor:	Sambasivarao Damaraju
Title:	Germline copy number variations as genetic susceptibility determinants in sporadic breast cancer
Authors:	Mahalakshmi Kumaran, Ashok Narasimhan, Roland Hubaux, Sambasivarao Damaraju
Affiliations:	University of Alberta
Research Activity:	Women's Health : Oncology
Investigation Type:	Quantitative Research

Introduction

Breast cancer (BC) susceptibility has genetic and environmental components. While familial BC is explained by heritable high penetrant mutations in Breast Cancer (BRCA) and other moderate penetrant genes, genetic predisposition to sporadic BC is largely unexplored. Copy number variations (CNVs) are an important class of polymorphisms. CNVs cover larger regions of the genome, may harbor gene regulatory elements or may function through gene dosage. We hypothesize that CNVs explain the heritable basis for sporadic breast cancer risk in populations.

Methods

Whole genome CNV profiles from germline DNA were generated on Affymetrix SNP 6.0 arrays. Quality assurance steps were carried out using Golden Helix SVS 8. Eigenstrat method was adopted for correcting population stratification. CNV analysis was carried out using Partek genomics suite 6.6 (genomic segmentation algorithm) using HapMap 270 samples to create a reference baseline (diploid copy status). For Stage 1 of the study, we used samples from The Cancer Genome Atlas project (TCGA, 308 BC cases) and Welcome Trust Case Control Consortium (WTCCC, 408 controls). For stage 2 of the study, we used 348 BC cases and 348 controls (in-house). All study subjects are women of European ancestry. Chi-square tests for association were used with a cut-off p-value of 0.05 as significant. The study was approved by institutional ethics board.

Results

In Stage 1 and 2 samples, we detected a total of 224,986 and 260,627 CNVs, respectively and these were tested for association with BC. Statistically significant ($p<0.05$) associations were observed for structural aberrations (copy gains or copy loss regions). Total aberrations (gain + loss) were 32,466 and 7,827 in the two independent data sets, respectively. We also observed 4,076 CNV aberrations that are common between the samples sets from the two stages of the study and pathways involved in BC are being investigated (Gene Ontology Classifications). We observed 300 CNVs in Stage 1 study showing very high frequency gains in cases only relative to controls. We tested for these CNVs in Stage 2 study and found 29 CNV gains to be statistically significant indicating that the high frequency gains are indeed reproducible. The 29 CNV regions span the RET, CSMD1, KIT, FERD3L, MEGF11 genes and are reported in literature with functional roles in BC etiology.

Conclusion

The concordant CNV signatures from germline DNA in independent data sets reflect reproducibility and robustness of the identified associations. These signatures will be validated using qRT-PCR.

Funded By: Canadian Breast Cancer Foundation

women & children's health research institute

Abstract #:	108
Presenter:	Ray Amith
Supervisor:	Larry Fliegel
Title:	Deletion of the Na+/H+ exchanger NHE1 results in decreased invasiveness of MDA-MB-231 breast cancer cells
Authors:	S. Ray Amith, Jodi M. Wilkinson, Shairaz Baksh, Larry Fliegel
Affiliations:	University of Alberta
Research Activity:	Women's Health : Oncology
Investigation Type:	Quantitative Research

Introduction

The pH gradient in normal cells is controlled by the activity of various pH regulatory membrane proteins including the Na^+/H^+ exchanger, NHE1. NHE1 becomes constitutively active in neoplastic cells, dysregulating pH homeostasis and altering the survival, differentiation, and proliferation of cells, causing them to become tumorigenic. In breast cancer cells, cytoplasmic alkalinization as a result of NHE1 hyper-activity results in an acidic tumour microenvironment that facilitates aggressive cellular proliferation, migration, and invasion leading to tumour metastasis. The pathophysiological role of NHE1 in tumour progression is becoming clearer, however, the manipulation of pH homeostasis and proton dynamics in and around tumour cells has only recently been considered a strategy in augmenting cancer therapy.

Methods

To highlight the importance of NHE1 function, we generated an NHE1- knockout of the MDA-MB-231 breast cancer cell line for comparison with parental cells that endogenously express the exchanger. Endogenous NHE1 was excised using CompoZr® Knockout Zinc Finger Nucleases (Sigma). Potential knockout cells were screened using anti-NHE1 antibody and re-selected using a proton suicide treatment to generate the complete knockout (231-KO). In vitro: Proliferation was studied using MTT assays. Migration rates were a measure of time to gap closure in wound-healing assays. Boyden chamber and 3D-scaffold assays were used to guage cell invasion rates through a Matrigel matrix. In vivo: Xenograft tumour growth of both cell types in athymic nude mice was evaluated over 60 days.

Results

The NHE1-knockout cell line (231-KO) showed no demonstrable Na^+/H^+ exchange activity and no NHE1 expression in western blot analysis compared to parental MDA-MB-231 cells (231-WT). 231-KO cells had lower rates of proliferation, migration and invasion compared to 231-WT cells. The tumorigenic potential of the 231-KO cells was assessed by their ability to form xenografts in athymic nude mice over 60 days. 231-WT cells grew tumours over time while tumour growth of 231-KO cells was minimal or not at all.

Conclusion

Since pH regulation appears to play an integral role in breast cancer cell development, from neoplasia to metastasis, these data lend further credence to the importance of NHE1 as a potential target in breast cancer chemotherapy.

Supported by the Canadian Breast Cancer Foundation and WHCRI.

Funded By: Innovation Grant

women & children's health research institute

Abstract #:	109
Presenter:	Matthew Benesch
Supervisor:	David Brindley
Title:	Autotaxin inhibition suppresses inflammatory cytokine production in mammary adipose tissue and delays breast tumor growth and metastasis in mice
Authors:	Matthew Benesch, Xiaoyun Tang, Jay Dewald, Todd McMullen, David Brindley
Affiliations:	University of Alberta
Research Activity:	Women's Health : Oncology
Investigation Type:	Quantitative Research

Introduction

Breast cancer is the most common malignancy among women and one-third of patients die from metastases once their cancers become resistant to therapy. We provide evidence that the lipid growth factor, lysophosphatidate (LPA), contributes to this treatment failure. Extracellular LPA is produced by the secreted enzyme autotaxin (ATX). ATX is important in tissue remodeling and wound repair, but ATX is overproduced in many inflammatory diseases including cancers. LPA promotes cancer progression, metastasis and resistance to chemotherapy and radiotherapy. No treatment currently targets LPA signaling and this provides an opportunity for introducing novel cancer therapies.

Methods

Female BALB/c mice were injected in breast adipose tissue with 20,000 4T1 BALB/c breast cancer cells. Tumor growth was monitored with caliper measurements and by weighing once excised. ATX mRNA was quantified by RT-PCR and activity was measured. We evaluated the efficacy of ONO-8430506, a novel oral ATX inhibitor (Ono Pharmaceuticals, Japan) by daily gavage. LPA species in plasma and tumors were measured by mass spectrometry. Cytokines in plasma, tumors and mammary adipose tissue were measured by enzyme-linked immunofluorescence assay (ELISA).

Results

1) Breast adipose tissue expresses >10,000-fold more ATX mRNA than 4T1 breast cancer cells. Adipose tissue ATX activity was induced 3-fold more by the adjacent tumor compared to the contralateral unaffected breast. 2) ONO-8430506 decreased plasma ATX activity by >90%, and almost completely decreased unsaturated LPA concentrations in plasma and tumors. 3) Initial tumor growth and subsequent lung metastasis was decreased by about 60% by ONO-8430506. 4) ATX inhibition decreased tumor and systemic pro-inflammatory cytokine levels such as TNF-α. 5) TNF-α potently increases ATX secretion from breast fibroblasts, which produce the majority of ATX in the breast tumors.

Conclusion

This study demonstrates for the first time that inhibiting ATX activity decreases breast cancer progression. Breast cancer cells produce negligible ATX relative to mammary adipose tissue. Instead, our work presents a novel paradigm where breast cancer progression depends on inflammation-induced ATX production from fibroblasts in the tumor stroma and the surrounding fat pad rather than the cancer cells themselves. ATX inhibition provides a completely new therapeutic strategy for breaking this vicious cycle of inflammatory cytokine and LPA production, which drives breast tumor growth, treatment resistance and metastasis. We now hope to translate this work in a first in man trial for an ATX inhibitor.

Funded By: Support services

women & children's health research institute

Abstract #: 110
Presenter: Shyambabu Chaurasiya
Supervisor: Mary Hitt

Title: Examining the therapeutic potential of mutant vaccinia viruses for Breast Cancer Therapy

Authors: Shyambabu Chaurasiya, Nicole Favis, Kyle Potts, Chad Erwin, David Evans, Mary Hitt
Affiliations: University of Alberta

Research Activity: Women's Health : Oncology
Investigation Type: Qualitative Research

Introduction

Breast cancer (BrCa) continues to be one of the leading causes of deaths in women worldwide. Oncolytic viruses designed to selectively kill cancer cells, may emerge as an alternative treatment for BrCa. Vaccinia virus (VV), a large DNA virus, has a proven safety record in human from its use as a vaccine against smallpox. VV encodes more than 200 genes, some of which are involved in deoxyribonucleoside triphosphate (dNTP) synthesis. These genes are critical for replication of the virus in non-cycling normal cells which typically display low levels of dNTP synthesis. Deletion of these viral genes should impair virus replication in normal cells but not in cancer cells since cancer cells have high levels of dNTP synthesis. *F4L,* homologous to cellular *ribonucleotide reductase* (*R2*), is an important viral gene involved in dNTPs synthesis that could be deleted to restrict virus replication to cancer cells. We hypothesize that *F4L*-mutant VV will be able to replicate in and kill cancer cells with high levels of *R2* such as BrCa and it will be harmless to normal cells with low levels of *R2*.

Methods

Mutant VVs were generated by homologous recombination method. Plaque assay and alamar blue assay were used to determine viral titer and resulting cytotoxicity, respectively. *In vitro* specificity of the mutant viruses were studied in 2-dimensional and 3-dimensional (spheroid) cell culture using confocal microscopy. siRNA against *R2* was used to show the dependence of *F4L*-mutant on cellular *R2* levels. Syngeneic and xenograft model of BrCa in mice were used to test the safety and anti-tumor efficacy of the mutant viruses *in vivo*.

Results

Replication of *F4L*-mutant VV depends on the level of cellular *R2* which is elevated in BrCa cells. *In vitro F4L*-mutant VV replicates to high levels and kill BrCa cells while being relatively harmless to non- cancerous cells. In mice, the virus titer was found to be very high in tumor but was undetectable in normal organs (liver, lungs and spleen). Moreover, the virus was able to significantly delay the tumor progression and increase the overall survival of mice both in case of xenograft and syngeneic mice models of BrCa.

Conclusion

Results from our *in vitro* and *in vivo* experiments support the hypothesis that *F4L*-mutant VV specifically replicates in and kill BrCa cells. *F4L*-mutant VV, therefore, holds a promise to be tested in human for the treatment of BrCa.

Funded By: Trainee Travel Grant

women & children's health research institute

Abstract #: 111
Presenter: Powel Crosley
Supervisor: Mary Hitt
Title: Effective treatments for granulosa cell tumour: The potential of small molecule drugs
Authors: Powel Crosley, Kate Agopsowicz, Michael Weinfeld, Mary Hitt
Affiliations: Other
Research Activity: Women's Health : Oncology
Investigation Type: Quantitative Research

Introduction

Granulosa cell tumour (GCT) is an uncommon form of ovarian cancer, constituting ~5% of ovarian neoplasms. While typically diagnosed in early stage, with 5-year survival >90%, it is marked by late recurrence and an 80% mortality rate for women who relapse or have advanced disease. Evasion of apoptosis is one hallmark of cancer. Caspase-3 (CASP3) is at the hub of multiple apoptotic pathways and, when active, contributes to an irreversible cascade of protease activity leading to programmed cell death. X-linked inhibitor of apoptosis (XIAP) facilitates cell survival by inhibiting CASP3 permitting unchecked proliferation of cancer cells.

Targeted, small-molecule cancer therapies are drugs designed to interact with the enzymatic activity of proteins affecting tumour growth and progression. Traditional cytotoxic chemotherapies usually kill rapidly dividing cells in the body by interfering with cell division, while targeted therapies fight cancer cells with more precision and potentially fewer side effects.

Procaspase activating compound-1 (PAC1) is a small-molecule drug which induces cleavage of Procaspase-3 into active CASP3 by sequestering an inhibitory zinc ion. Embelin is a small, monovalent inhibitor of XIAP. This study reports on preliminary experiments testing our hypothesis that use of complementary, small-molecule drugs affecting the apoptotic pathway will result in increased killing of GCT cells, and may represent a novel therapeutic approach.

Methods

GCT cell line, KGN, was treated *in vitro* with various concentrations of PAC1, for selected time points, and evaluated for viability using a metabolic assay. High-content screening of similarly-treated cells was used to quantify PAC1 activation of CASP3-mediated apoptosis. KGN cells were then treated *in vitro* with selected concentrations of embelin to assess the effect of XIAP inhibition, and combined with 10 µM PAC1 to look for additive effect by combining these small-molecule drugs.

Results

Preliminary *in vitro* tests showed PAC1 induces significant cytotoxicity in KGN in both a dose and time-dependent manner (p<0.05) with an estimated effective concentration (EC50) of ~10 µM. High-content screening confirmed significant reduction in cell number and increased CASP3-mediated apoptosis in both a dose and time-dependent manner (p<0.05). Combination of 10 µM PAC1 with selected embelin concentrations produced significant increase in cytotoxicity in a dose-dependent manner (p<0.05).

Conclusion

These *in vitro* results support the hypothesis that combining small-molecule drugs to affect CASP3 activation and XIAP inhibition is potentially an effective, novel treatment for GCT that warrants further study.

Funded By: Innovation Grant

women & children's health research institute

Abstract #: 112
Presenter: Saima Hirani
Supervisor: Dr. Gerri Lasiuk
Title: Gender and the study of resilience: A critical review
Authors: Saima Hirani, Dr. Gerri Lasiuk, Dr. Kathleen Hegadoren
Affiliations: University of Alberta
Research Activity: Women's Health : Mental Health
Investigation Type:

Introduction

Resilience is an evolving construct that has a direct association with positive mental health as it enables individuals to adapt in rapidly changing or chaotic life circumstances. Although resilience has been the focus of study for almost a century, research in the area is fraught with definitional and methodological issues, making it difficult to compare research findings, perform meta-analyses, and operationalize and measure this important construct.

Purpose

The purpose of this critical literature review was to examine the hypothesis that current conceptualizations of and methods for measuring resilience lack sensitivity to gender, social, cultural, and environmental factors that shape women's experiences and their responses to adversity.

Method

A critical review aims to present, analyse and synthesize literature from diverse sources. Theoretical and research-based articles as well as books and chapters in edited books were located through electronic searches of CINAHL, MEDLINE, Science Direct, and PubMed. Search terms included a controlled vocabulary and free text phrases related to 'resilience', 'adaptability', 'psychological constructs similar to resilience', 'women', 'gender', and 'gender based analyses. Literature was included in the full review if it was published in the English language between 1979 and 2014 and its primary focus was resilience and women.

Results

The review discusses the origins of resilience and related constructs across several disciplines and traces its evolution to the present. The critical analysis of the literature reveals significant gaps in gender sensitivity and the theoretical and methodological approaches to defining and measuring resilience. Compared with men, women score lower on measures of resilience and coping; however, the literature does not address gender-related social and environmental experiences that may contribute to the observed differences. These gaps are problematic because they influence the quality of scientific knowledge and its practical implications for the health and well-being of women and their families. We argue that resilience cannot be understood in isolation from context because social and cultural influences play a critical role in determining women's capacity to address adversity.

Conclusion

Gender is a determinant of health and incorporating gender and other social dynamics into the conceptualization of resilience offers a coherent theoretical framework for conducting resilience research that will inform the development of effective interventions to promote women's health and well-being.

women & children's health research institute

Abstract #:	113
Presenter:	Elaine Hyshka
Supervisor:	T. Cameron Wild
Title:	The Royal Alexandra Hospital's addiction recovery and community health team: Addressing health inequities faced by women in Edmonton's inner city
Authors:	Elaine Hyshka, Ginetta Salvalaggio, John Budgell, Kathryn A Dong, Christopher McCabe, Rhonda Rosychuk, Shireen Surood, T. Cameron Wild
Affiliations:	Other
Research Activity:	Women's Health : Mental Health
Investigation Type:	Quantitative Research

Introduction

Many women living in Edmonton's inner city experience homelessness, unstable income, and/or problematic substance use, and are at increased risk for a host of negative health outcomes and repeat hospitalizations. Intimate partner violence, past histories of trauma, and participation in the sex trade can exacerbate these risks. Based at the Royal Alexandra Hospital and launched in July 2014, the Addiction Recovery and Community Health (ARCH) team attempts to mitigate health inequities faced by inner city women through an in-hospital consultation service and post-discharge transitional clinic that provides alcohol and drug withdrawal management, stabilizes and treats addictions, and provides harm reduction and sexual health services. Beyond medical services, the team assists patients with applying for housing and/or income support, transitioning to residential treatment programs, and connecting to primary care. A comprehensive outcome evaluation has been developed to measure the ARCH team's impact on patients' substance use and health and social outcomes, and generate knowledge on addressing health inequities in an acute care setting.

Methods

The ARCH patient outcome evaluation employs a pre-post quasi-experimental design. ARCH patients will be asked to provide informed consent allowing for collection of primary survey data, secondary administrative data, and data linkage. Surveys will be administered at baseline, 6 months, and 12 months; administrative data will be retrieved for 6 months prior to, and 12 months after enrolment. Outcomes of particular interest include 1) substance use stabilization or reduction; 2) uptake into housing and income support, 3) healthcare utilization; and 4) linkage to primary care and other community supports. Descriptive analyses and appropriate inferential statistical tests adjusted for covariates, will be performed on all outcome measures.

Results

ARCH launched its service in July 2014 and conducts approximately 19 patient consults weekly. Early program data suggest that ARCH patients have high rates of alcohol and other drug use, past histories of violence and trauma, and are engaged in a number of health risk behaviours. Study enrollment has commenced, and we will present preliminary baseline characteristics of our female sample (approximately 46%). Unique characteristics of female patients and the implications for clinical care and program outcomes will be discussed.

Conclusion

The ARCH program addresses health inequities faced by socially vulnerable women residing in Edmonton's inner city. Comprehensive characterization of this population will enable care providers and policymakers to improve acute care, better tailor community-based programs and services, and improve health and social outcomes.

Funded By: Support services

women & children's health research institute

Abstract #:	114
Presenter:	Katherine Wyper
Supervisor:	Jacqueline Pei
Title:	The use of alternative therapies at the 2nd Floor Women's Recovery Centre
Authors:	Katherine Wyper, Marnie Hutchison, Audrey McFarlane, Paula Dewan, Darlene Fader, Michele Huszar, Jacqueline Pei
Affiliations:	University of Alberta
Research Activity:	Women's Health : Mental Health
Investigation Type:	Mixed Methods

Introduction

The 2nd Floor Women's Recovery Centre is an innovative residential addictions treatment program delivered by the Lakeland Centre for Fetal Alcohol Spectrum Disorder in Cold Lake, Alberta. The program serves women who are pregnant (or who may be likely to become pregnant) and dealing with substance abuse issues. It is a long-term holistic program aimed at strengthening clients' physical, mental, spiritual, and emotional well-being. In addition to traditional programming such as individual counselling and group sessions, clients of the 2nd Floor are also offered a range of alternative therapies such as yoga, massage, reflexology, reiki, art therapy, meditation, and drumming. In this presentation we will share data from client feedback forms completed after each therapy session, as well as exit interviews completed at the end of their 2nd Floor stay.

Methods

The current study is a retrospective review of activity feedback forms and exit interviews completed by 2nd Floor clients between November 2013 and June 2014. Fifty-eight activity feedback forms and 11 exit interviews were reviewed and descriptive statistics were examined to identify the types of therapies accessed by clients, and client perceptions of these activities.

Results

The most frequently accessed alternative therapies were meditation, massage therapy, and reflexology. Clients reported the most positive feedback for massage therapy, drumming, art class, and iridology, and used a range of positive descriptors (e.g., stress relief, calm, peaceful) to characterize their experiences with these therapies. Importantly, on almost all (91.5%) of the feedback forms, women reported that they would like to participate in these alternative therapy activities again in the future. They also offered a variety of suggestions on what might enhance their experience with these activities, as well as other activities in which they would like to engage during treatment.

Conclusion

This study provides insight into innovative practices currently being delivered at the 2nd Floor Recovery Centre for women dealing with addictions. It highlights the positive experiences of clients at the 2nd Floor and sheds some light onto practices that may be particularly helpful when working with this group. This work is especially important in terms of maximizing our potential to support at-risk women before and/or during pregnancy, which ultimately leads to healthier mothers and babies.

women & children's health research institute

Abstract #: 115
Presenter: Sarah Elliott
Supervisor: Rhonda Bell
Title: Postpartum Calorimetry (PCAL) Study: Baseline anthropometric and body composition data
Authors: Sarah Elliott, Leticia Pereira, Emannuel Guigard, Linda McCargar, Rhonda Bell, Carla Prado
Affiliations: University of Alberta
Research Activity: Women's Health : Nutrition
Investigation Type: Qualitative Research

Introduction

Changes in body weight and composition in response to the energetic needs of the postpartum period, including lactation are variable among and within different populations. Differences in regional patterns of fat deposition (android/gynoid ratio) and mobilisation during lactation may contribute to varying levels of weight loss success following pregnancy. However, little is known about the trajectory of postpartum weight and regional fat patterning change. Here we present the baseline physical characteristics of women participating in the Postpartum Calorimetry (PCAL) Study. One aim of the PCAL study is to investigate changes in weight retention and body composition at three and nine month's postpartum.

Methods

Twelve women aged 31.8 ± 4.3 years have participated in the study thus far. Pre pregnancy age, height, weight, and gestational weight gain (GWG) were self-reported. Excess GWG was calculated as the difference between recommended (Health Canada 2010) and actual GWG. Anthropometric variables (height, weight and waist circumference) and body composition (via Dual energy X-ray absorptiometry [DXA]) were measured at three months postpartum. Three-day breast feeding diaries were used to estimate daily total duration of breastfeeding (minutes/day).

Results

Eight women (66 %) were exclusively breastfeeding at 14 ± 1 (12-15) weeks postpartum. Total duration of breastfeeding per day was 156 ± 68 minutes. Pre pregnancy body mass index (BMI) was 25.92 ± 6.91 kg/m^2 and BMI at three months postpartum was 27.86 ± 7.22 kg/m^2. Average body fat % and waist circumference were 40.6 ± 7.7 % and 87.3 ± 14 cm, respectively. The android/gynoid fat ratio was 0.89 ± 0.12. Average excess GWG was 3.5 ± 2.1 kg with 75% of women gaining more weight than recommended by Health Canada guidelines (2010). Weight retention at three months was 5.5 ± 2.7 kg. A significant inverse association between weight retention and duration of breastfeeding was observed ($r=-0.65$, $p=0.04$). Body fat percentage and the android/gynoid ratio was also significantly associated with weight retention ($r=0.65$, $p=0.04$; $r=0.70$, $p=0.02$, respectively).

Conclusion

These preliminary results suggest that women who breastfed for more time each day, retained less weight at three months postpartum. Women with an android fat distribution and a higher percent of body fat had retained more weight. Further data collection (at nine months postpartum) and analysis, will offer a greater understanding of the factors that impact maternal body composition and weight retention throughout the postpartum period.

Funded By: ENRICH Program Grant

Abstract #: 116
Presenter: Leticia C. R. Pereira
Supervisor: Linda J. McCargar
Title: Estimated energy costs of exclusive breastfeeding: Preliminary data from the Postpartum Calorimetry study
Authors: Leticia C. R. Pereira, Sarah A. Elliott, Linda J. McCargar, Emmanuel Guigard , Rhonda C. Bell, Carla M. Prado
Affiliations: University of Alberta
Research Activity: Women's Health : Nutrition
Investigation Type: Quantitative Research

Introduction

Postpartum energy requirements comprise those of the pre-pregnancy period, plus the additional demands for milk production and secretion. However, postpartum energy recommendations are based on observations made decades ago and may not be appropriate for contemporary women. The energy cost of lactation can be determined by the amount of milk produced and secreted, its energy content, and the efficiency with which dietary energy is converted to milk energy [1]. The objective of this sub-study is to present descriptive data on the energy cost of lactation in women at approximately three months postpartum. These data were collected as part of a longitudinal study of energy expenditure in postpartum women, the Postpartum Calorimetry (PCal) study.

Methods

Maternal and infant age, anthropometric variables, and breastfeeding practices were recorded. A 3-day breast-feeding diary and 1-day of infant test weighing assessed the milk volume produced/day. Infant test weighing estimates breastmilk production by weighing the infant before and after each breastfeeding episode on an electronic scale (BabyWeigh™ II Scale, Medela), precision of ± 2.0 g. The energy cost of lactation was calculated according to the WHO Human Energy Requirements Report [1], in which the milk volume produced/day was corrected for insensible water losses (5%); the energy content of human milk was assumed to be 0.67 Kcal/g; and an efficiency factor of 80% was applied.

Results

Eight of the 12 women enrolled in the PCal study were exclusively breastfeeding and provided complete data related to breastfeeding practices at 3 months postpartum. All infants were full term with a mean birth weight of 3,760 ± 551g. Data were collected when infants were aged 3.3 ± 0.2 months old. Women (n=8) were 31.5 ± 2.8 years old and had a body mass index of 27.9 ± 7.2 kg/m^2. Women nursed their infants 10 ± 3 times/day for an average of 18 ± 5 minutes/feeding episode. Mean milk volume produced was 766 ± 145 g/day, which equated to an estimated energy cost of 646 ± 122 kcal/day.

Conclusion

Breastfeeding is a significant component of total energy expenditure in the postpartum period. This information will be combined with information about total energy expenditure and energy mobilization from body stores and considered in light of present energy recommendations for postpartum women.

[1] WHO Human energy requirements. Report of a Joint FAO/WHO/UNU Expert Consultation. FAO Food and Nutrition Technical Report Series No. 1. Rome: Food and Agriculture Organization, 2004.

Funded By: AIHS

women & children's health research institute

Abstract #:	117
Presenter:	Sarah Lee
Supervisor:	Noreen Willows
Title:	A qualitative investigation of the experience of food insecurity among students with children who use the Campus Food Bank
Authors:	Sarah Lee, Geoff Ball, Anna Farmer, Noreen Willows
Affiliations:	University of Alberta
Research Activity:	Women's Health : Nutrition
Investigation Type:	Qualitative Research

Introduction

Food insecurity is the limited or uncertain availability of nutritionally adequate and safe foods or limited or uncertain ability to acquire acceptable foods in socially acceptable ways. The condition is associated with adverse nutritional and health outcomes. The University of Alberta (UAlberta) Campus Food Bank (CFB) provides students in need and their dependents with hampers containing a 4-day supply of non-perishable foods (e.g., canned and dried foods), and if available, perishable items (e.g., produce, dairy, bread). About one-fifth of students requesting food hampers have children living with them. The purpose of this qualitative descriptive study was to explore the experience of food insecurity among a purposive sample of students with children under 18 years of age who had received emergency food hampers from the UAlberta CFB during the 2013-2014 academic year.

Methods

Semi-structured face-to-face interviews were digitally recorded. Transcripts underwent conventional content analysis permitting codes and categories to be drawn from the data using participants own words.

Results

Nine participants (n=4 women, n=5 men) were interviewed. Several themes related to food insecurity. These were unexpected financial crisis, insufficient income or financial resources, inappropriate foods, time management, and negative academic outcomes. Coping strategies used to deal with food insecurity included borrowing money, lowering food quality and utilizing additional emergency food resources. Students protected their children from food insecurity by preferentially giving them foods higher in nutritional quality. Participants noted that they did not feel the food provided in the CFB food hamper was nutritionally adequate enough to meet the needs of their children. To overcome this perceived shortcoming parents would opt to serve their children store bought food if available while they consumed the food hamper items. Some students mentioned that their children did not like to eat the food provided in the food hamper due to unfamiliarity with food items. One participant mentioned that their children were concerned that some foods in the hampers were bad to eat because they were past their expiry date.

Conclusion

Some postsecondary students with children may be at risk of nutritional inadequacies and poor academic performance due to financial crises that lead to food insecurity. Students with children may jeopardize their own well-being as a result of consuming lower quality foods and going hungry to protect their children from hunger. Increasing financial resources, enhancing nutrition education and developing food assistance policies for post-secondary students with children may reduce food insecurity among this group.

women & children's health research institute

Abstract #: 118
Presenter: Ernst Hoppenbrouwers
Supervisor: Simon Urschel
Title: Functional echocardiography as non-invasive method to detect cardiac allograft vasculopathy in children post cardiac transplantation
Authors: Dr. Ernst Hoppenbrouwers, Dr. Nee Scze Khoo, Dr. Michael Kaestner, Dr. Simon Urschel
Affiliations: University Of Alberta
Research Activity: Pediatrics
Investigation Type:

Chronic allograft vasculopathy (CAV) in pediatric recipients after cardiac transplantation is the leading cause for late graft failure and death after more than one year post cardiac transplantation. Diagnostic assessment of CAV can be challenging since early detection is difficult and typical clinical signs are lacking. Routine echocardiography currently compares findings to the normal range of healthy hearts and therefore detects CAV only in advanced stages. Angiography is the standard diagnostic technique but is invasive and poses a risk to the coronaries and the vascular access site. Improved techniques such as intracoronary vascular ultrasound (IVUS) are not practical for younger children.

This study examines parameters of heart function derived from routine functional echocardiographic studies after cardiac transplantation that may detect and predict CAV earlier. A blinded, retrospective study of standardized echocardiographic studies performed on 30 pediatric heart transplant recipients is described. Echocardiographic measurements will be analyzed against angiographically determined CAV status. Statistical analysis will determine if standardized assessments of changes over time for each individual are helpful in the non-invasive detection of CAV. Functional echocardiographic tests expected to correlate to CAV such as increasing rigidity and diastolic dysfunction will be assessed with dimensional measurements, Tissue Doppler Imaging, isovolumetric relaxation and atrial ejection force calculations. We aim to compare longitudinal changes in functional echocardiography in patients with and without progressive CAV in order to define thresholds of individual change that correlate with development of graft vasculopathy in coronary angiogram. Generation of a score including the various parameters and validation of the score in a dataset including all transplanted patients for sensitivity, specificity and predictive value is planned. The ultimate goal is to develop a reliable non-invasive monitoring protocol for early detection of graft vasculopathy.

women & children's health research institute

Abstract #:	119
Presenter:	Mohamed Elgendi
Supervisor:	Ian Adatia
Title:	The voice of the heart: the heart sound signature of children with pulmonary artery hypertension
Authors:	Mohamed Elgendi, , Prashant Bobhate, Shreepal Jain, Long Guo, Jennifer Rutledge, Yashu Coe, Roger Zemp, Dale Schuurmans, Ian Adatia
Affiliations:	University of Alberta
Research Activity:	Child and Youth Development : Cardiology
Investigation Type:	Mixed Methods

Introduction (Purpose)

We hypothesized that vibrations created by the pulmonary circulation would create sound like the vocal cords during speech and that subjects with pulmonary artery hypertension (PAH) might have a unique sound signature.

Methods

We recorded heart sounds at the cardiac apex and 2nd left intercostal space (LICS) using a digital stethoscope from 27 subjects (12 males) with a median age of 7 years (range 3 months to 19 years) undergoing simultaneous cardiac catheterization. Thirteen subjects had a mean pulmonary artery pressure (mPAP) < 25 mmHg (range 8-24 mmHg). Fourteen subjects had a mPAP ≥ 25 mmHg (range 25-97 mmHg). We extracted the relative power of the frequency band,theentropy, and the energyofthesinusoid formants from the heart sounds. We applied linear discriminant analysis with leave-one-out cross-validation to differentiate children with and without PAH. The significance of the results was determined using a *t*-test and rank-sum test.

Results

The entropy of the first sinusoid formant contained within an optimized window length of 2 seconds of the heart sounds recorded at the 2nd LICS was decreased significantly in subjects with a mPAP ≥25 mmHg versus subjects with a mPAP < 25 mmHg with a sensitivity of 93% and specificity of 92%.

Conclusion

The reduced entropy of the first sinusoid formant of the heart sounds in children with PAH suggested the existence of an organized pattern. The analysis of this pattern revealed a unique sound signature, which could be applied to a non-invasive method to diagnose PAH.

Funded By: Cardiovascular CMERF for pulomnary hypertension

women & children's health research institute

Abstract #:	120
Presenter:	Lindsay Mills
Supervisor:	Nee Khoo
Title:	Premature infants have increased left ventricular twist from enhanced apical rotation and deformation
Authors:	Lindsay Mills, Etienne Fortin-Pellerin, Akiko Hirose, Winnie Savard, Lisa K Hornberger, Nee S Khoo
Affiliations:	University of Alberta
Research Activity:	Child and Youth Development : Cardiology
Investigation Type:	Quantitative Research

Introduction

Premature hearts have altered myocardial cellular prperties compared to term infant hearts. Preterm infants are exposed to higher afterload in the postnatal circulation relative to the fetal circulation for the same gestational maturity. In studies of pressure loaded ventricles, the left ventricle (LV) has been observed to compensate by augmenting twist to improve ejection. We sought to determine if preterm infants have different LV twist mechanics compared to postnatal age-matched term infants.

Methods

Echocardiograms were prospectively performed on 30 healthy preterm (gestational age (GA) at birth 27.8 ±1.9 weeks) and 28 healthy term (> 37 weeks GA) infants at a mean chronological age of 29 ±7 days. Frame rate optimized LV basal and apical parasternal short-axis echocardiography images were analyzed by speckle-tracking imaging on Echopacs software. Circumferential strain and strain rate (SR), peak rotation and rotation rate, twist and twisting rates were recorded. Time to peak for each parameter was normalized to the systolic interval and expressed as a percentage of systole. Untwist performance in diastole was determined as a ratio of the twist value at 110%, 120%, and 130% of systole compared to the peak twist value.

Results

Preterm infants had similar mean blood pressure, but slightly higher heart rates compared to term infants (mean 152 vs. term 142, p=0.013). There was increased peak twist in preterm infants (mean 13.1 ± 4.6 º vs. term 10.4 ± 4.2º, p= 0.029). Basal peak rotation was not different, however the apical peak rotation was significantly higher in preterms (mean 7.59 ± 3.5º vs. term 5.2 ± 2.5º, p=0.006). Premature infants' apical peak systolic strain (mean -24.2 ± 7.1% vs. term -20.0 ± 5.4 %, p=0.016), peak systolic SR (p=0.035), as well as early diastolic SR (p=0.023) and late diastolic SR (p<0.001) were all greater than term infants. The untwist performance at 110%, 120% and 130% of systole were not different, although the peak untwisting rate (mean -205 ± -58º /sec vs. term -174 ± -69º /sec, p=0.079) and the untwisting rate at mitral valve opening (p=0.073) trended towards greater values in preterm infants. Both groups had similar rotational deformation delay between the base and the apex and there was no difference in the time to peak twist or peak untwist rate.

Conclusion

Preterm infants have greater LV peak twist, generated through increased apical rotation and deformation. This enhanced LV twist may represent a compensatory mechanism in premature hearts adapting to the demands of the relative increase in afterload of the postnatal circulation for their gestational maturity.

Funded By: Innovation Grant

women & children's health research institute

Abstract #:	121
Presenter:	Tarek Kaddoura
Supervisor:	Dr. Ian Adatia
Title:	Automated measurement of electro-mechanical activation time differentiates pulmonary hypertensive patients with and without right ventricular failure
Authors:	Tarek Kaddoura, Prashant Bobhate, Mohammed Elgendi, Long Guo, Shreepal Jain, Shine Kumar, James Coe, Dale Schuurmans, Roger Zemp, Ian Adatia
Affiliations:	University of Alberta
Research Activity:	Child and Youth Development : Cardiology
Investigation Type:	Mixed Methods

Introduction

Electromechanical activation time (EMAT), defined as the time between onset of the QRS complex and the first heart sound (S1), is prolonged in patients with left ventricular dysfunction. However EMAT has not been studied in right ventricular failure. We sought to investigate EMAT in patients with pulmonary hypertension and right ventricular failure.

Methods

Heart sounds were recorded from the tricuspid area with an external phonocardiogram simultaneously with the electrocardiogram (EKG) and pulmonary artery (PA) pressure in patients in sinus rhythm with mean PA pressure ≥ 25 mmHg undergoing right heart catheterization. Right ventricular fractional area change (RVFAC) was calculated from an echocardiogram within 3 months of the cardiac catheterization. EMAT was automatically calculated using Matlab (2011, Massachusetts USA) as a mean of EMAT recorded over 20 seconds.

Results

43 patients met inclusion criteria for the study. Accurate automated analysis of EMAT were possible in 28/43 (65%) patients. Subjects had a median age of 45 yrs (0.4-45) and median body surface area (BSA) of 1.6 m^2. There were 17 female and 11 male subjects. Seven of 28 patients had severe right ventricular dysfunction (RVFAC<25%). Hemodynamics in patients with RVFAC<25% were comparable to those with normal RV function: median values were mean PA pressure of 31 mmHg (range 25-60) vs 29 mmHg (25-40) (p=0.1), mean PA wedge pressure 15 mmHg vs 11 mmHg (p=0.1), mean aortic pressure 77 mmHg (38-111) vs 90 mmHg (36-108) (p = 0.09) and cardiac index 2.8 L/min/m^2 (2-5.4) vs 3.4 L/min/m^2 (1.8-3.6) (p=0.8). The median EMAT was significantly prolonged in patients with severe RV dysfunction (RVFAC<25%) compared with subjects with normal right ventricular function [113 msec (91-165) vs 68 msec (31-110)], p<0.001.

Conclusion

EMAT differentiates patients with PH and severe RV dysfunction. Automated measurement of EMAT could be developed as a clinical tool to detect RV dysfunction.

Funded By: CMREF for Pulmonary Hypertension

women & children's health research institute

Abstract #:	122
Presenter:	Santokh Dhillon
Supervisor:	Lisa K Hornberger
Title:	Myocardial mechanics of the systemic right ventricle in hypoplastic left heart syndrome through the perinatal transition
Authors:	Santokh Dhillon, Akiko Hirose, Nee Khoo, Lindsay Mills, Tim Colen, Winnie Savard, Po-Yin Cheung, Lisa K Hornberger
Affiliations:	University of Alberta
Research Activity:	Child and Youth Development : Cardiology
Investigation Type:	Quantitative Research

Introduction

Rapid changes occur in myocardial loading during the transition from the fetal to postnatal circulation. In healthy neonates, the LV output almost doubles within hours of delivery but decreases to levels slightly higher than the fetal LV output within the first few days. In contrast, we have found in Hypoplastic left heart syndrome (HLHS) the combined cardiac output (CO) is initially similar to that of the late gestation fetus with a gradual but progressive increase occurring within the first 3-5 days. We sought to define the functional changes of the systemic right ventricle (RV) during the perinatal transition in the neonate with HLHS.

Methods

We prospectively recruited 11 pregnancies with fetal HLHS. Echocardiograms were performed in late gestation and at 4 -12, 20-24, 44-48 hours (hrs) and 3-5 days after birth. Hemodynamics including stroke volume (SV), heart rate (HR), CO, blood pressure (BP), and RV size and fractional area change (FAC) were measured. High frame rate images were used for offline strain and strain rate (SR) analysis using speckle tracking. ANOVA with repeated measures and paired t-test for parameters and Pearson's correlations were used.

Results

In the first 24 hrs, CO increased ($p=0.03$) which was accompanied by an increase in RV longitudinal strain ($p=0.03$). From 24 hrs to 5 days, although CO and SV continued to increase ($p<0.001$ for both) along with progressive increase in RV end diastolic size ($p<0.002$), no further increase in longitudinal strain and SR was observed. There was no change in HR, systolic BP or RV FAC between intervals. Longitudinal strain and SR correlated with CO ($r=-0.44$; $p=0.007$ & $r=-0.60$; $p=0.0001$ respectively) and SV ($r=-0.46$; $p=0.004$ & $r=-0.55$; $p=0.0006$ respectively). Longitudinal SR also correlated with RV FAC ($r=-0.40$; $p=0.01$) and RVEDV ($r=0.37$; $p=0.02$).

Conclusion

The RV in neonatal HLHS appears to compensate by initially increasing its longitudinal deformation in the first 24 hrs to meet the postnatal circulatory demands. Thereafter, subsequent increase in CO relies on increasing SV through progressive increase in ventricular preload. Further studies using deformation imaging are needed to explore RV adaptation in early transition in HLHS neonates and its implication on management and outcome.

Funded By: CIHR

women & children's health research institute

Abstract #:	123
Presenter:	Rebecca Peat
Supervisor:	Gary Lopaschuk
Title:	Role of protein succinylation in the regulation of energy metablism in the newborn heart.
Authors:	Rebecca Peat, Osama Abo Alrob, Cory Wagg, Gary Lopaschuk
Affiliations:	University of Alberta
Research Activity:	Child and Youth Development : Cardiology
Investigation Type:	Quantitative Research

Background

Dramatic cardiac developmental changes in energy metabolism occur in the neonate, which includes a shift from glycolytic to mitochondrial oxidative metabolism in the heart shortly after birth. Lysine succinylation has recently been identified as a potentially important pathway involved in the control of energy metabolism. However, the role of lysine succinylation in regulating the dramatic changes in energy metabolism in the newborn heart is not clear. Therefore, we investigated the role of changes in protein succinylation in the maturational changes in energy metabolism in the newborn rabbit heart.

Methods

1-day, 7-day, and 21-day old rabbit hearts were perfused with Krebs-Henseleit solution (containing 2.5 mM Ca2+, 5 mM glucose, 0.4 mM palmitate, 3% albumin, 1 mM lactate, and 100 µU/mL insulin). The palmitate, glucose, and lactate were appropriately radiolabeled in order to measure glycolysis, and the oxidation of fatty acids, glucose, and lactate. At the end of the perfusion, hearts were immediately frozen in liquid N2 and processed for succinylation status.

Results

Cardiac fatty acid β-oxidation rates were significantly increased in 21-day vs 1-day and 7-day old rabbits (555±26, 299±10 and 364±24 nmol.g dry wt-1.min-1, respectively, $p<0.05$) Overall succinylation was increased in 21-day vs 1-day and 7-day old rabbits. Expression of the mitochondrial desuccinylase, SIRT5, did not change. The activity of the major fatty acid β-oxidation enzymes, β-hydroxyacyl CoA dehydrogenase (β-HAD) and long chain acyl CoA dehydrogenase (LCAD) was decreased in hearts from 21-day vs 1-day and 7-day old rabbits. Despite the increase in overall succinylation, the succinylation of the fatty acid β-oxidation enzymes, β-hydroxyacyl CoA dehydrogenase (β-HAD) and long chain acyl CoA dehydrogenase (LCAD) was decreased in hearts from 21-day vs 1-day and 7-day old rabbits.

Conclusion

We conclude that alterations in lysine succinylation contribute to the increase in cardiac fatty acid β-oxidation and the low carbohydrate metabolism in the newborn period.

Funded By: Summer Studentship

women & children's health research institute

Abstract #:	124
Presenter:	Amin Shah
Supervisor:	Sandra Davidge
Title:	Effect of resveratrol on cardiovascular and metabolic function in intrauterine growth restricted male and female rats on a high-fat diet
Authors:	Amin Shah, Laura Reyes, Jude Morton, Sandra Davidge
Affiliations:	University of Alberta
Research Activity:	Child and Youth Development : Cardiology
Investigation Type:	Quantitative Research

Introduction

Cardiovascular diseases cause the greatest mortality in the world today. Fetal hypoxia, leading to intrauterine growth restriction (IUGR), is one of the most common consequences of complicated pregnancies worldwide. Our laboratory observed that IUGR male rat offspring are more susceptible to develop metabolic and cardiovascular disorders in later life. In the early stages of life, consumption of a high-fat (HF) diet has been shown to exacerbate these adverse effects. Resveratrol (Resv), a polyphenol found in grape skin, has been shown to protect against cardiovascular and metabolic disease in mice on a HF diet. Our laboratory has shown that Resv treatment in IUGR male rat offspring prevented or reduced the observed cardiovascular and metabolic dysfunction. However, mechanism of Resv action for cardioprotection is unclear and the impact on female offspring has not been assessed. We hypothesized that Resv treatment will also prevent the deleterious cardiovascular and metabolic effects in female IUGR offspring exposed to a HF diet.

Methods

Male and female, control or IUGR rat offspring (created by exposing pregnant dams to hypoxia, 11.0±0.5% O_2, for the last third of pregnancy) were randomly assigned to receive a HF diet or a HF diet supplemented with Resv (4g/kg of diet) from 3-12 weeks of age. Metabolic parameters were assessed using a glucose tolerance test and echo MRI, and cardiac susceptibility to ischemia/reperfusion (I/R) injury was assessed using a Langendorff heart system.

Results

Resv did not affect body weight gain, energy intake or body composition in male and female IUGR offspring. We did not observe any changes in glucose tolerance in female offspring, however, it was impaired in male IUGR offspring and improved by Resv treatment. In both male and female IUGR offspring, cardiac function recovery after I/R injury was decreased and Resv improved the cardiac function recovery in both sexes.

Conclusion

Prenatal hypoxia and postnatal HF diet impaired cardiac function in female offspring; however both cardiac and metabolic functions are impaired in male IUGR offspring. Postnatal Resv supplementation improved metabolic function in male IUGR offspring and prevented cardiac dysfunction after I/R injury in both male and female IUGR. These studies will ultimately lead to early intervention strategies to reduce cardiovascular risk in the susceptible population.

Funded By: Start-up or Retention Funding

women & children's health research institute

Abstract #:	125
Presenter:	Vanessa Lam
Supervisor:	Michael van Manen
Title:	Retrospective review of death in the NICU
Authors:	Vanessa Lam, Nicole Kain, Chloe Joynt
Affiliations:	University of Alberta
Research Activity:	Other
Investigation Type:	Quantitative Research

Introduction

In Canada the majority of infant deaths occur in level III neonatal intensive care units (NICUs). Although research has been conducted describing health practitioner and patient-family perspectives of end-of-life care and decision-making, there is a paucity of research actually describing neonatal palliative care. The purpose of this study was to obtain a pragmatic description of how palliative care unfolds at the bedside in the NICU.

Methods

We completed a retrospective chart review using a structured, data gathering tool of all deaths occurring under level III NICU-led care from January 2009 to December 2013 in Edmonton, Alberta. We excluded case-room deaths as well as deaths occurring outside of the NICU in the home or hospital ward.

Results

In total, we identified 227 level III NICU deaths. Median gestational age and birth weight was 29weeks and 1375g respectively. The most common reasons for admission included: prematurity (54.2%), prematurity with congenital anomaly/syndrome (18.1%), term congenital anomaly (11.5%), and hypoxic ischemic encephalopathy (12.8%). Median age at death was 7days. Death tended to follow a decision to withdraw medical treatments while the babies were held by their family members in the NICU or in a parent room off cardiorespiratory monitors. Median time to death following withdrawal of life sustaining medical treatments was 53minutes. After withdrawal, medications and intravenous fluids were variably continued. New medications were rarely initiated. Autopsy was uncommonly pursued.

Conclusion

Death in the NICU tends to occur following a decision to withdrawal life sustaining medical treatments. Death following withdrawal generally is not a protracted event. Medical treatments are inconsistently provided following withdrawal.

Funded By: Start-up or Retention Funding

women & children's health research institute

Abstract #:	126
Presenter:	Laura Reyes
Supervisor:	Sandra Davidge
Title:	The effect of aerobic exercise training in the femoral arteries from intrauterine growth restricted offspring.
Authors:	Laura Reyes, Jude Morton, Raven Kirschenman, Sandra Davidge
Affiliations:	University of Alberta
Research Activity:	Maternal Research : Fetal Origins of Adult Disease
Investigation Type:	Quantitative Research

Introduction

Fetal hypoxia is one of the most common consequences of complicated pregnancies worldwide. We have demonstrated that prenatal hypoxia leads to intrauterine growth restriction (IUGR) and impairs later-life endothelial-dependent vascular function, demonstrating that fetal environment during early development is important for cardiovascular health. Alterations in the balance between nitric oxide (NO), endothelial-dependent hyperpolarization (EDH) and prostaglandins results in endothelial dysfunction. Early interventions are needed to ultimately reduce later life risk for cardiovascular disease. We tested whether aerobic exercise prevents IUGR-induced endothelial dysfunction. We hypothesized that aerobic exercise training would improve vascular function in IUGR offspring by increasing NO bioavailability.

Methods

Pregnant Sprague-Dawley rats were exposed to control (21% oxygen) or hypoxia (11% oxygen) conditions from gestational day 15 to 21. Male and female offspring from normoxic (control) and hypoxic (IUGR) pregnancies were randomized at 10 weeks of age to either an exercise-trained or sedentary group. After acclimatization, rats ran on a treadmill for 6 weeks; 5 consecutive days/week, 30 min/day at 20 m/min. After a recovery period of 24 hours, animals were euthanized and second order femoral arteries were mounted on a wire myograph. Cumulative concentration response curves to methacholine were performed in the absence or presence of the NO synthase inhibitor (L-NAME, 100µM), a combination of Apamin (0.1 µM) and TRAM-34 (100 µM) to block SK_{Ca} and IK_{Ca} channels, or indomethacin (5 µM), a cyclooxygenase inhibitor.

Results

In sedentary males, NO ($p<0.01$) and EDH ($p<0.05$) contributed to vasodilation in control but not IUGR offspring. Exercise increased EDH-mediated vasodilation (11.9 ±32.7 vs. 142.5 ± 20.5 delta change area under the curve [AUC], $p<0.05$) and enhanced prostaglandin-mediated vasoconstriction in male IUGR offspring ($p<0.01$). Being born growth restricted was associated with impaired maximal vasodilator capacity in female offspring (93.1 ± 0.3% vs. 77.6 ± 6.8% E_{max}, $p=0.02$). In sedentary IUGR female offspring, the NO component of vasodilation was abolished and only EDH contributed to vasodilation ($p<0.01$). Exercise increased a prostaglandin-mediated vasoconstriction in female IUGR offspring (61.5 ± 17.1 vs. -30.1 ± 19.9 delta change AUC, $p=0.002$) and decreased NO-mediated vasodilation (123.7± 14.2 vs. 65.8 ± 14.2 delta change AUC, $p=0.007$).

Conclusion

The results from the present study highlight that understanding the mechanisms by which exercise impacts the cardiovascular system in a susceptible population, and the consideration of sexual dimorphism is essential. Exercise may not prove to be a beneficial therapy for specific vascular pathways affected by prenatal insults, particularly in female offspring.

Funded By: Start-up or Retention Funding

women & children's health research institute

Abstract #:	127
Presenter:	Nikytha Antony
Supervisor:	Joanna MacLean
Title:	Effects of preterm birth and bronchopulmonary dysplasia on asthma presentation in middle childhood.
Authors:	Nikytha Antony, Joanna MacLean
Affiliations:	University of Alberta
Research Activity:	Child and Youth Development : Sleep and Breathing Disorders
Investigation Type:	Qualitative Research

Introduction

Bronchopulmonary dysplasia (BPD) is one of the common complications of preterm birth. It is characterized by inflammation and scarring of the lungs due to barotrauma, and hyperoxia that is administered to the preterm infant to aid in their pulmonary needs. Preterm children with BPD are more likely to have respiratory symptoms such as coughing and wheezing and use asthma medications compared to preterm children without BPD in middle childhood. The aim of this study was to determine whether the pathophysiology of asthma is similar in preterm and term born children. We hypothesize that the BPD will complicate the pathophysiology of asthma, change the asthma symptom profile and reduce the quality of life of the patients more severely compared to both preterm children without BPD and term born children.

Methods

We recruited children 7-15 years of age born extremely preterm (<28 weeks) and term born children. Pulmonary function tests and cardiopulmonary exercise tests were done to assess lung health while questionnaires were given to both parent and child to assess general health, respiratory symptoms, activity and quality of life.

Results

We studied 168 children who were born either preterm with BPD (n=50), preterm without BPD (n=52) or at term (n=60) with significant differences in asthma prevalence across these groups (26%, 24%, 9%, chi-square 6.62, $p<0.05$). Among the three groups, preterm children with BPD had the highest incidences of wheezing and hospitalizations since birth for respiratory illnesses. For those children with asthma across these 3 groups, family history of asthma, maternal smoking during pregnancy, household smoking, and history of wheeze were comparable as were measurements of lung function. History of allergies and eczema, hospitalizations due to respiratory illnesses, and shortness of breath during activity showed the highest associations with asthma. BPD and family history of asthma were not strongly associated with asthma prevalence in our cohort.

Conclusion

These results suggest that while rates of asthma are higher in preterm children, the pathophysiology of asthma is similar to term born children. The children with asthma in all three groups report similar values in the quality of life variables, asthma symptoms and have very similar pulmonary function test and cardiopulmonary test values. This suggests that changes in lung health in our cohort are attributable to the consequences of preterm birth and BPD rather than a difference in asthma presentation.

Funded By: Summer Studentship

women & children's health research institute

Abstract #: 128
Presenter: Megan Fowler
Supervisor: Dawn Hartfield
Title: Spontaneous Pneumothorax in Children: Examining the Epidemiology and Etiology
Authors: Megan Fowler, Dawn Hartfield, Manisha Witmans, Bryan Dicken, Ambikaipakan Senthilselvan
Affiliations: University Of Alberta
Research Activity: Pediatrics
Investigation Type:

Introduction:

Spontaneous pneumothorax (SP) in the pediatric population can be a serious and sometimes a life-threatening event, especially in asthmatic patients. SP does not commonly occur in the pediatric population and there are very few studies examining the epidemiology and etiology of primary and secondary SP. The goal of this study is to describe the epidemiology and etiology of primary SP and secondary SP in children with asthma. In addition, we also want to assess and describe the prevalance of poorly controlled asthma, a history of allergies and/or anaphylaxis and use of certain asthma medications in asthmatic children with secondary SP. Lastly, we hope to identify any risk factors for recurrence of SP in children.

Methods:

This study will be a retrospective chart review of patients between the ages of 1 month to 17 years admitted to the Stollery Children's Hospital between April 2002 to January 2013 with spontaneous pneumothorax.

Results:

We are currently in the process of completing our chart review, therefore, we do not have any results to date.

Conclusion:

We hypothesize that: 1) primary SP will typically affect adolescent males with below average BMIs, 2) secondary SP will affect a younger age group in asthmatic patients, when compared to non-asthmatics and a similar male predominance in the asthmatic group, 3) poorly controlled asthma, history of allergy and anaphylaxis, and non-compliance with medication will be risk factors for recurrence of secondary SP in asthmatic children.

Funded By: Resident Trainee Grant

women & children's health research institute

Abstract #:	129
Presenter:	Ann L. Revill
Supervisor:	Gregory D. Funk
Title:	Muscarinic modulation of persistent inward currents in motoneurons that control airway patency
Authors:	Nathan Chu, Ann L. Revill, Gregory D. Funk
Affiliations:	University of Alberta
Research Activity:	Child and Youth Development : Sleep and Breathing Disorders
Investigation Type:	Quantitative Research

Introduction

Obstructive sleep apnea (OSA) is characterized by repeated upper airway obstructions and apneas (periods of no airflow) during sleep despite ongoing central respiratory efforts. It is increasingly prevalent among children (~5%). A major factor in OSA is low hypoglossal motoneuron (XII MN) excitability, which leads to decreased airway muscle tone, increased risk of airway collapse and apnea. Reduced MN excitability in sleep results from a fall in excitatory modulators and an increase inhibitory modulators. Recent data suggest that during sleep acetylcholine (ACh) levels increase and that this reduces XII MN excitability by activating muscarinic receptors (mAChRs). The ion channel target(s) of mAChRs are not known. Our objectives were therefore to test the hypotheses that mAChRs modulate persistent inward currents (PICs; currents that amplify synaptic inputs and greatly increase excitability) in XII MNs and that this effect changes developmentally.

Methods

Medullary slices were generated from neonatal (0-3 days old) and juvenile (14-17 days old) rats. XII MNs were voltage-clamped at -65 mV and triangular voltage ramps (-80 to 0 to -80 mV, 14 mV/s) were applied in control and during bath application of the mAchR agonist, muscarine (25 µM) to the measure the PIC.

Results

Muscarine significantly attenuated the PIC in neonates (-224 ± 26 to -197 ± 25 pA, $n = 8$, $p < 0.001$), but had no effect in juveniles (-442 ± 78 to -494 ± 58 pA, $n = 6$, $p > 0.05$). Neither MN input resistance nor the voltage onset of the PIC were affected by muscarine.

Conclusion

These data suggest that mAChR activation inhibits the PIC and depresses XII MN excitability in neonates but not juveniles. If ACh levels rise during sleep in human as in rat, mAChR-mediated inhibition of PICs may play a role in OSA, particularly in children.

Funded By: Summer Studentship

women & children's health research institute

Abstract #:	130
Presenter:	Andre Isaac
Supervisor:	Hamdy El-Hakim
Title:	The correlation between Acoustic Rhinometry, subjective symptoms and endoscopic findings in symptomatic children with nasal obstruction
Authors:	Andre Isaac, Michael Major, Manisha Witmans, Yaser Alrajhi, Mohamed Korayem, Carlos Flores-Mir, Paul Major, Hamdy El-Hakim
Affiliations:	University of Alberta
Research Activity:	Child and Youth Development : Sleep and Breathing Disorders
Investigation Type:	Quantitative Research

Purpose

To explore the correlation between acoustic rhinometry (AR), subjective symptoms, and endoscopic findings in children presenting with nasal obstruction.

Methods

We conducted a cross-sectional diagnostic study over a two-year period. Eligible patients included non-syndromic children ≥ 7 years of age, presenting with persistent nasal obstruction. The children were all assessed on the same day by the otolaryngologist, orthodontist, and pulmonologist. We collected demographics, subjective nasal obstruction scored on a visual analogue scale (VAS), information on allergic rhinitis, and asthma. The adenoid size, septal position, and visual severity of chronic rhinitis (endoscopic rhinitis score, or ERS) were rated on nasal endoscopy by two independent reviewers. AR was undertaken before and after use of a decongestant. Correlation and multiple regression analyses were performed to explore interrelationships between VAS, AR and nasal endoscopy.

Results

65 children were included in the study (38 boys), with a mean age 10.3 ± 2.5 years (7-14 years). 14 had allergic rhinitis, and 10 had asthma. Significant correlations were found between VAS and ERS ($r = -0.364$, $p=0.003$), ERS and minimal cross sectional area pre-decongestion ($r=-0.278$, $p=0.03$), and adenoid size and calculated nasal resistance post-decongestion ($r=0.430$, $p<0.01$). Multiple regression analysis showed that the ERS was the only significant predictor of VAS (B of -22.089, $p= 0.002$, 95% CI -35.56 to -8.61). No predictors were identified for AR variables.

Conclusion

Among the evaluated tools, endoscopy appears to be the most reliable tool to estimate the degree of subjective nasal symptoms.

women & children's health research institute

Abstract #: 131
Presenter: Allison Carroll
Supervisor: Piush Mandhane

Title: 3D modeled custom-made non-invasive positive pressure mask in an infant

Authors: Allison Carroll, Israel Amirav, Roger Marchand, Deb Olmstead, Carina Majaesic, Joanna MacLean, Piush Mandhane
Affiliations: University of Alberta

Research Activity: Child and Youth Development : Sleep and Breathing Disorders
Investigation Type:

Introduction

Often, commercially available non-invasive positive pressure ventilation (NIPPV) masks are ineffective at certain stages of infant and child growth due to discomfort, poor seal or intermittent nasal obstruction. Custom-made masks may have higher utility in infants or patients with craniofacial abnormalities who have poor fit with standard masks. We explored the use of three-dimensional (3D) camera face image acquisition and 3D printer rapid prototyping procedures to produce customizable NIPPV masks.

Case

A 2 month old male, weighing 3.5 kg with trisomy 21 and complex congenital heart disease required a central aortopulmonary shunt to allow growth before complete repair of his underlying cardiac defect. The infant returned to hospital after discharge with worsening stridor and increased work of breathing. Bronchoscopy showed pulsatile narrowing of the trachea and CT angiography confirmed vascular impingement with 50% tracheal compression. High flow nasal cannula relieved the stridor. Surgical plan was to proceed with complete cardiac repair at 5 kg. Continuous positive airway pressure (CPAP) NIPPV was explored to facilitate discharge home until the patient reached goal weight. Standard outpatient commercial masks were not tolerated because of discomfort and nasal obstruction.

Methods

Four stage development of a custom mask:

1. 3D facial photography to determine optimal mask dimension based on the child's facial morphology.
2. Modification of stereolithographic (STL) files of a commercially available mask using the infant's facial morphology.
3. Produce a rapid prototype (RP) of the mask using a 3D printer to establish optimal mask fit.
4. RP to develop a mold to produce a final mask using medical grade silicone.

Results

Facial data acquisition was performed at the bedside using topographic 3D photography. A STL file of a standard infant NIPPV nasal interface was input to computer-assisted design (CAD) software and the 3D facial imaging was subtracted from the mask. A RP was developed using an Objet Eden 350v 3D printer to test fit on the patient. A negative image mold was created using 3D printing and a medical grade silicone mask was produced.

Conclusion

Nasal NIPPV interfaces are important in ensuring efficacy and compliance with positive pressure regimes. Development of custom techniques for NIPPV masks may allow for improved delivery of NIPPV in a number of populations. Future direction includes laboratory comparison of air leak in custom and industry standard masks, qualitative analysis of important features of mask fit and compliance and a clinical trial of custom NIPPV masks in children.

Funded By: Trainee Research Grant

women & children's health research institute

Abstract #:	132
Presenter:	Maria Castro Codesal
Supervisor:	Joanna MacLean
Title:	Long- term noninvasive ventilation in children in Alberta (2002-2014): Trends of the Home Ventilation Program in Edmonton
Authors:	Maria Castro Codesal, Prabh Bedi, Kassi Shave, Joanna MacLean
Affiliations:	University of Alberta
Research Activity:	Child and Youth Development : Sleep and Breathing Disorders
Investigation Type:	Quantitative Research

Introduction

Long-term non-invasive ventilation (NIV) in children is an increasingly common modality of breathing support where pressure is provided through a mask interface. Rates of long-term NIV in children have increased worldwide but there is no data on the trends in Alberta. The aim of this study is to describe the longitudinal trends of the home NIV program at the Stollery Children's Hospital, Edmonton, over the last 12 years.

Methods

The study design is a retrospective chart review of all children receiving NIV for ≥3 months and cared for through the NIV clinic at the Stollery. Outpatient medical charts and sleep laboratory records were reviewed. Data was subdivided into three 4-year epochs, 2003-2006, 2007-2010, and 2011-2014. Descriptive variables are presented as mean± standard deviation or percentages within epochs.

Results

We identified 345 children commenced on NIV during the 12-year period. Eighty-nine charts have been reviewed to date. The number of children commencing NIV each year increased significantly across the epochs (Kruskal-Wallis, $p< 0.05$): 9 children started in the first epoch, 32 in the second and 48 in the third. As a result, the total number of children followed by the home NIV program also increased across epochs (Kruskal-Wallis, $p<0.05$). Mean age of NIV initiation across the epochs differed; age was similar in the first and second epochs (7.9± 2.5 y, 10.7± 5.1) but lower in the third epoch compared to the second (7.2±5.4 y; post-hoc ANOVA $p<0.05$). Children <2 years of age were only represented in the third epoch with 24 children initiated on NIV in this epoch. The reason for NIV initiation differed across epochs; for example, NIV was initiated after acute illness in 11%, 13% and 37% respectively across epochs (Chi-square 10.33, $p<0.05$). There is no difference in the proportion of children started on continuous positive airway pressure (CPAP) versus Bilevel support across epochs. Overall, 56% were started on CPAP versus 44% on Bilevel support. The interface type does change across epochs with a higher proportion of nasal masks over time (6%, 27%, 67% respectively, Chi-square 15.6, $p<0.001$).

Conclusion

NIV use in children has increase over the last 12 years at the Stollery home NIV clinic. More recently, younger children are receiving NIV. While the type of ventilation has not changed over time, more nasal mask interfaces have been used progressively. This interim analysis supports trends in NIV are similar to those reported from other areas of the world.

Funded By: Trainee Research Grant

women & children's health research institute

Abstract #: 133
Presenter: Beatriz Carvalho Henriques
Supervisor: Katherine Aitchison

Title: CYP2D6: Detecting new structures for clinical practice

Authors: Beatriz Carvalho Henriques, Caitlin Slomp, David Rossolatos, Evangelia Tsapakis, Logos Curtis, Paramala Santosh, Jose Paya-Cano, Sarah Curran, Ian Craig, Katherine Aitchison
Affiliations: University of Alberta

Research Activity: Other
Investigation Type: Qualitative Research

Introduction

Research in pharmacogenomics aims to elucidate the contribution of genetic variation to the response to medications used in clinical practice. Once an individual's genetic profile is determined, the range of adverse reactions - from side effects to potentially lethal reactions – can be predicted. Within this field, a gene that has been the focus of extensive research is the cytochrome P450 enzyme 2D6 (*CYP2D6*). The gene coding for this enzyme is highly polymorphic, thus a wide range of variants are currently known. Identifying such variants and understanding how they differ in their interaction with a given chemical compound is desirable because the *CYP2D6* enzyme metabolizes over 50 medications. Of particular interest is tamoxifen, a drug used in the treatment of breast cancer, and for which there is some evidence that *CYP2D6* genotype may predict remission status. This enzyme has four levels of activity: an individual may be classified as a poor, intermediate, extensive or ultrarapid metabolizer. The unusual variants referred to above are complicated variants that may be associated with no active enzyme. This project continues work that has identified individuals that would have been classified by standard techniques as having rapid enzyme activity but in fact appear to have unusual variants that may have no enzyme activity. In this manner, the improvement in technology gained will enable correct identification of a wider range of variants of this enzyme than was previously possible, which can be translated into clinical practice in the form of personalized and hence more efficient medical care.

Our objective is to identify precisely which unusual variants are present, in order to correctly deduce the activity of the relevant enzyme for the individual.

Methods

The methodology applied to investigate samples likely carrying *CYP2D6* hybrid alleles was the polymerase chain reaction (PCR) approach to identify complex *CYP2D6* functional variants using the technique described by Kramer *et al*. (2009) and Black *et al*. (2011), including agarose gel electrophoresis for fragment delineation.

Results

Preliminary data show the presence of a fragment of the expected length in a sample for which the *CYP2D6* TaqMan copy number data were consistent with a *CYP2D6* hybrid allele.

Conclusion

Preliminary data are encouraging; further analysis, is in progress.

Acknowledgements

Dr Aitchison holds a Government of Alberta funded Alberta Centennial Addiction and Mental Health Research Chair; BCH is funded by this Chair fund to conduct this research.

Funded By: Undergraduate Research Initiative

women & children's health research institute

Abstract #:	134
Presenter:	Suzan Shenouda
Supervisor:	Consolato Sergi
Title:	Combined morphometric and immunohistochemichal algorithm for identification of ganglion cells
Authors:	Suzan Shenouda, Catherine Takawira, Braikhna Yousafzai, Gregor Mikuz, Consolato Sergi
Affiliations:	University of Alberta
Research Activity:	Child and Youth Development : Congenital Abnormalities
Investigation Type:	Mixed Methods

Introduction

The absence of ganglion cells in suction biopsies of distal colon specimens is still the golden rule in diagnosing Hirschsprung disease, a multigenic pediatric disease. However, the identification of those cells may be difficult especially for the inexperienced pathologist and may lead to a dilemma or overtreatment for the management of those patients. Many immunohistochemical studies have been applied to aid in detection of ganglion cells and especially synaptophysin, CD56, and calretinin have been the focus of most recent research becoming daily practice in some institutions.

Our study objective is to combine morphometry and different immunohistochemical stains used to detect ganglion cells in different stages of maturation. In cooperation with external institutions, we have been able to compare the morphometric and immunohistochemical pattern of ganglion cells at time of suction biopsy with the Haematoxylin and Eosin (H&E) specimens of maturing fetal gut (5-24 weeks of gestation). The results will be analyzed to detect the stages of maturation of ganglion cells and neural gut development.

Material and Methods

Paraffin embedded blocks from the distal gastrointestinal tract of miscarried fetuses ranging from 5-24 weeks of gestation were obtained from Austria following external institutional approval. H&E tissue slides were prepared and compared with other immunohistochemical stains to outline the value of using different methods for detection of ganglion cells. Morphometric imaging using imageJ (http://rsb.info.nih.gov/ij/) were applied to quantify cell types and parameters. The threshold was also used for stain contrasting.

Results

Mature ganglion cells were significantly larger than all other cell types including immature ganglion cells. We could also identify stages of gut development using histological and immunohistochemical analysis of the tissue slides provided. These results enabled us to identify anomalies and phenotypic errors in the early stages of neural gut development.

Conclusion

We hope to use these results in correlation with genetic mutations to outline the pathogenesis and genetic subgroups of Hirschsprung disease.

women & children's health research institute

Abstract #: 135
Presenter: Quang Vo
Supervisor: Edmond Lou

Title: In-vivo measurements of axial vertebral rotation using a 3D spinal image: A pilot study
Authors: Quang Vo, Edmond Lou, Lawrence H. Le
Affiliations: University of Alberta
Research Activity: Other
Investigation Type: Quantitative Research

Review Introduction

Adolescent Idiopathic Scoliosis (AIS) is a three-dimensional deformity of the spine associated with vertebral rotation and their cause is unknown. The axial vertebral rotation is one of the important parameters to assess the severity of scoliosis, estimate the risk of progression, and evaluate the treatment outcomes. Several methods have been developed to measure the axial vertebral rotation from radiographs, but the two-dimensional measurement may under estimate its true value. Our group has demonstrated that it is feasible to reconstruct 3D ultrasound spine images on scoliotic patients. The coronal curvature measurements from the ultrasound images have been validated with radiographic measurements.

Purpose

The objective of this pilot study is to investigate if 3D spinal ultrasound images can be used to measure the axial vertebral rotation.

Methods

Five subjects who were diagnosed with AIS and their major Cobb angles were less than 40^{o} were recruited. A medical ultrasound system and a 2.5 MHz convex probe with a built-in positioning system were used in this study. All subjects were scanned while they were instructed in a standard standing position. Their 3D ultrasound spinal images were then reconstructed. Among the 5 subjects, a total of 20 vertebrae were measured. On the ultrasound images, the centre of lamina method was used, while the Stokes method was used on radiographs. The ultrasound images were measured by rater 1, but the radiographs were measured by rater 2. The Student's paired t-tested was used to determine the correlation. The mean absolute difference was used to determine the differences between the ultrasound and radiographic measurements.

Results

The range of the vertebral rotation measurements from the ultrasound and radiographs were $0 – 11^{o}$ and $1 – 21^{o}$, respectively. The p-value of the Student's t-test was 0.46 which meant there was a weak correlation between the two measurements. The mean absolute difference between the two sets of measurements was $3.8^{o} \pm 0.8^{o}$ with the absolute errors ranging from 0 to 14^{o}.

Conclusion

This pilot study showed that there was a discrepancy of axial vertebral rotation measurements between the 3D ultrasound images and the 2D radiographs. To truly evaluate the vertebral rotation measurements from the ultrasound images, 3D spinal images from other image modalities may be required.

Funded By: Trainee Travel Grant

women & children's health research institute

Abstract #:	136
Presenter:	Lina Becerra
Supervisor:	Kim Adams
Title:	Using robots to assess skills and access play and problem solving for children with severe disabilities
Authors:	Adriana Rios, Liliana Alvarez, Isabela Sa, Lina Becerra, Paola Esquivel
Affiliations:	University of Alberta
Research Activity:	
Investigation Type:	Mixed Methods

Introduction

Children who have severe physical limitations may also have cognitive delays and difficulty participating in play. Cognitive evaluation tests require fine motor tasks or speech so it is difficult to determine the cognitive ability of these children. However, when children control robots, they can access play and problem solving activities and demonstrate cognitive skills.

Children with disabilities often have a delay in their play and problem solving skills because adults or peers manipulate their toys for them. These children do not have opportunities for meaningful exploration or manipulation of objects; therefore they need a means for manipulating objects in play in order to develop symbolic play and problem solving skills.

This study aims to develop robotic tasks that will allow non-disabled children to perform play and problem solving activities. To understand how the robot tasks reflect cognitive ability, we will first evaluate the performance of typically developing children in tasks that become developmentally more complex.

Methods

We have performed 6 pilot trials with typically developing children between the ages of 3 and 7. First, the child performs three tasks with a mobile car-like robot to determine their level of understanding of cause and effect, inhibition, laterality and sequencing (in a protocol used in several previous studies). Next, the child is exposed to two conditions, robot or no robot in a problem solving activity known as "truck loading". This is a reverse sequencing task in which the child must deliver invitations while considering a route in advance to load a delivery truck. The child receives a level score from 1 to 4 depending on how many items they match. Finally, the child does free play with and without the robot with conventional and unconventional toys. The play activities of the child are assessed for evidence of play skills (from functional to symbolic play).

Results

The problem solving task appears to be useful in discriminating cognitive ability, e.g., 3 year olds accomplish level 1, 7 year olds level 4. Further analysis will determine if using the robot influences performance. Children are showing more symbolic play without the robot, but after modeling how the robot can be incorporated in symbolic play, they can achieve a higher level in that condition.

Conclusion

The next steps involve performing the tasks with 25 typically developing children between the ages of 3 and 7 to validate the developmental sequence of the tasks.

Funded By: Innovation Grant

women & children's health research institute

Abstract #:	137
Presenter:	Mark Assmus
Supervisor:	Peter Metcalfe
Title:	Postnatal Surveillance of Pediatric Hydronephrosis due to Utero-Pelvic Junction Obstruction
Authors:	Mark Assmus, Darcie Kiddoo, Ryan Hung, Peter Metcalfe
Affiliations:	University of Alberta
Research Activity:	Child and Youth Development: Congenital Abnormalities
Investigation Type:	Quantitative Research

Introduction

Ubiquitous use of prenatal ultrasounds (US) has identified antenatal hydronephrosis (ANH) in 1% of all pregnancies. Sequential postnatal US and declining renal function on Tc99m-Mag-3 renography can identify surgical candidates before the advent of morbidity, however consensus prognostic factors and optimal surveillance strategies remain controversial. Therefore, we examined Mag-3 surveillance in pediatric patients with hydronephrosis due to utero-pelvic junction obstruction (UPJO). We hypothesize that patients with asymmetric differential function on intial Mag-3 have a higher odds ratio for deterioration and/or pyeloplasty when compared to patients whose initial scans are symmetrical.

Methods

We performed a retrospective chart review of 1,124 pediatric patients with hydronephrosis seen at the Stollery Children's Hospital over 15 years. Of those, 387 patients met database inclusion criteria and were grouped by intial postnatal function. Data collection included; postnatal Mag-3 surveillance, need for surgery and post-pyeloplasty outcomes.

Results

Of the 152/387 (39%) patients with 50/50 function on initial postnatal Mag-3; 10/152 (7%) experienced a ≥10% decrease in function and 27/152 (18%) proceeded to pyeloplasty. Of the 235/387 (61%) patients with asymmetrical initial Mag-3 function; 112/235 (48%) started ≤40% on the affected side, 28/235 (12%) showed a ≥10% decrease in function and 52/235 (22%) proceeded to pyeloplasty. Odds ratio for a ≥10% decrease in differential function or progression to pyeloplasty in patients with asymmetrical initial differential function compared to patients with symmetrical scans is 1.92 (95% CI: 0.90, 4.08) and 1.32 (95% CI: -0.24, 0.79) respectively.

Conclusion

Asymmetrical differential function on initial postnatal Mag-3 indicates increased odds of progressing to pyeloplasty. Taken together, these results help to further educate patient families regarding pediatric hydronephrosis surveillance.

Funded By: Northern Alberta Urology Foundation

women & children's health research institute

Abstract #: 138
Presenter: Bo Bao
Supervisor: Toshifumi Yokota

Title: Optimizing exon 51 skipping as a treatment of Duchenne Muscular Dystrophy

Authors: Bo Bao, Yusuke Echigoya , William Duddy , Toshifumi Yokota
Affiliations: University of Alberta

Research Activity: Other
Investigation Type: Quantitative Research

Introduction

Duchenne muscular dystrophy (DMD) is a common lethal genetic disorder characterized by progressive muscle degeneration and loss of muscle function, causing premature death due to respiratory and cardiac failure. Statistically, DMD affects 1 in 3,500 newborn boys. It is caused by a mutation in the DMD gene that encodes the muscle-supporting protein dystrophin. Becker muscular dystrophy (BMD) is also caused by a mutation in the DMD gene, however it displays a much milder phenotype than DMD. While there are no effective treatments for DMD, current therapeutic approach attempts to convert DMD into BMD. To date, exon skipping therapy is a very promising approach to treat DMD by using short DNA-like molecules, called antisense oligonucleotides (AOs), to splice sections of the premature mRNA resulting in truncated yet functional protein. While clinical trials of AO-mediated exon skipping therapy targeting exon 51 are ongoing they have not achieved desired therapeutic effects due to a lack of desirable efficacy. Thus, our objective is to identify AOs with higher efficiency by using an AO prediction tool we recently developed.

Methods

We began by designing eight new AOs called phosphorodiamidate morpholino oligomers (PMOs) for exon 51 skipping using our new prediction algorithms. Next, we conducted a time course analysis of dystrophin mRNA expression in two DMD skeletal muscle cells harboring exons 48-50 and exon 52 deletion mutations to determine the optimal timing for PMO transfection in vitro. Based on our result, we transfected the cells with PMOs three days after differentiation and collected the cells to evaluate effects of them with RT-PCR and Western blotting analyses.

Results

Our results revealed that our newly designed PMO could induce 10 times the level of exon skipping and dystrophin expression compared to current drugs under clinical trials called eteplirsen and drisapersen. Recently, drisapersen developed by Prosensa has failed Phase III clinical trial due to lack of effect. Dose-dependent analysis at three different PMO concentrations (1, 3 and 10 µM) also demonstrated superiority of our PMO over eteplirsen. In fact, treatment at 1 µM of our PMO produced even higher exon skipping levels than that of eteplirsen at 10 µM.

Conclusion

Our results indicated that our newly developed PMO outperformed current drug candidates suggesting that our PMOs could eventually be able to achieve practical effectiveness to treat DMD in the future. With the emerging potential of exon-skipping therapy, optimizing drug efficiency brings us closer to obtaining treatment for DMD.

Funded By: Summer Studentship

women & children's health research institute

Abstract #:	139
Presenter:	Jose Luis Cabeza Gonzalez
Supervisor:	Alvaro Osornio Vargas
Title:	The interactions of economic, legal and political factors on environment and their potential child health effects
Authors:	Jose Luis Cabeza Gonzalez, Deliwe Ngwezi
Affiliations:	University of Alberta
Research Activity:	Child and Youth Development : Congenital Abnormalities
Investigation Type:	Qualitative Research

Introduction

The congenital heart defects rate, specifically septal defects, decreased in Alberta between 2006 and 2010. This decline can be attributed to reductions in pollutant emissions from the manufacturing industry since this sector showed a significant decrease in the emissions of certain organic compounds over the same period. Organic compounds such as benzene, toluene, and 1, 3-butadiene have links with a range of adverse health effects, including congenital heart defects. The purpose of this research is to identify economic, legal, and political rationale for contaminant emissions reduction into the environment in Alberta in the 2003-2010 period. The study attempts to identify the economic factors; legislation -or the lack thereof - and 3) political strategies; that could have influenced (alone or in combination), the observed industrial environment behavior.

Methods

This research identified chemicals with known developmental toxicity according to the Office of Environmental Health Hazard Assessment (CalEPA, *Proposition 65)*. Additionally, we consulted the National Pollutant Release Inventory to identify the volume of developmental toxicants emitted by the manufacturing sector from 2003-2010. Ultimately, we studied Canada-based environmental protection Acts and regulations at both federal and provincial levels, directives, industry's emissions control best management practices, and reports on Alberta economy and its manufactures markets. All of the above, with the purpose of determining which factor (or combination of factors), was responsible for pollutant emissions reduction in Alberta in that specified period.

Results

We identified 13 known developmental toxicants (i.e. 1,3-Butadiene, Toluene, Hexachlorobenzene, Carbon Monoxide, Methanol, Benzene, Sulphur Dioxide, Carbon Disulphide, Ethylene Oxide, Arsenic, Cadmium, Lead, and Mercury) as released by manufacturing industry in Alberta between 2003-2010. Specifically, we found that the emissions of Benzene, 1,3-Butadiene, Carbon Disulphide, Ethylene Oxide, Hexachlorobenzene, and Toluene drastically decreased between 2006 and 2009. In the particular case of Benzene, industry and government focused on reducing benzene emissions either, by implementing environmental codes of practices or by endorsing a Standard for Benzene emission. Concurrently, the North America's economic and financial crisis also determined reductions of benzene emissions due to decreased industrial activity.

Conclusion

While this research is still in the process, it can be asserted that a combination of several factors (economic, legal and political) contributed to a reduction in pollutant emissions in Alberta.

women & children's health research institute

Abstract #:	140
Presenter:	Anthony Chiu
Supervisor:	Joseph Casey
Title:	Identifying chemical correctors for the folding defect in corneal dystrophy-causing mutants of SLC4a11
Authors:	Anthony M. Chiu, Jake Mandziuk, Joseph R. Casey
Affiliations:	University of Alberta
Research Activity:	
Investigation Type:	Mixed Methods

Purpose

Congenital Hereditary Endothelial Dystrophy (CHED) and Fuchs Endothelial Corneal Dystrophy (FECD) are two forms of genetic corneal blindness. CHED is recessive whereas FECD is dominant with a 4% occurrence. Some cases of these diseases are caused by mutations in the membrane protein, SLC4a11, which has been identified as forming a water translocation pathway. In normal function, SLC4a11 at the plasma membrane facilitates water flow out of the stroma and into the aqueous humor. When mutated, SLC4a11 is unable to perform its function because it is either retained in the endoplasmic reticulum or is catalytically dead. Current treatments for these diseases, including corneal transplant, are wholly inadequate. Our goal is to identify compounds that could be used as drugs to correct these protein folding defects.

Methods

We have developed an assay to identify chemical correctors that enable diseased SLC4a11 to target to the plasma membrane. SLC4a11 with a hemagglutinin epitope tag inserted into an extracellular loop is stably expressed in HEK293 cells, seeded on a 96 well plate and then incubated with the potential correcting compound of choice. Cells are then incubated with anti-HA antibody, followed by secondary antibody conjugated to horseradish peroxidase (HRP). In the presence of H_2O_2, HRP metabolizes AmplexRed to create a red fluorescence product, read in a 96 well plate reader. A higher relative amount of fluorescence indicates a higher proportion of protein at the plasma membrane. Mutants being tested include G709E (FECD), A269V, E143K and R869C (CHED). The assay enables screening of large numbers of compounds against many different mutants.

Results

The ability of the assay to differentiate plasma membrane versus ER retained SLC4a11 was assessed by measurement of fluorescence arising from cells expressing WT protein with an intracellular or extracellular HA tag. Fluorescence was six fold higher in cells expressing the extracellular tagged protein. Compounds screened for their ability to correct SLC4a11 misfolding include, DMSO, glycerol, 4-phenylbutyrate and the Hsp90 inhibitor; geldanamycin.

Conclusion

We have developed an assay that enables rapid, sensitive and accurate screening of compounds that correct the folding defect in SLC4a11 mutants. By screening potential correcting compounds already approved for drug testing in humans, our work could very quickly lead to a marketable pharmaceutical based treatment for FECD and CHED.

Funded By: Trainee Travel Grant

women & children's health research institute

Abstract #:	141
Presenter:	Michelle Young
Supervisor:	Edmond Lou
Title:	The use of ultrasound for guided pedicle screw insertion: A Preliminary Investigation
Authors:	Michelle Young, Douglas Hill, Rui Zheng, James Mahood, Edmond Loug
Affiliations:	University of Alberta
Research Activity:	Other
Investigation Type:	Mixed Methods

Introduction

Pedicle screw fixation is used in conjunction with vertebral fusion to correct severe spinal deformities. For optimal results, the diameter of pedicle screw used for surgery should be 1-2 mm smaller than the width of the pedicle bone into which it is inserted. Therefore, even a slight misalignment can cause perforation of the cortical bone and damage to nearby neurological and vascular tissue. Computer-assisted navigation has been introduced to improve the accuracy of screw placement. Existing navigation techniques either use preoperative images that require lengthy and invasive registration to the patient's anatomy, or use intraoperative images that expose the patient and surgical team to radiation. This study aims to determine if intraoperative ultrasound images can be registered to preoperative CT images to non-invasively determine the optimum trajectory and depth for pedicle screw placement.

Methods

A CT scan of a bovine tibia and a radiograph of a bovine vertebra were obtained. Ultrasound scans were completed before and after 2 mm diameter guide holes were drilled at various angles, depths, and locations. Actual depths were measured using calipers. Ultrasound and CT/radiograph frames were registered using a landmark based image registration technique implemented on in-house software developed in Matlab.

Results

Bone surfaces and guide holes could be visualized with ultrasound. Qualitative analysis suggests that an accurate guide hole trajectory and position can be determined by using landmark based registration to align ultrasound and CT frames. Depth measurements were performed on two registered ultrasound images. Three measurements were performed on each image resulting in measured depths of 3.9-4.1 mm (true depth 4.3 mm), and 16.6-16.8 mm (true depth 16.5 mm).

Conclusion

Preliminary results show that ultrasound may be helpful for intraoperative registration of preoperative CT scans to the surgical frame of reference, and for visualization of pedicle screw guide holes.

Funded By: Summer Studentship

women & children's health research institute

Abstract #:	142
Presenter:	Renee Leduc
Supervisor:	Heather McDermid
Title:	Identification and analysis of genetic variants contributing to anencephaly.
Authors:	Renee Leduc, Deidre Krupp, Natalie Mola, Erica Davis, Nicholas Katsanis, Simon Gregory, Allison Ashley-Koch, Heather McDermid
Affiliations:	University of Alberta
Research Activity:	Child and Youth Development : Congenital Abnormalities
Investigation Type:	Quantitative Research

Introduction

Anencephaly is an invariably lethal birth defect that is characterized by the failure of the cranial portion of the neural tube to close during early embryonic development. To illuminate the mechanistic underpinnings of neural tube closure, we have investigated genetic variation in mice and humans. In mice, a homozygous mutation of the gene *Cecr2* causes exencephaly (equivalent to the human anencephaly phenotype). The manifestation of exencephaly is strain dependent, where approximately 54% of BALB/c *Cecr2* mutant mice develop exencephaly compared to 0% of FVB/N *Cecr2* mutant mice. This suggests the presence of DNA sequence variants that modify the penetrance of the exencephaly phenotype.

Methods

To look for the genomic region containing these variants, linkage analysis was previously performed and identified a modifier region on mouse chromosome 19. Microarray analysis was then performed to discover genes differentially expressed between BALB/c and FVB/N within this region. To detect possible functional variants, whole exome sequencing (WES) was also performed on BALB/c and FVB/N.

Results

A combination of microarray and WES analyses yielded a list of 24 candidate modifier genes. It is possible that the human homologues of *Cecr2* and the 24 candidate modifier genes identified in mice are involved in the etiology of anencephaly in humans. Therefore, we performed custom capture sequencing of the coding regions of human *CECR2* and the 24 candidate modifier genes in a human anencephaly cohort of 157 probands. Fifty coding variants with a minor allele frequency (MAF) ≤ 0.03 were identified in 18 genes, including *CECR2*. All fifty variants were Sanger sequence verified in the probands and in available parental DNA samples.

Conclusion

These data demonstrate the utility of comparative genomics in dissecting the mechanisms of neural tube closure. Functional assays are underway to determine whether the identified variants may contribute to causality.

Funded By: Innovation Grant

women & children's health research institute

Abstract #: 143
Presenter: Alexandria Tiffinger
Supervisor: Andrew Waskiewicz

Title: Role of bmpr1ab in ocular developmental disease

Authors: Alexandria Tiffinger, Sonya Widen, Andrew Waskiewicz
Affiliations: University of Alberta

Research Activity: Child and Youth Development : Congenital Abnormalities
Investigation Type: Mixed Methods

Introduction

Microphthalmia, anophthalmia, and coloboma (MAC) represent a group of related congenital eye disorders that can lead to severe visual impairment. A coloboma is a developmental abnormality where an opening in the iris persists. MAC disorders can occur syndromically or independently. The importance of such MAC disorders is highlighted by their frequently blinding effects, with MAC collectively representing 11% of pediatric blindness. The role of the crucial developmental signaling pathway Bone Morphogenic Protein (BMP) signaling has been previously evaluated in MAC. Our lab has recently discovered a novel structure in the developing vertebrate eye, the superior fissure, which is a transient fissure in the dorsal eye. If this fissure fails to close, it can result in a superior coloboma. A cause of this new coloboma is currently being examined, and a specific mutation in Bone Morphogenic Protein Receptor 1A (BMPR1A) has been identified in one of the patients. The current study tests the hypothesis that the identified variant in BMPR1A is pathogenic and that this receptor plays a critical role in early vertebrate eye development at the superior fissure.

Methods

The zebrafish (*Danio reiro*-) homologue of human BMPR1A, *bmpr1ab*, was cloned and used for mRNA synthesis. *In situ* hybridizations (ISH) were used for gene expression analysis in zebrafish embryos.

Results

When the sequence of *bmpr1ab* was compared to that of human BMPR1A, the site of the point mutation in BMPR1A was found to be conserved in *bmpr1ab*. Zebrafish *bmpr1ab* was successfully cloned. Expression of *bmpr1ab* using ISH showed it is strongly expressed in the eye during early eye development.

Conclusion

The laboratory work completed this summer has laid the foundation for this new study, by suggesting that using a zebrafish homologue is an appropriate model to study human eye development. The study is now moving forward to examine the specific sequence variant found in human patients and its effects on eye development and congenital disease.

Funded By: Summer Studentship

women & children's health research institute

Abstract #: 144
Presenter: Sonya Widen
Supervisor: Andrew Waskiewicz

Title: The role of BMP3 in eye development and pediatric ocular disease

Authors: Sonya Widen, Prajakta Desai, Mika Asai-Coakwell, Benson Matt, Ordan Lehmann, Andrew Waskiewicz
Affiliations: University of Alberta

Research Activity: Child and Youth Development : Congenital Abnormalities
Investigation Type: Mixed Methods

Introduction

Microphthalmia (small eyes), anophthalmia (no eyes) and coloboma are a group of related, frequently blinding conditions that result from abnormal embryonic eye development. Collectively referred to as MAC, these defects represent up to 11% of all pediatric blindness. Our lab has previously implicated bone morphogenetic protein (BMP) signaling, a crucial developmental signaling pathway, in causality of MAC. However, our understanding of direct causes of MAC only represents a fraction of documented cases. Our goal is to elucidate the genetic causes of these pediatric diseases. Here, we describe our work on an intriguing new candidate, *BMP3*.

Methods

To identify the genetic causes of MAC, we performed Sanger and exome sequencing. We employed morpholino-based gene knockdown to investigate the role of *bmp3* in ocular development, in situ hybridization (ISH) for gene expression analysis and transgenic zebrafish for fluorescent microscopy and cell migration analysis. We utilized luciferase reporter assays, western blots and *in silico* ANOLEA modeling to investigate the pathogenicity of identified mutations.

Results

Exome sequencing of a family of affected individuals identified a sequence variant in *BMP3*, with two additional variants identified within the mature protein domain through Sanger sequencing of a MAC patient panel. *In silico* modeling indicates these variants are highly damaging to protein structure, while *in vitro* assays suggest BMP3 variants have altered biological activity. To investigate the role of *bmp3* in ocular development, we performed *in vivo* experiments in zebrafish. Morpholino (MO) knockdown of Bmp3 causes MAC, lens defects and other ocular abnormalities, highlighting a key role for *bmp3* in eye formation. ISH previously revealed *bmp3* is expressed not in the eye but in periocular mesenchyme (POM), an extraocular group of migratory cells that has been implicated in causality of MAC. However, the role of BMP signaling in this process is unknown. Consistent with lens defects, a POM-derived structure, and the incidence of MAC, MO knockdown of *bmp3* causes defects in POM development.

Conclusion

We have identified a novel candidate in causality of MAC, *BMP3*. Sequence variants identified in MAC patients are predicted to be damaging to both protein structure and biological activity. Zebrafish experiments suggest loss of *bmp3* causes not only MAC, but maldevelopment of POM cells, suggesting a possible mechanism for the action of Bmp3 in ocular development. Further characterization of Bmp3 may greatly expand our understanding of MAC disorders and the causes of pediatric blindness.

Funded By: Graduate Studentship

women & children's health research institute

Abstract #:	145
Presenter:	Sukhpreet Tamana
Supervisor:	Carmen Rasmussen
Title:	Neuropsychological functioning in children and adolescents with FASD and comorbid seizure disorder
Authors:	Sukhpreet Tamana, Gail Andrew, James Reynolds, Jacqueline Pei, Carmen Rasmussen
Affiliations:	University of Alberta
Research Activity:	Child and Youth Development : Fetal Alcohol Syndrome
Investigation Type:	Quantitative Research

Introduction

Children and adolescents with Fetal Alcohol Spectrum Disorders (FASD) exhibit a range of neurobehavioral outcomes including impairments in cognitive, neuropsychological, behavioral, and adaptive skills (Chudley et al., 2005). Children and adolescents with FASD are also at risk for comorbid seizure disorder and epilepsy (Bell et al., 2010), which may have temporary or long-lasting structural and neurobehavioral effects. However, it is unknown whether children and adolescents with FASD, with and without seizure history, show a different pattern of neurobehavioral impairments. The *purpose* of this study is to compare the neurobehavioral profile of children and adolescents with FASD to those with FASD and seizure history to determine whether seizure comorbidity is associated with more severe neurobehavioral deficits in FASD.

Methods

A sample of 26 children and adolescents with FASD (11 with seizure history and 15 without) and 15 typically developing controls aged 7 to 16 years were included in this study. Data examined is a subset from the FASD NeuroDevNet Demonstration Project. Groups were matched on age and gender where possible. All participants were assessed on selected subtests from the NEPSY-II that included measures of attention and executive functioning, memory, visual-spatial processing; math subset from the Woodcock Johnson III; as well as two parent rating scales measuring executive functioning (BRIEF) and adaptive behavior (ABAS-II).

Results

Overall, as expected children and adolescents with FASD (with and without seizures) performed worse on most tests as compared to typically developing controls. In children and adolescents with FASD, participants with FASD and seizures performed significantly worse than those without seizures on a measure of inhibition. We also found that the FASD and seizure group showed trends towards greater impairments in some areas involving more complex-inhibition, but similar performance in cognitive flexibility and attention. No group differences were found on the BRIEF and ABAS-II.

Implication

Preliminary findings from this study indicate that for children and adolescents with FASD having a seizure comorbidity may negatively affect some neurobehavioral domains. However, further research is needed in this area to understand the profile of strengths and needs for children with FASD and seizure comorbidity. These results also have implications for developing appropriate intervention strategies for individuals with FASD and seizure history. Importantly, these results highlight healthcare professionals and caregivers awareness of the risks and implications of having a seizure comorbidity in this population.

Funded By: NeuroDevNet

women & children's health research institute

Abstract #:	146
Presenter:	Punit Virk
Supervisor:	Oana Caluseriu
Title:	Antisense-mediated gene therapy in cells from patients with Fibrodysplasia Ossificans Progressiva
Authors:	Punit Virk, Yusuke Echigoya, William Duddy, Oana Caluseriu, Toshifumi Yokota
Affiliations:	University of Alberta
Research Activity:	Child and Youth Development : Congenital Abnormalities
Investigation Type:	Quantitative Research

Introduction

Fibrodysplasia Ossificans Progressiva (FOP) is a rare autosomal dominant, highly disabling, genetic disease characterized by progressive bone formation in the soft tissue. In 98% of cases the disease is caused by a recurrent R206H missense mutation in the *activin receptor-like kinase-2 (ALK2)* gene (coding for a type 1 bone morphogenetic protein receptor), resulting in overactive receptor activity and aberrant osteogenesis. While no cure or recognized treatment for FOP currently exists, exon-skipping is a promising therapeutic approach, employing synthetic DNA-like molecules, called antisense oligonucleotides (AONs), such as phosphorodiamidate morpholino oligomers (PMOs). PMOs can be used to target and splice out the mutated portion of the gene or target the transcriptional start site, blocking the translation of the entire mutant protein. A recent *in vitro* mouse cell study has shown successful skipping of the exon that is found to carry the recurrent mutational hotspot in FOP cells. The study also showed downregulation of ALK2 expression; however antisense-mediated therapy in human FOP cells has not been demonstrated to date.

Methods

The aim of our study is to skip the mutant exon and reduce ALK2 activity in FOP patient cells. FOP fibroblasts were transfected with a variety of PMOs, either targeting the FOP mutation site in exon 6 or the ALK2 transcriptional start site in exon 3 (for overall ALK2 protein reduction). Statistical algorithms were used to design AON sequences with the greatest binding energy differential between the exon 6 mutant and normal alleles. RT-PCR and western blotting were used to analyze ALK2 mRNA and protein expression in PMO-treated FOP cell-lines.

Results

DNA sequencing revealed that both FOP cell-lines used in our experiments carry the recurrent R206H missense mutation. RT-PCR confirmed successful exon-skipping by newly designed oligonucleotides as well as the human analog of an AON previously found effective in mouse cells. Preliminary western blotting results analyzing ALK2 protein expression levels in PMO-treated FOP cell-lines versus healthy control fibroblast cells are currently pending.

Conclusion

These findings will allow us to use successful AON sequences to further target human FOP cells and assess the downregulation of ALK2 activity and the downstream molecules (activated by the ALK2 receptor), involved in SMAD signaling pathways. Promising AON sequences will also be used to test whether osteogenic activity is reduced post-skipping in patient cells.

Funded By: URI (Undergraduate Research Initiative)

women & children's health research institute

Abstract #:	147
Presenter:	Conrad Tsang
Supervisor:	Amanda Newton
Title:	Predicting return emergency department visits and hospital admissions for deliberate self-harm in children and adolescents: A cohort study
Authors:	Conrad Tsang, Xiaoqing Niu, Rhonda Rosychuk, Stanley Kutcher, Amanda Newton
Affiliations:	University of Alberta
Research Activity:	Child and Youth Development : Mental Health
Investigation Type:	Quantitative Research

Introduction

Death by self-inflicted injury is the second leading cause of mortality worldwide for adolescents aged 15 to 19, with greater risk for those presenting to hospital than those who do not. However, the health services trajectory of these patients discharged from the emergency department (ED) after deliberate self-harm (DSH) is poorly understood. In pediatric patients, we sought to determine the physician-based features and sociodemographics associated with ED re-visits and hospital admission, for mental health care, after discharge from an ED for DSH.

Methods

A province-wide retrospective cohort study of all pediatric ED visits for DSH from 2002-2011 was conducted. Ambulatory care, physician claims, and hospitalization files were linked and generalized linear models were used to test the association between variables of interest and ED re-visit and hospital admission. Variables included the number and type of physician visits made 30 days prior to and after index ED visits, self-harm acuity at the index visit, child age and sex, and a socioeconomic proxy (First Nations status or family health care premium subsidy status: government subsidy, human services subsidy, no subsidy). Multivariable Cox proportional hazards models were used to estimate the risk between variables and time to ED re-visit and hospital admission. Outcomes were measured within 90-days after ED discharge.

Results

3,133 children's ED visits for DSH were captured. First Nations children (adjusted hazard ratio 1.43; 95% CI 1.09-1.87) had shorter times to ED re-visit compared to others. Children who made a physician visit in the month following an ED visit had an increased time to ED re-visit (0.58; 0.36-0.92) compared to those without a physician visit, while children who made >1 physician visit had a shorter time to ED re-visit (2.41; 1.64-3.55) and hospital admission (5.98; 3.14-11.39). Physician follow-up visits for mental health increased the risk of time to earlier ED re-visit (3.30; 2.51-4.33) and hospital admission (1.64; 1.06-2.54) compared to visits for other reasons. Sociodemographics and acuity of the index ED visit were not associated with risk of time to hospitalization.

Conclusion

These independent risk factors for ED re-visit and hospital admission and time to these events following DSH can alert clinicians to children who are at continued risk for DSH and may signal a need for different post-crisis care models to prevent subsequent hospital-based service use and improve outcomes. Whether multiple physician visits in the post-ED period reflect health care utilization patterns or unmet need is important to clarify.

Funded By: CIHR

women & children's health research institute

Abstract #: 148
Presenter: Marghalara Rashid
Supervisor: Amanda Newton

Title: The impact of pediatric traumatic brain injury (TBI) on family functioning: A Systematic Review

Authors: Marghalara Rashid, Helly Goez, Neelam Mabood, Samah Damanhoury, Jerome Yager, Anthony Joyce, Amanda Newton
Affiliations: University of Alberta

Research Activity: Other
Investigation Type: Qualitative Research

Introduction

In young children, traumatic brain injury (TBI) is the most frequent cause of disability. A growing body of literature proposes that parenting style can facilitate or impede behavioural recovery after a TBI, and interventions to address these roles may ameliorate emerging behavioural problems in the child and facilitate a more adaptive home environment and functioning for the family. To date there has been no systematic review conducted regarding the impacts pediatric TBI has on family functioning. Thus, the objective of this systematic review was to explore the impact moderate to severe traumatic brain injury (TBI) in a child has on family functioning.

Methods

The search was conducted using 9 bibliographic databases for articles published between 1980 and 2013. Two reviewers independently screened for inclusion and assessed study quality. Two reviewer extracted study data and a third checked for completeness and accuracy. Findings are presented by three domains: injury-related burden and stress, family adaptability, and family cohesion.

Results

Nine observational studies were included. Across the studies, differences between study groups for family functioning varied, but there was a trend for more dysfunction in families whose child had a severe TBI as compared to families whose child had a moderate TBI or orthopedic injury. In three studies, injury-associated burden was persistent post-injury and was highest in families whose child had a severe TBI followed by families with a child who had a moderate TBI. One study found fathers reported more family dysfunction caused by their child's injury compared to mothers. Two studies found that mothers' adaptability depended on social support and stress levels while fathers' adaptability was independent of these factors and injury severity.

Conclusion

Moderate to severe TBI has a significant, long-standing impact on family functioning. There are different factors that can be considered to assist with families' adaptability. The evidence from this systematic review provides a strong platform to understand the parental challenges that arise after a child's TBI, and guide family-based program development that can positively impact the well-being of children with TBI, their families, and their communities.

Funded By: supervisor

women & children's health research institute

Abstract #:	149
Presenter:	Rohit Lodhi
Supervisor:	Katherine Aitchison
Title:	Antipsychotic associated metabolic syndrome: clinical course and vulnerability factors
Authors:	Rohit Lodhi, Leslie Roper, Bret Granger, Carol Bolt, Sudhakar Sivapalan, Adrian Heald, Katherine Aitchison, Scot Purdon
Affiliations:	University of Alberta
Research Activity:	Child and Youth Development : Mental Health
Investigation Type:	Quantitative Research

Introduction

Weight gain and metabolic syndrome can be major side effects of antipsychotic medications. Medication concordance, quality of life and self esteem of patients may be affected by aspects of the metabolic syndrome. Several genes have been associated with aspects of the metabolic syndrome, including *HTR2C, LEP, LEPR, DRD2, TNF, SNAP-25* and *MC4R*.

Methods

Edmonton Early Psychosis Intervention Clinic manages young patients who are sometimes as low as 14 years old. These patients with first episode psychosis received prospective monitoring for metabolic dysfunction as part of good clinical practice: weight gain, fasting glucose and lipid profile, blood pressure, and waist circumference were recorded at intake and at 9, 27, 53 and 104 weeks. We intend to seek consent from patients to investigate biomarkers conferring vulnerability to metabolic dysfunction. SNP's in the *MC4R* and *FTO* gene regions, methylation of promoters of genes such as *POMC*, selected cytokines and neurohormonal markers, and substance abuse will be investigated for their effect on antipsychotic induced weight gain and metabolic syndrome.

Results

From the clinical data available we can conclude that the proportion of patients with dysglycemia was less than 5% at baseline. In addition there are significantly higher rates of abnormal body mass index (BMI, p =0.001) and central obesity (p = 0.002) in subjects who took antipsychotic medications for one year compared to those who had not been on any medication. In work conducted in parallel with other collaborators, we have shown an association between weight gain on treatment with an antipsychotic and a mutation in the leptin receptor gene (*LEPR*; Almandil *et al*., 2014). We will be seeking to replicate and extend this finding to other relevant biomarkers as described above.

Conclusion

By one year, the percentage of patients on antipsychotic medications with increased central obesity and body mass index is concerning. This has implications for early provision of appropriate healthy lifestyle interventions. The availability of replicated biomarkers would have significant public health implications.

Acknowledgement

Dr Aitchison holds a Government of Alberta funded Alberta Centennial Addiction and Mental Health Research Chair, and Dr Lodhi is funded by this Chair fund. Dr Katherine Aitchison and Dr Scot Purdon are joint senior authors for this submission.

women & children's health research institute

Abstract #:	150
Presenter:	Vanessa Carias
Supervisor:	Rachel Wevrick
Title:	The role of MAGEL2, a protein implicated in Prader-Willi syndrome, in the regulation of various RING-zinc finger-type E3 ubiquitin ligases
Authors:	Vanessa Carias, Rachel Wevrick
Affiliations:	University of Alberta
Research Activity:	Child and Youth Development : Neuro-cognitive Development
Investigation Type:	Qualitative Research

Introduction

Ubiquitylation is a posttranslational modification in which proteins are targeted for modification and degradation. Ubiquitylation is involved in various cell processes such as cell cycle, regulation of transcription, circadian rhythm, and neuronal development. *MAGEL2*, a gene inactivated in children with Prader-Willi syndrome (PWS), encodes a member of the MAGE (melanoma antigen) protein family. This family of proteins interacts with and enhances the function of RING-zinc finger-type E3 ubiquitin ligases (E3 ligases) through a conserved MAGE homology domain. Mutations in *MAGEL2* have also been identified in children with Autism Spectrum Disorder (ASD). The rate of ASD among children with PWS is estimated to be between 25-48%, where disrupted cellular mechanisms due to the lack of *MAGEL2* could contribute to their phenotype. This project will elucidate the relationship between MAGEL2 and various E3 ligases implicated in PWS and ASD. It will help in the understanding of how loss of MAGEL2 can contribute to symptoms associated with PWS, including ASD.

Methods

Using the Gateway Cloning vector system, various constructs have been created for expression in mammalian cells (HA-MAGEL2, V5-TRIM32, V5-TRIM55, V5-RNF41, and V5-RBX1) or bacteria (GST-MAGEL2). Transfections in HEK293T cells and U2OS cells and subsequent immunoblots have been performed to confirm protein expression. Immunofluorescence of transfected HEK293T cells is ongoing to determine whether subcellular localization of E3 ligases changes in the presence of MAGEL2. Co-transfections of each V5-E3 ligase and HA-*MAGEL2* at various ratios were performed in U2OS cells to determine if there are effects on the abundance of either protein. GST-pull down assays will be performed using bacterially produced GST-MAGEL2 and HEK293T cell lysate transfected with each E3 ligase, to detect protein interactions.

Results

Expression constructs produced appropriate epitope-tagged proteins as confirmed by immunoblotting. Preliminary data indicates MAGEL2 has an effect on the abundance of TRIM32, TRIM55, and RNF41 co-expressed in U2OS cells.

Conclusion

The identification of interactions between MAGEL2 and E3 ligases and their effects on their ubiquitylation protein substrates will be useful in determining the underlying cellular mechanisms disrupted in children with PWS and ASD. The results from this project will elucidate the role of protein ubiquitylation that contribute to PWS and ASD. Discovery of new protein interactions with MAGEL2 and its downstream effects could potentially generate targets for therapeutic intervention.

Funding for this research was provided by the Department of Medical Genetics, University of Alberta, Women and Children's Health Research Institute, and the Simons Foundation Autism Research Initiative.

Funded By: Graduate Studentship

Abstract #: 151
Presenter: Ain Kamaludin
Supervisor: Rachel Wevrick
Title: Investigating autophagy in a mouse model of Prader-Willi Syndrome
Authors: Ain Kamaludin
Affiliations: University of Alberta
Research Activity: Child and Youth Development : Neuro-cognitive Development
Investigation Type:

Introduction

Autophagy is a cellular degradation process that is essential for intracellular maintenance by eliminating proteins targeted for degradation. The targeted proteins reach lysosomes through incorporation into double-membrane vesicles, autophagosomes or delivery within endosomes and are degraded by lysosomal enzymes. Neurons are particularly susceptible to disruption of autophagy as the brain ages. Mutations in autophagy-regulating genes causes neurodegenerative disease and impairs axonal outgrowth. Loss of autophagy specifically in pro-opiomelanocortin (POMC) neurons of the hypothalamus interrupts the regular function of these neurons and causes increased body weight and other endocrine defects. Prader-Willi syndrome (PWS) is an imprinted genetic disorder characterized by inactivation of several genes including *MAGEL2*. We found that POMC neurons in the arcuate nucleus of hypothalamus are defective and there are fewer POMC neurons in mice lacking Magel2. The phenotype of mice that lack autophagy in POMC neurons similar to the phenotypes seen in our Magel2-null mice. We hypothesize that loss of Magel2 in the hypothalamus leads to autophagy impairment and causes interruption in the maturation of POMC neurons. Our objectives are to examine whether the inactivation of Magel2 in mice inhibits autophagy in the hypothalamus and mouse embryonic fibroblast (MEFs), and determine whether re-expressing Magel2 in cultured neurons from mice lacking Magel2 can rescue autophagy defects in these neurons.

Methods

We have performed immunoblots to measure the level of autophagy protein markers; p62, ubiquitin, and LC3B in the protein lysates from brain regions (hypothalamus and cortex) and MEF cell lines from wild-type and Magel2-null adult mice. Cell treatment of MEFs with autophagy inhibitor, thapsigargin has been performed to observe the accumulation of autophagy protein markers as the process is inhibited.

Results

Results from immunoblot experiments illustrated no significant different between genotypes for the level of p62, ubiquitin, and LC3B. Cell treatment of MEFs with thapsigargin demonstrated accumulation of p62 and LC3B due to autophagy impairment. However, there was no significant difference in the accumulation of autophagy protein markers between genotypes when cells were treated with thapsigargin.

Conclusion

Our results do not support the hypothesis that the inactivation of MAGEL2 inhibits autophagy in the hypothalamus and disrupts the maturation of POMC neurons. Experiments are still ongoing to assess the autophagy protein markers expression in the brain slices through immunostaining.

Funding for this research was provided by the Department of Medical Genetics, University of Alberta Graduate Program in Maternal and Child Health, and the Canadian Institutes of Health Research.

Funded By: CIHR

women & children's health research institute

Abstract #: 152
Presenter: Preeti Kar
Supervisor: Dr. Jerome Yager

Title: A study of biomarkers for oxidative stress and metabolism following broccoli sprout ingestion

Authors: Preeti Kar, Bretton Hari, Pavel Medvedev , Dr. Jerome Yager
Affiliations: University of Alberta

Research Activity: Child and Youth Development : Perinatel Stroke
Investigation Type: Quantitative Research

Introduction

Perinatal brain injury (PBI) is the underlying etiology for a multitude of cognitive and physical disabilities such as cerebral palsy. As a natural neuroprotective strategy, cruciferous vegetables such as broccoli sprouts (BrSp) are a promising therapy to prevent/treat PBI. BrSp contain the precursor for a potent anti-oxidant, sulforaphane (SFN), known for its therapeutic efficacy against cancer and cardiovascular disease. Our lab has previously established the role of BrSp as preventative in a model of placental insufficiency and as a treatment strategy in a model of PBI. This project aims to determine the safety, metabolism, and bioavailability of BrSp and SFN in healthy humans. Establishing these factors will aid in the therapeutic translation of BrSp to the clinical prevention/treatment of PBI.

Methods

Healthy human volunteers (aged 18-40; n=20) consumed their regular diets, without cruciferous vegetables, throughout the 22 day study. Following a 7 day washout period, participants were allocated to one of the following four groups: 50g, 100g, or 200g of juiced BrSp made up to 120mL with apple juice, or only 120mL of apple juice. Participants consumed their assigned dose of BrSp or apple juice from day 8-14 followed by a second washout period until day 22. Blood and urine samples were collected on days 7, 10, 14, and 22 and analyzed for renal, liver, thyroid, clotting, and pancreatic functions. Lipid profile, uric acid, oxidative and inflammatory markers were also assessed.

Results & Conclusion

Our results from healthy humans show no significant alterations in any of the factors measured between groups over time. Thus, the consumption of BrSp, even at high doses, has no apparent adverse effects on systemic/organ function. Our data indicate that BrSp consumption could be a potential prophylactic therapy for mothers during pregnancy to prevent brain injury to the newborn.

Funded By: AIHS

women & children's health research institute

Abstract #: 153
Presenter: Basma Al Jabri
Supervisor: Helly Goez

Title: Case report of Infantile Neuronal Ceroid Lipofuscinoses: a novel mutation in CLN1/PPT1

Authors: Basma Al Jabri, Helly Goez
Affiliations: University of Alberta

Research Activity: Child and Youth Development : Neuro-cognitive Development
Investigation Type: Quantitative Research

Introduction

Neuronal-Ceroid-Lipofuscinoses (NCL) is the most common group of neurodegenerative disorders in childhood. These conditions are autosomal-recessive in trait. They are characterized by accumulation of autofluorescent lipopigment in different tissues. The clinical presentation includes: visual impairment, seizures, motor and cognitive regression. Based on clinical and pathological grounds, the disorder is subdivided into four types: The Adult NCL, Infantile NCL (INCL), Late Infantile NCL (LINCL) and Juvenile NCL (JNCL) types. Classically, INCL type present between 8-12 months of age, and LINCL type present between 24-48 months. Up to 20% of NCL cases may present atypically. Identifying the genetic-mutation assists in determining the subtype. The identification is detrimental for genetic counseling to families and planning for palliative care.

A 19 months old boy presented with a rapid developmental regression starting at age 17 month. The parents initially observed a decrease in eye-contact and regression in social skills. This was followed by regression in previously normally acquired gross motor skills. He had frequent falls and apparently refused to walk. His behavior changed, and he became irritable and lost previously acquired words.

The past medical history was unremarkable. He was born after an uneventful pregnancy and normal delivery at term. His growth and development were normal till 17 month of age. The family is originally from the province of Tamalnadu at the southern part of India. Parents are healthy and non-consanguineous. The family history is remarkable for a paternal brother and sister who died at 12-months and 5-years, respectively from an undiagnosed neurodegenerative condition. A second-degree paternal-cousin presented with an undiagnosed neurodegenerative disorder at age of 4 years. The neurological-examination was remarkable for increased tone in upper and right lower limbs, with Choreiform movements in both hands. The child was irritable and did not make eye-contact with his parents or the examiner. He had early signs of retinitis-pigmentosa. A non-specific cerebral atrophy was demonstrated on brain MRI.

Methods

Skin biopsy, enzymatic assay and genetic sequence analysis assisted in diagnosing INCL.

Results

The skin biopsy revealed granular-osmiophilic deposits that are characteristically seen in INCL. PPT enzyme activity was abnormal. The gene sequence analysis was supportive of defect in CLN1 gene with a novel variation in PPT1 gene: p.P238L:c713C>T.

Conclusion

To the best of our knowledge social-regression in infancy has not been described as an initial clinical presentation of INCL. We highlight the need to include neurodegenerative disorders, other than Autism and Epileptic-Encephalopathies in the differential diagnosis of social-regression in infancy.

women & children's health research institute

Abstract #:	154
Presenter:	FangChao Ding
Supervisor:	Lonnie Zwaigenbaum
Title:	Predicting Autism Spectrum Disorder using 12 and 18 months behavioural data: Novel risk classification using decision tree models
Authors:	FangChao Ding, Lori Sacrey, Lonnie Zwaigenbaum
Affiliations:	University of Alberta
Research Activity:	Child and Youth Development : Neuro-cognitive Development
Investigation Type:	Qualitative Research

Introduction

Autism Spectrum Disorder (ASD) is characterized by atypical behavioural patterns that may be exhibited as early as 12 months of age. The Autism Observation Scale for Infants (AOSI) is a 16 item scale that was developed to monitor early behavioural signs of ASD in high-risk (HR) infants (younger siblings of children diagnosed with ASD), to support earlier diagnosis. We aimed to use Classification and Regression Tree (CART) analysis to identify a subset of AOSI items that would enable individual prediction of either ASD, Atypical, or typical development diagnostic outcomes at 3 years of age using 12 and 18 months AOSI data.

Method

The sample included toddlers diagnosed with ASD (n=110), toddlers with atypical development (n=113), and toddlers with typical development (n=181). All infants were assessed at 6, 12, and 18 months using the AOSI. CART analyses was applied to 12 and 18 months data.

Results

12 months AOSI data found the presence of atypical sensory behaviours to most strongly predict an ASD outcome. Combined with other behavioural profiles, the 12 months CART model had a sensitivity of 0.38 and specificity of 0.71. At 18 months, absence of eye contact most strongly predicted ASD, with an overall model sensitivity of 0.85 and specificity of 0.66. The results are complicated by the instability of the tree models, the broad spectrum of ASD symptom presentation, and the variable pattern of symptom emergence.

Conclusion

The 18 months decision tree model based on AOSI data shows high sensitivity in predicting ASD diagnosis. However, due to the heterogeneity of ASD presentation, the model's usage may be limited to the specific context for which it was developed (i.e., HR toddlers).

Funded By: Summer Studentship

women & children's health research institute

Abstract #:	155
Presenter:	David Rossolatos
Supervisor:	Katherine Aitchison
Title:	COMT genotype predicts age of diagnosis in substance-induced psychosis
Authors:	Yabing Wang, Brodie Heywood, Beatriz Henriques , David Rossolatos, Darren Bugbee, Alexandra Loverock, Carol Bolt, Aleksandra Dimitrijevic, Georgina Macintyre, Philip Tibbo
Affiliations:	University of Alberta
Research Activity:	Child and Youth Development : Mental Health
Investigation Type:	Mixed Methods

Introduction

Cannabis use in adolescence is a known risk factor for the development of psychotic disorders. Clinical and preclinical genetic studies provide increasing evidence that genes related to dopamine signaling and neuroprotection are implicated in the cannabis-psychosis association. Arseneault *et al*. (2002) found that individuals using cannabis at ages 15 and 18 years had higher rates of psychotic symptoms at age 26 years compared with non-users.

Methods

204 patients with psychotic disorders were recruited in Edmonton and Halifax, Canada. DSM-IV diagnosis was made using the SCID. Data on cannabis use and other relevant variables were collected. DNA has been extracted from salivary samples using Oragene kits. Genotyping for *COMT* rs4680 and ancestry informative markers (AIMs) is being conducted using TaqMan and SnaPshot.

Results

The genotypic distributions were in Hardy-Weinberg equilibrium and there was 100% concordance between different SNP methodologies (TaqMan and SNaPshot). The results of linear regression analysis with gender, age at regular use of cannabis, and *COMT* genotype showed that *COMT* genotype was not a significant predictor of log age of onset of illness for the whole sample (p=0.197). However, for those with a diagnosis of schizophrenia spectrum disorder or substance-induced psychosis, there was a borderline significant p value (p=0.055, N=139). *COMT* genotype was a significant predictor of log age at diagnosis (p=0.046) only in the substance-induced psychotic disorder subsample (N=44). Age of regular use of cannabis was not included in the final model as it was correlated with age at onset of psychotic disorder.

Conclusions

In summary, we found an association between *COMT* rs4680 SNP and age of diagnosis of psychotic disorder in the schizophrenia and substance-induced subsample, which appeared to be driven by the association within the substance-induced psychosis group. This deserves further exploration and investigation in similar datasets.

Acknowledgements

This study was funded by the Canadian Institutes of Health Research (CIHR): NPAS3 variants in schizophrenia and other psychoses. KJA holds an Alberta Centennial Addiction and Mental Health Research Chair, funded by the Government of Alberta, Canada. Genotyping was conducted by The Applied Genomics Core (TAGC; University of Alberta) and by the Aitchison laboratory.

Funded By: CIHR, Government of Canada

women & children's health research institute

Abstract #: 156
Presenter: Leslie Roper
Supervisor: Katherine Aitchison
Title: Stressful prenatal and childhood events and adolescent mental health
Authors: Leslie Roper, Philip Tibbo, Cam Wild, Jody Wolfe, Katherine J Aitchison, Scot E Purdon
Affiliations: University of Alberta
Research Activity: Child and Youth Development : Mental Health
Investigation Type:

Introduction

Several studies have suggested that early life stressors may be implicated in future ill health[1], in particular for psychosis proneness[2] and depression[3]. Our goal was to examine the effects of prenatal psychological and medical events as well as early childhood adverse events on the psychological health of adolescents.

Methods

High school students (n=222) were recruited from Edmonton and surrounding areas to complete an online questionnaire containing measures of psychological health: the Magical Ideation Scale (MIS), the Social Anhedonia Scale (SAS), and the Mood and Feelings Questionnaire (MFQ). The students also completed a measure of childhood adversity: the (amended) Childhood Life Events Scale. In addition, mothers of the students (n=81) also supplied information in a self-report questionnaire regarding prenatal events such as medical difficulties and psychological stressors.

Results

On preliminary analysis, there was a significant association between maternal prenatal psychological stressors and MFQ scores in the students ($p=0.023$). Moreover, students whose mothers had experienced 1 or 2 prenatal medical events had significantly higher MIS scores than those reporting no medical events ($p=0.044$), and there was also a trend towards higher MFQ scores ($p=0.083$). Some associations were in addition found on individual stressor items. Mothers who experienced financial difficulty during pregnancy were associated with higher SAS scores in the students ($p<0.05$), while mothers who reported bleeding during gestation were associated with elevated MFQ scores ($p<0.01$). In addition, students who reported being extremely ill or injured in childhood had significantly higher MIS scores ($p<0.01$).

Conclusion

Prenatal stressors and adverse childhood events appear to affect the psychological health of individuals into late adolescence and may have implications for their future mental health. These investigations appear to suggest that prenatal psychological events may affect the offspring's mood, while prenatal medical events may affect psychosis proneness. Moreover, our findings suggest that specific early life stressors may modulate scores on these measures of mental health.

Acknowledgements: Dr Aitchison holds a Government of Alberta funded Alberta Centennial Addiction and Mental Health Research Chair. Leslie Roper is supported by Chair funds to conduct an MSc in Psychiatry at the UofA. Study funding was provided by an operating grant from the Faculty of Medicine & Dentistry/Alberta Health Services. Kind thanks to the Edmonton Public and St. Albert School Boards, and to all the participants.

[1]Felitti VJ et al. (1998) *Am J Prev Med* 14:245-258,[2]Heins et al. (2011) *Am J Psychiatry* 168:1286-94,[3]Heim and Nemeroff (2001) *Biol Psychiatry* 12:1023-39

Funded By: Faculty of Medicine and Dentistry operating grant, Alberta Centennial Addiction and Mental Health Research Chair

women & children's health research institute

Abstract #: 157
Presenter: Geetha Venkateswaran
Supervisor: Sujata Persad

Title: Role of β-catenin/Active β-catenin in Osteosarcoma progression

Authors: Geetha Venkateswaran, Li Hao, Sujata Persad
Affiliations: University of Alberta

Research Activity: Child and Youth Development : Oncology
Investigation Type: Quantitative Research

Background

Osteosarcoma (OS) is the most common primary bone malignancy with high incidence in children and adolescents. Although the overall survival rate has increased in OS patients over years, it still remains as one of the childhood cancer with lowest overall survival rate. Wnt signaling pathway is one of the signaling pathways deregulated in most cancers. Although a number of studies have shown deregulation of this pathway to be implicated in OS, role of β-catenin (regulator of Wnt signaling) in this cancer is unclear. While some studies support the involvement of β-catenin in OS, others suggest contrary. All these studies investigate the role of β-catenin rather than Active Beta Catenin (ABC) which is transcriptionally active form of β-catenin. ABC transcribes genes involved in cell proliferation, invasiveness and hence promotes cancer. Therefore in our study we are interested in investigating the role of ABC in OS progression and its potential regulation by PI3K pathway, yet another pathway that is deregulated in OS.

Methods

We used a panel of cell line comprising normal human osteoblast and OS cell lines U2OS, Saos2, Saos2-LM7 and 143B. OS specific markers of progression, Ezrin, MMP2, were used as measure of aggressiveness. Cellular β-catenin, ABC and PI3K pathway components were determined by Western Blot (WB). RT-PCR was used for detection of changes in the expression of Wnt-10b with OS progression.

Results

Preliminary results from WB shows increase of ABC in OS cell lines compared to normal osteoblasts. There were moderate differences in ABC levels amongst the OS cell lines. In general, the OS cell lines with high p-AKT levels also showed higher levels of ABC. RT-PCR analysis of Wnt-10b mRNA expression shows a similar trend such that there was greater expression of Wnt-10b in OS cell lines compared to normal osteoblast with moderate differences among the OS cell lines investigated.

Conclusion

Our results show that there is a difference in ABC levels in OS compared to normal osteoblasts with moderate difference within the OS cell lines. However, WB of whole cell lysates may not be representative of changes in ABC. Therefore we plan to evaluate ABC levels in nuclear/cytoplasmic fractions and perform immuno-fluorescence analysis to study alterations in cellular localization of ABC in OS progression. However, our present result indicates that ABC levels are increased in cells with high p-AKT suggesting a possible correlation between the Wnt and PI3K pathway in regulation of ABC in OS.

Funded By: Graduate Studentship

women & children's health research institute

Abstract #: 158
Presenter: Sabina Baghirova
Supervisor: Richard Schulz

Title: Determining the nuclear localization and targets of nuclear matrix metalloproteinase-2 in ischemia-reperfusion injury

Authors: Sabina Baghirova, Marcia Kondo, Bryan Hughes, Frank Fan, Richard Schulz
Affiliations: University of Alberta

Research Activity: Other
Investigation Type: Mixed Methods

Introduction

Matrix metalloproteinases (MMPs) are zinc-dependent proteases which are known to be involved in extracellular matrix remodeling associated with developmental processes and disease progression. MMP-1,-3,-9,-13,-14, and -26 have all been found in the nucleus. However the function and substrates of nuclear MMPs are mostly unknown. MMP-2 has a C-terminal nuclear localization sequence that is exposed on the protein surface. We hypothesize that MMP-2 is present in the nucleus under normal physiological conditions but increases during oxidative stress induced myocardial ischemia-reperfusion (I/R) injury, proteolyzing structural and DNA repair proteins. Lamin A/C, a possible nuclear MMP-2 target, is an intermediate filament protein that provides structural support to the inner part of the nuclear envelope. It has newly identified functions: gene expression, DNA replication, transcription and repair. Novel actions of MMP-2 in the nucleus during oxidative stress contribute to the development of cardiovascular disease, the number one cause of mortality amongst women, and understanding this may result in new therapeutic targets.

Methods

Cytosolic, membrane and nuclear fractions were extracted from isolated rat hearts that were perfused aerobically or subjected to I/R injury. Western blots for lamin A/C (nuclear marker), SERCA2 (membrane marker) and GAPDH (cytosol marker) were used to demonstrate the purity of the nuclear extracts. Gelatin zymography was used to determine MMP-2 activity in fractionated samples. The presence of nuclear MMP-2 was also examined by immuno-fluorescence confocal microscopy in the HT1080 fibrosarcoma cell line. Recombinant lamin A/C was incubated with MMP-2 for 0.5 hr at 37^{o}C.

Results

Western blotting showed that the nuclear fraction was free of cytosolic and membrane contamination. Gelatin zymography of the nuclear extracts showed 64kDa cleaved form of MMP-2 in contrast to 72kDa full length MMP-2 in the cytosolic and membrane fractions. Nuclear fractions from I/R hearts by zymography showed increased MMP-2 activity in the nucleus of I/R versus aerobic heart nuclear fractions. Lamin A/C recombinant protein was proteolyzed in vitro by MMP-2 in a concentration dependent manner and this proteolysis was prevented by the addition of an MMP inhibitor o-phenanthroline.

Conclusions

MMP-2 is present in the nuclear fraction obtained from aerobic rat heart tissue and in intact nuclei of HT1080 cells. The activity of MMP-2 increased in the nucleus after I/R injury. MMP-2 can proteolyse lamin A/C in vitro in a concentration dependent manner. Future experiments will focus on determining MMP-2 colocalization with nuclear bodies, determining nuclear substrates and further discovering the novel function inside the nuclei.

Funded By: FoMD, CIHR

women & children's health research institute

Abstract #:	159
Presenter:	Brandon Chan
Supervisor:	Richard Schulz
Title:	Doxorubicin-induced oxidative stress activates intracellular matrix metalloproteinase-2 in human fibrosarcoma cells
Authors:	Brandon Chan, Bryan Hughes, Frank (Xiaohu) Fan, Richard Schulz
Affiliations:	University of Alberta
Research Activity:	Other
Investigation Type:	Quantitative Research

Introduction

Matrix metalloproteinases (MMPs) are a family of extracellular matrix proteases with important roles in both developmental processes and disease progression. MMP-2 can be secreted as a 72 kDa zymogen which is activated upon extracellular release by the proteolytic removal of its autoinhibitory domain to produce a 64 kDa MMP-2. In addition to its important roles in extracellular matrix remodeling, the Schulz lab was the first to show that MMP-2 can proteolyze intracellular targets including sarcomeric proteins. Intracellular MMP-2 can be activated in vitro by peroxynitrite-mediated S-glutathiolation of its Cys102 residue located on the propeptide domain. MMP-2 activity is involved in several heart pathologies resulting from increased oxidative and nitrosative stress including myocardial ischemia-reperfusion injury. Doxorubicin, a potent chemotherapeutic drug used for childhood and women's cancer, is cardiotoxic in part because it stimulates peroxynitrite biosynthesis. Though effective for the treatment of cancer, cumulative dosing of doxorubicin may cause heart failure in patients undergoing chemotherapy.

Hypothesis

Doxorubicin-induced oxidative stress activates intracellular MMP-2 in both heart and cancer cells.

Methods

To test this, neonatal rat ventricular myocytes (NRVMs) and human fibrosarcoma cells (HT1080 cells) were treated with 0-1 µM doxorubicin for 0.5 and 2 h. MMP-2 activity was measured by gelatin zymography. MMP-2 protein levels were assessed by immunoblotting. Oxidative stress was measured by changes in mitochondrial aconitase activity. Cell death was measured by lactate dehydrogenase release.

Results

In HT1080 cells, 2 h treatment with 0.1-1 µM doxorubicin increased intracellular MMP-2 activity by 60% without any change in MMP-2 protein level. In NRVMs, doxorubicin did not significantly increase intracellular MMP-2 activity. However doxorubicin significantly increased oxidative stress as measured by aconitase activity in a concentration and time dependent manner. At the conditions used, doxorubicin did not induce significant cell death.

Conclusion

Our results support the hypothesis that oxidative stress, stimulated by doxorubicin, may activate intracellular MMP-2 by peroxynitrite-mediated post-translational modification. Doxorubicin-induced intracellular MMP-2 activity can cause intracellular remodeling, which may explain the cases of heart failure in patients undergoing chemotherapy. To visualize changes in intracellular MMP-2 activity in real time, future experiments will use a genetically encoded fluorescence resonance energy transfer (FRET)-based MMP-2 biosensor. This construct contains the MMP-2-selective cleavage site in troponin I genetically fused between two fluorescent proteins. The FRET-based biosensor will allow us to better understand how oxidative stress affects intracellular MMP-2 activity and its specific substrates.

Funded By: CIHR

women & children's health research institute

Abstract #:	160
Presenter:	Brodie Heywood
Supervisor:	Katherine Aitchison
Title:	ABCB1: From target validation to clinical utility
Authors:	Brodie Heywood, Dawon Lee, Yabing Wang, Sarah Curran, Jose Payo-Cano, Amalia Lafuente, Ian Craig, Paramala Santosh, Peter McGuffin, Katherine Aitchison
Affiliations:	University of Alberta
Research Activity:	Other
Investigation Type:	Quantitative Research

Introduction

The ABCB1 gene encodes P-glycoprotein (P-gp), also known as multidrug resistance protein 1 (MDR1), an ATP-dependent xenobiotic efflux pump with broad substrate specificity. ABCB1 polymorphisms can affect P-gp functionality and expression, thus influencing drug absorption at the level of multiple organs including the brain and gut. As a result, ABCB1 genotype may be a valuable predictor of individual treatment response to therapeutic drugs; for example, paclitaxel chemotherapy commonly used in women with ovarian or breast cancer and tacrolimus used in paediatric liver and kidney transplants (Gao et al, 2014; Zhao et al, 2008). Currently, St. Jude Children's Research Hospital employs a subset of targets available on the Affymetrix DMET™ Plus microarray for clinical genotyping in paediatrics; this subset does not include ABCB1. If consistent, accurate results can be confirmed for this gene using the DMET™ Plus microarray method, our research will be a proof-of-concept that this relatively quick and cheap method of genotyping can be useful in the clinic.

Methods

To confirm the accuracy of the DMET™ Plus method of ABCB1 genotyping, we are comparing our results with genotypic data previously obtained from these samples using different SNP-based assays. In addition, we are comparing data generated from different sample types for the ABCB1 markers on the DMET™ Plus microarray.

Results

Preliminary results show a high call rate for ABCB1 SNPs on the DMET™ Plus microarray, and we have confirmed that the DMET™ Plus assay can accurately genotype the tri-allelic ABCB1 SNP rs2032582. Notably, sample type (blood, saliva, or buccal cells) appears to affect the call rate for some SNPs. Additionally, our up-to-date Affymetrix analysis software appeared to be able to more accurately interpret data for a SNP (rs28381915) that an older (2011) version of the software.

Conclusion

By confirming the accuracy of DMET™ Plus ABCB1 genotyping, this target may progress within the DMET™ Plus assay to being one that could be used for predicting treatment outcomes for women and children. Delineating any differential results by sample type will be valuable information for difficult-to-sample patient groups, such as paediatric patients, for whom sampling by saliva may be more feasible than by blood. Additionally, the DMET™ Plus assay can accurately genotype the tri-allelic SNP rs28381915 which may be difficult to genotype.

Acknowledgments

KJA holds an Alberta Centennial Addiction & Mental Health Research Chair.

Funded By: Alberta Addiction & Mental Health Research Partnership Program

women & children's health research institute

Abstract #: 161
Presenter: Xiaoyun Tang
Supervisor: David Brindley

Title: Expression of lipid phosphate phosphatase-1 in cancer cells attenuates lysophosphatidatesignaling, tumor growth and metastasisin mice

Authors: Xiaoyun Tang, Matthew Benesch, David Brindley
Affiliations: University of Alberta

Research Activity: Child and Youth Development : Oncology
Investigation Type:

Introduction

Lipid phosphate phosphatase-1 (LPP1) degrades lysophosphatidate (LPA) and attenuates receptor-mediated signaling. LPP1 expression is low in many cancer cells and tumors compared to normal tissues. It was hypothesized from studies with cultured cells that increasing LPP1 activity would decrease tumor growth and metastasis. This hypothesis has never been tested *in vivo*. To do this, we inducibly expressed LPP1 or a catalytically inactive mutantin cancer cells.

Methods

Lentivirus generation and establishment of stable cell lines, Assays for LPP1, LPA, phosphatidate and diacylglycerol, Real-time PCR, Western blotting and Immunohistochemistry, Intracellular Ca^{2+}-mobilization assay, Small GTPase activation assay, Cell proliferation assay in monolayer and three-dimensional culture, Cell migration assay, Mouse tumor models.

Results

Expressing active LPP1 increased extracellular LPA degradation by 5-fold. It also decreased the stimulation of Ca^{2+}-transients by LPA, a non-dephosphorylatable $LPA_{1/2}$ receptor agonist and a protease-activated receptor-1 peptide. The latter results demonstrate that LPP1 has effects downstream of receptor activation. Decreased Ca^{2+}-mobilization and Rho activation contributed to the effects of LPP1 in attenuating the LPA-induced migration of MDA-MB-231 breast cancer cells and their growth in 3D culture. Increasing LPP1 expression in breast and thyroid cancer cells decreased tumor growth and the metastasis by up to 80%compared to expression of inactive LPP1 or green fluorescent protein in syngeneic and xenograft mouse models.

Conclusion

The present work demonstrates for the first time that increasing the LPP1 activity in three lines of aggressive cancer cells decreases their abilities to produce tumors and metastases in mice.

Funded By: Trainee Travel Grant

women & children's health research institute

Abstract #:	162
Presenter:	Allison Norris
Supervisor:	Shannon Scott
Title:	Developing a knowledge translation tool with families about pediatric chronic pain: a study protocol
Authors:	Shannon Scott, Kathy Reid, Allison Norris, Samina Ali, Lisa Hartling
Affiliations:	University of Alberta
Research Activity:	Child and Youth Development: Pain Management
Investigation Type:	Mixed Methods

Introduction

A patient revolution is on the horizon – one where patients, families and health care professionals work together in partnership. Essential to achieving this ambitious mission and simultaneously improving children's health outcomes is actively engaging children and their families in health care decision making. One such health care issue being increasingly recognized as a significant clinical problem is pediatric chronic pain. Pediatric chronic pain affects between 15-39% of children and their families, yet is it is often under-recognized and under-treated by clinicians. Three types of interventions comprise pediatric chronic pain treatment: pharmacological, physical and psychological interventions. Treatment also must address education and support of families' reactions to their child's pain and how they best support their child. It is well established, however, that conventional modes of communicating complex health information are insufficient and unintentionally may push families into passive bystanders, rather than active decision makers. Building upon recent Stollery Chronic Pain Clinic research that highlighted children and parents' desire for more information about their children's chronic pain condition and its treatment, the purpose of this study is to develop and evaluate an arts based KT tool for families about pediatric chronic pain.

Methods

This study will use a multi-method approach to determine usability of an e-Book prior to widely spread use in the Stollery Hospital. The design of the study will occur over five phases. In the first phase, the research team will conduct semi-structured qualitative interviews of a sample of children with chronic pain and their parents from the Stollery Chronic Pain Clinic. Using the information gained from the interviews, an e-Book prototype will be developed in the second phase, and subsequently shared with pediatric chronic pain experts in the third phase to ensure evidence accuracy and interpretation. Following feedback gained from chronic pain experts, the e-Book will then be tested for usability with parents and children in the Stollery Chronic Pain Clinic. Focus groups will be conducted in the fourth phase with children with chronic pain and their parents to refine the e-Book and test the short term knowledge translation impact of the tool. The dissemination of the e-Book throughout the Stollery Children's Hospital is the final phase.

Results

Currently, we are not in the data collection phase of this project.

Conclusion

The relevance of this study is that children and parents will be empowered to be meaningful partners in the creation of an e-Book about pediatric chronic pain.

Funded By: Innovation Grant

women & children's health research institute

Abstract #: 163
Presenter: Qendresa Beka
Supervisor: Padma Kaul

Title: Impact of diabetes during pregnancy on maternal mental health

Authors: Qendresa Beka, Anamaria Savu, Dawn Kingston, Jeff Johnson, Padma Kaul
Affiliations: University of Alberta

Research Activity: Maternal Research : Perinatal Mental Health
Investigation Type: Quantitative Research

Introduction

Gestational diabetes mellitus (GDM) is diabetes first recognized in women during pregnancy and is an established risk factor for the subsequent development of type 2 diabetes for both mother and child. Mental health disorders have been shown to be more prevalent in people with diabetes. However, less is known about the association between GDM and mental health disorders, and is the focus of our study.

Methods

Our patient population consists of all Albertan women who delivered babies between April 1, 1999 and March 31, 2009. For the study time period, data from the the Alberta Perinatal Health Program (APHP) was linked to administrative data on hospital discharges, emergency department visits, and outpatient visits (clinic and physician office). We restricted our analysis to the first delivery for each woman in the study time period. Anxiety and affective mood disorders 2 year prior to delivery and one year post delivery were identified using established ICD 9/ICD 10 CM codes. Trends in GDM and mental health issues were examined by year.

Results

Among 248 960 women, the annual prevalence of GDM in Alberta increased from 3.3% in 1999 to 4.6% in 2009. During the same time period the prevalence of mental health disorders (anxiety and affective disorders combined) two years prior to pregnancy decreased from 22.7% to 18.5% ($p<0.01$). The prevalence of mental disorders during one year following delivery decreased from 16.5% to 12.7% ($p<0.01$). However, the prevalence of anxiety and affective disorders was higher among women with GDM than among women without GDM (Figure).

Conclusion

The prevalence of mental health issues is considerable among pregnant women in Alberta. The presence of GDM may be a marker for higher risk of mental health issues in this population.

women & children's health research institute

Abstract #:	164
Presenter:	Katherine Bannar-Martin
Supervisor:	Shannon Scott
Title:	A protocol for a systematic review of the use of process evaluations in knowledge translation research
Authors:	Shannon Scott, Thomas Rotter, Katherine Bannar-Martin, Rachel Flynn, Thane Chambers, Lisa Hartling
Affiliations:	University of Alberta
Research Activity:	Other
Investigation Type:	Quantitative Research

Introduction

Experimental designs for evaluating knowledge translation (KT) interventions for professional behavior change can provide strong estimates of intervention effectiveness but offer limited insight into *how* the intervention worked, and how it may be moderated. The ability to generalize study findings to different contexts, organizations or clinical problems is therefore compromised. Consequently, researchers have started exploring the *causal mechanisms* in KT intervention studies through complementary studies (process evaluations), yet there are no methodological standards to guide their design. This study focuses on improving KT process evaluations by synthesizing current evidence to provide methodological recommendations.

Methods

A medical research librarian developed and implemented peer-reviewed search strategies. Studies had to be in English, published since 1996, and were not excluded based on design. A two-step screening process occurred. First, a single reviewer screened all titles and abstracts, and studies had to be or contain: (1) a process evaluation of a KT intervention study in health; (2) a primary research study; and (3) a licensed health care professional (HCP) providing or receiving the KT intervention. A second reviewer screened a random sample of 6% of the titles with 94% inter-rater reliability. Data to be extracted includes: (1) study design, (2) data collection types, timing and approaches, (3) theoretical influences, (4) approaches to evaluate the KT intervention dose delivered, dose received, fidelity, (5) data analysis, and (6) study outcomes. A multi-method scoring tool will be used to assess the methodological quality of the studies. Extracted data will be analyzed by study design, study quality, and KT intervention. Where appropriate, sensitivity analysis will be conducted to explore sources of heterogeneity and data will be pooled for meta-analysis using a random effects model.

Results

Screening of the initial set of 9690 articles is complete, and 214 studies fit our inclusion criteria. Of those 214 studies, 165 studies included HCPs as the intervention recipients and used qualitative and/or multiple quantitative process measures. These 154 studies are now undergoing detailed data extraction and analysis.

Conclusion

There is widespread acceptance that the generalizability of quantitative trials of KT interventions would be enhanced through complementary process evaluations alongside trials. This systematic review serves as a 'state of the science' on methodological approaches to process evaluations and will allow us to: (1) take stock of current research approaches, and (2) develop concrete recommendations and a standard guide for designing and implementing KT process evaluations for multiple end-user groups.

Funded By: CIHR

women & children's health research institute

Abstract #: 165
Presenter: Colin Andrews
Supervisor: Silvia Pagliardini

Title: Abdominal recruitment and expiratory activity In REM sleep

Authors: Colin Andrews
Affiliations: University of Alberta

Research Activity: Other
Investigation Type: Mixed Methods

Introduction

Breathing is more vulnerable to apneas and irregular breathing patterns during rapid eye movement (REM) sleep. Results from in vivo sleep studies in rats show enhanced recurrent expiratory activity due to the recruitment of the abdominal muscles (ABD, the principal expiratory muscles). To develop an understanding of the characteristics of ABD recruitment during REM periods and their relationship with the breathing pattern and its irregularities, we sought to characterize REM epochs that displayed ABD muscle recruitments and compare them with REM epochs that did not. Further, we compared within the same REM epoch respiratory values before and during recruitment of ABD muscles.

Methods

We implanted adult rats with electroencephalograph (EEG) electrodes to determine sleep stages, and with electromyography (EMG) electrodes in the diaphragm (the principal inspiratory muscle), ABD and neck muscles to measure respiratory activity and posture. Rats were recorded inside a whole body plethysmograph to determine tidal volume and ventilation.

Results

Epochs of REM sleep containing ABD recruitments (ABD+), were preceded by periods of increased respiratory variability. Further, we observed that ABD+ periods had increased diaphragm EMG activity, along with increased tidal volume when compared to the periods prior to ABD muscle activation.

Conclusion

These results suggest that expiratory muscle activity is recruited when respiration is more irregular and its recruitment improve ventilation. Further study of the role of expiratory ABD recruitments could translate to a greater understanding of respiration during sleep in humans, particularly concerning those with sleep-disordered breathing.

Funded By: Summer Studentship

women & children's health research institute

Abstract #:	166
Presenter:	Rachel Flynn
Supervisor:	Shannon Scott
Title:	A theory based evaluation of Lean process improvement in pediatric healthcare-research proposal
Authors:	Rachel Flynn, Thomas Rotter, Shannon Scott
Affiliations:	University of Alberta
Research Activity:	Other
Investigation Type:	Mixed Methods

Introduction

Globally, pediatric health services research has been largely underrepresented. Pediatric healthcare requires quality improvement (QI) and knowledge translation (KT) energies to ensure the best research evidence informs practice. Lean is a QI program that has gained increasing attention across healthcare agendas, its values of quality, customer needs, waste reduction and cost efficiency have made it an attractive approach for healthcare systems to adopt. However there is a paucity of theory based research on how lean can be best implemented in various healthcare contexts and what factors shape the success of lean. Without understanding the exclusive patterns, mechanisms and nuances of lean implementation, there is no way to ensure the best available research can be predictably and consistently implemented in pediatric healthcare settings to improve quality and to benefit Canadian children.

Knowledge Gap

There is a lack of evidence about the process, use and effectiveness of lean implementation activities (Rapid Improvement Workshops, Value Stream Mapping, 5S) in improving the quality of pediatric healthcare.

Objectives

The objectives of my PhD research are to:1)Determine the current research evidence about lean implementation activities in healthcare.2)Explore the perceptions of frontline healthcare providers and leadership on lean implementation activities in their pediatric work setting (barriers, facilitators, process and use). 3)Evaluate the process and use of these lean implementation activities in these settings and the impact on patient care, cost and practice.

Methods

A mixed methods theory-based evaluation of lean activities across acute pediatric healthcare settings in one health region (Saskatoon), where lean implementation has been in place since 2012.

Conclusion

This research holds the potential to contribute to the science and evidence base of lean, on the implementation and use of lean activities to improve pediatric healthcare and whether lean is a viable QI program for pediatric healthcare.

Funded By: Graduate Studentship

women & children's health research institute

Abstract #:	167
Presenter:	Michelle Foisy
Supervisor:	Lisa Hartling
Title:	Overviews of reviews: A new publication type and an emerging method of knowledge synthesis
Authors:	Michelle Foisy, Denise Thomson, Donna M Dryden, Lisa Hartling
Affiliations:	University of Alberta
Research Activity:	Other
Investigation Type:	Qualitative Research

Introduction

Overviews of reviews (overviews) are an emerging method of knowledge synthesis in the field of evidence-based medicine; they integrate information from multiple systematic reviews (SRs) to provide a single synthesis of relevant evidence for clinical decision-making. Overviews may be preferred by front-line clinicians and other decision-makers because they provide a single synthesis of all systematic reviews regarding the health condition or intervention in question.

Objectives

To describe what overviews are, when overviews should be conducted, and the steps involved in conducting overviews.

Methods

Descriptive summary of our experience conducting over 30 overviews in pediatric medicine, including recommendations and practical considerations for issues commonly encountered.

Results

Overviews are broader in scope than any individual SR, but use methods similar to SRs (i.e. searching, screening, inclusion, methodological quality assessment, data extraction). In addition, there are several preconditions that must be met prior to undertaking an overview. We have been developing overviews since 2006 and have produced overviews on a wide range of topics related to the treatment of common pediatric conditions, such as chronic abdominal pain, bronchiolitis, attention deficit hyperactivity disorder, sore throat, and eczema. While some steps of the overview process are typically straightforward, we have encountered two key challenges when conducting overviews. First, since the unit of analysis is the SR, overview authors are limited by the scope and methods of the original SRs. This can create challenges if the SRs are not methodologically rigorous or if overview authors need to re-analyze outcome data to answer specific clinical questions. Second, there are often multiple SRs published on a given topic area, and it can be challenging to decide which SRs to include in an overview. Overview authors need to critically assess the SRs to identify theose most likely to contribute valid, high-quality data.

Conclusion

Overviews bring together the highest quality evidence into a "friendly front end" for decision-makers. However, overviews are a relatively new publication type, and their methodology has not yet been standardized. As a result, published overviews show considerable variation in their methods and reporting, which has implications for the validity of their results and conclusions. We are currently conducting a series of projects designed to refine and advance overview methods. Our end goal is to publish evidence-based recommendations for both the conduct and reporting of overviews. Ultimately, this information will ensure that overviews represent the most valid evidence to support clinical decision-making and optimize health outcomes.

Funded By: CIHR, KT Canada

women & children's health research institute

Abstract #:	168
Presenter:	Aimee Gonzalez de Armas
Supervisor:	Shannon Scott
Title:	Engaging consumers to evaluate knowledge translation approaches in a Pan-Canadian child health study
Authors:	Aimee Gonzalez de Armas, Shannon Scott
Affiliations:	University of Alberta
Research Activity:	Other
Investigation Type:	Mixed Methods

Purpose and Overview

Translating Emergency Knowledge for Kids (TREKK) is a Pan-Canadian initiative aimed at ensuring the latest research in pediatric emergency care is applied within general EDs (S. Scott, a Co-Director, T. Klassen, Network Director). TREKK's vision is to improve the outcomes of children cared for in all Canadian Emergency Departments (EDs), as the majority of Canadian children requiring emergency care are treated in general EDs. The foundation of the TREKK initiative is a large, pan-Canadian multi-method needs assessment of the knowledge needs and preferences of health consumers and health care professionals in general EDs (led by Scott and her team). The needs assessment was conducted in 32 EDs spanning 9 provinces and 1 territory, using iPads and an online survey to assess the information needs and knowledge mobilization preferences of health consumers and health care professionals in these sites. The needs assessment data is informing TREKK's national knowledge priorities and resource allocation.

Question

What are the most effective KT approaches to present data to healthcare consumers?

Methods

Using the TREKK health consumer data and findings report, we met and consulted with the TREKK Parental Advisory Board to understand consumer preferences for data presentation. Next we developed three different KT approaches (infographics, videos, traditional graphs) to present the data based on this consumer engagement. Then we conducted a survey of health consumers (assessing clarity, comprehensibility, aesthetic appeal) using www.trekk.ca to determine preference. Data were cleaned and analyzed using SPSS to obtain means and modes for the respondents' assessment of each KT approach, and frequencies of the demographic data.

Findings

40 responses were analyzed. Although all three KT approaches received similar scores, the infographic approach received higher scores overall.

Conclusion

The similarity of scores received suggests that a combination of KT approaches may be most effective.

Funded By: CIHR Health Professional Student Research Award, AIHS Summer Studentship, Faculty of Nursing Student Research Award

women & children's health research institute

Abstract #:	169
Presenter:	Humam Saltaji
Supervisor:	Carlos Flores-Mir
Title:	Assessing methodological quality of clinical trials included in orthodontic and pediatric dental systematic reviews
Authors:	Humam Saltaji, Susan Armijo-Olivo, Greta Cummings, Maryam Amin, Carlos Flores-Mir
Affiliations:	University of Alberta
Research Activity:	Other
Investigation Type:	Quantitative Research

Background and Objectives

Assessing the methodological quality of clinical trials is an essential step when selecting the best clinical evidence and conducting systematic reviews (SRs) of dental interventions. The goal of this study was to identify the tools used to assess methodological quality of studies included in orthodontic and pediatric dental SRs.

Methods

An electronic search of seven databases was performed. Studies were included if they were therapeutic or non-therapeutic orthodontic and pediatric dental SRs. Data were extracted from all the included SRs on key descriptive characteristics and methodological quality assessment tools used in these SRs.

Results

174 (21 Cochrane and 153 non-Cochrane) SRs were identified. 81.9% of the orthodontic SRs were categorized as therapeutic, with 92.9% examining non-drug interventions, while approximately third of the non-therapeutic SRs were classified as epidemiological SRs. 16 (9%) of the SRs used the Cochrane tool/Handbook, 12 (6.8%) used methodological quality items adapted from more than one risk of bias tool, while 15% (n = 27) of the SRs used a non-validated methodological checklist.

Conclusion

Methodological and descriptive characteristics varied extensively. There is a clear need for more dental primary studies, and for a methodological quality assessment tool designed specifically for assessing quality of dental trials.

Funded By: Graduate Studentship

women & children's health research institute

Abstract #: 170
Presenter: Carissa Samoluk
Supervisor: Jill Konkin

Title: Contraception use and delivery on campus

Authors: Carissa Samoluk, Dana MacIntyre
Affiliations: University of Alberta

Research Activity: Other
Investigation Type: Qualitative Research

Introduction

Currently half of all pregnancies in Canada are unplanned. Access to information about contraception is an important element in reducing unplanned pregnancies. Many women begin seeking contraception education in their late teens and early adulthood, coinciding with when many women begin their university careers. We were curious to find out how women at the University of Alberta educate themselves on contraception and decide which contraceptive method is the best option for them and to determine how to improve contraception education and delivery on campus.

Methods

Through focus groups with UofA female students, we inquired into their specific experiences with contraception using a semi-structured interview script. Women were recruited through posters placed around campus; participation was voluntary with no incentives given; formal consent was obtained; and, they were made aware that they could refrain from answering questions. Each woman attending a focus group completed an anonymous survey outlining contraceptive options they had used. Each focus group was recorded and transcribed. The transcripts were analyzed using thematic analysis. Descriptive statistical methods were used to analyze the surveys.

Results

Major themes identified were lack of patient education, poor access to correct information, and the influence of public perception on contraception. Reasons for lack of patient education included poor reproductive health education, short patient visits with healthcare providers, and lack of counseling by physicians about contraceptive options. Access to correct information was a barrier as many women were unaware of credible online resources, had received conflicting information from physicians, and found family and friends to be unreliable resources. Lastly, public perception of contraception affected a woman's choice, with many women perceiving the oral contraceptive pill to be the most popular option, and thus would be the best choice for them.

Conclusion

The results of this study point to a need to improve the informational resources available to young women at the UofA about contraception and their access to knowledgeable healthcare providers. Further areas for research include identifying the effectiveness of various educational modalities such as pamphlets, websites, seminars, healthcare professional counseling, and then implementing that educational modality to ultimately decrease the proportion of unplanned pregnancies.

women & children's health research institute

Abstract #:	171
Presenter:	Shannon Scott
Supervisor:	
Title:	Information needs and preferences of parents seeking care for their children in general emergency departments in Canada
Authors:	Shannon Scott, Lisa Given, Lauren Albrecht, Lisa Hartling, David Johnson, Mona Jabbour, Terry P. Klassen
Affiliations:	University of Alberta
Research Activity:	Other
Investigation Type:	Quantitative Research

Introduction

In Canada, the majority of children requiring emergency care are treated in general emergency departments (EDs). Simultaneously, there is a growing trend in healthcare towards increased consumer participation, leading to an unprecedented demand for consumer friendly, research-based health information and family-centred care. The Translating Emergency Knowledge for Kids (TREKK) initiative is a multi-phase, pan-Canadian project aimed at ensuring the latest research in pediatric emergency medicine is implemented in general EDs.

Objectives

To partner with 32 general EDs to determine knowledge needs and preferences of parents seeking care for their children in general EDs across Canada.

Methods

An electronic survey was developed to collect asynchronous survey data via an interactive iPad 'app'. Data was analyzed using SPSS.

Results

Data collection occurred from May 2012 to October 2013 and resulted in 897 parental surveys. It was determined that 39% had sought health information prior to coming to the ED. Participants typically found health information by talking to trusted professionals (69%) or through internet search engines (53%); however, 74% indicated that they would prefer to learn health information by talking in-person with a healthcare professional. Parents reported additional information is needed about being in the ED with their child, including explanation of the child's illness/condition (47%), treatment information (44%), and care instructions (42%).

Conclusion

The findings from this study will be of value to multiple stakeholders and will enable the TREKK Knowledge Mobilization Initiative to offer evidence-based information and interventions to ensure the best quality care for all Canadian children.

Funded By: Start-up or Retention Funding

women & children's health research institute

Abstract #: 172
Presenter: Lauren Albrecht
Supervisor: Shannon D. Scott

Title: Knowledge translation tools for parents with children with croup and gastroenteritis

Authors: Shannon D. Scott, Lisa Hartling, Lauren Albrecht, Mandy Archibald, Michele Hamm, Lisa Knisley, Terry P. Klassen
Affiliations: University of Alberta

Research Activity: Other
Investigation Type: Quantitative Research

Introduction

It is well established that conventional modes of communicating complex health information to parents with ill children are substandard due to overuse of complex medical jargon, as well as differences in literacy skills and language competencies. Ensuring that families fully understand essential health information about caring for their ill child is critical to the efficient use of health services and improving health outcomes. Recently novel approaches have been developed to engage with parents and translate complex health information, including the use of stories, arts and digital media.

Purpose

To actively engage health care consumers (i.e., parents) in the development, implementation, and evaluation of art-based, digital knowledge translation (KT) tools (i.e., RSA animation whiteboards and eBooks with embedded audio and visual features) for two common pediatric conditions, croup and gastroenteritis.

Methods

Partnering with Translating Emergency Knowledge for Kids (TREKK) and Pediatric Emergency Research Canada (PERC) for access to families with acutely ill children, we will use mixed methods approaches, including qualitative interviews and focus groups and quantitative surveys and online analytics, to develop the KT tools and determine consumers' usability of these tools. Social media will be used for widespread implementation and mainstream digital evaluation frameworks will be employed to evaluate uptake of these tools.

Results/Conclusion

This research will develop new art-based, digital KT tools to implement, high quality evidence on croup and gastroenteritis treatment and management. This approach has the potential to yield large dividends for life long health and quality of life of Canadian children, as well as the Canadian health care system.

Funded By: CIHR

women & children's health research institute

Abstract #:	173
Presenter:	Samir H Barghout
Supervisor:	YangXin Fu
Title:	RUNX3 and Wnt signaling pathway contribute to carboplatin resistance of epithelial ovarian cancer cells
Authors:	Samir H Barghout, Nubia Zepeda, Krista Vincent, Abul K Azad, Zhihua Xu, Christine Yang, Helen Steed, Lynne M Postovit, YangXin Fu
Affiliations:	University of Alberta
Research Activity:	Women's Health : Oncology
Investigation Type:	Mixed Methods

Introduction

Ovarian cancer is the leading cause of death due to gynecologic malignancies and the fifth leading cause of cancer-related mortalities in women. Epithelial ovarian cancer (EOC) is the major type of ovarian cancer, constituting approximately 90 % of all ovarian malignancies. Despite the initial positive response to the current first-line treatment (platinum-paclitaxel combination), relapse occurs in most EOC patients and the recurrent disease is resistant to current chemotherapy regimens. Identifying the molecular mechanisms underlying chemoresistance will help to develop more effective therapeutic strategies.

Methods

EOC cell line A2780s (cisplatin-sensitive) and its derivative A2780cp (cisplatin-resistant) cells were studied using DNA microarray, ingenuity pathway analysis (IPA), quantitative real-time polymerase chain reaction (qRT-PCR), Western blotting, neutral red uptake assay, clonogenic assay and LEF/TCF-driven luciferase reporter assay. RUNX3 expression in human primary EOC cells and primary ovarian surface epithelium (OSE) cells was determined by Western blotting.

Results

The gene expression profile analysis showed that RUNX3 expression was elevated in cisplatin-resistant A2780cp cells compared to the cisplatin-sensitive counterpart A2780s cells, which was confirmed by qRT-PCR and Western blotting. Analysis of the microarray data from the Gene Expression Omnibus (GEO) database for RUNX3 and cisplatin resistance showed that RUNX3 expression was significantly higher in EOC tissues from chemoresistant patients compared to EOC tissues from chemosensitive patients. We also confirmed that RUNX3 expression was elevated in human primary EOC cells compared to primary OSE cells. Overexpression of RUNX3 rendered A2780s cells more resistant to carboplatin and overexpression of the dominant-negative RUNX3 (dnRUNX3) resulted in a moderate chemosensitization of A2780cp cells to carboplatin. Mechanistically, dnRUNX3 sensitizes A2780cp cells to carboplatin-induced apoptosis likely by decreasing the expression of the cellular inhibitor of apoptosis 2 (cIAP2). The gene expression profile analysis also suggested that Wnt/β-catenin signaling pathway was more active in A2780cp cells compared to A2780s cells, because the endogenous Wnt inhibitory proteins (DKK1, SFRP1 and FRZB) were down-regulated and Wnt ligands (WNT3, WNT11 and WNT3A) and Wnt target genes (*JUN*, *CCND1*, and *AXIN2*) were up-regulated in A2780cp cells. Using the LEF/TCF-driven luciferase reporter assay, we confirmed that β-catenin transcriptional activity was higher in A2780cp cells than in A2780s cells. Combined treatment of carboplatin and CCT036477 (a β-catenin inhibitor) was more effective in killing A2780cp cells than either agent alone.

Conclusion

Our data demonstrate that RUNX3 and Wnt/β-catenin signaling contribute to carboplatin resistance of A2780cp cells, suggesting that they could be potential therapeutic targets to treat resistant the disease.

Funded By: Trainee Travel Grant

women & children's health research institute

Abstract #: 174
Presenter: Juliana Valencia Serna
Supervisor: Hasan Uludag
Title: Cell and tumor growth arrest of chronic myeloid leukemia cells by siRNA delivery with lipid-modified polymers carriers
Authors: Juliana Valencia-Serna, Nicole Chan, Xiaohong Yang, Hamid M Aliabadi, Manoj B Parmar, Xiaoyan Jiang, Hasan Uludag
Affiliations: University of Alberta
Research Activity: Women's Health : Oncology
Investigation Type: Quantitative Research

Introduction

Chronic Myeloid Leukemia (CML) is initialized at the hematopoietic stem cells after a chromosomal translocation (BCR-ABL fusion oncogene) which causes uncontrolled myeloid cell expansion and accumulation in the blood system. Drug resistance and insensitivity to current leukemia treatments call for development of new treatments. To control the expression of BCR-ABL or other aberrant genes, synthetic small interfering RNA (siRNA) can be delivered into cells to interact with target mRNA and silence protein expression. The aim of this project is to deliver siRNA moieties that reach the BCR-ABL mRNA of CML cells with the use of a novel polymeric carrier, which consists of low molecular weight polyethylenimine (PEI) grafted with linoleic acid (LA) (PEI1.2-αLA), and to evaluate its potential in the reduction of CML cell and tumor growth.

Methods

Decrease in green mean fluorescence (protein silencing) of PEI1.2-αLA was assessed by flow cytometry and compared with commercial reagents using GFP-expressing K562 cells. Cell viability changes after BCR-ABL siRNA delivery were assessed by MTT experiments. CML tumors grown in mice were injected in their vicinity with PEI1.2-αLA/siRNA complexes 3 times every 72 h, and tumor volume was measured every 3 days. Tumors were processed for BCR-ABL mRNA quantification by PCR.

Results

Based on flow cytometry results, commercial reagents show a silencing of 80% while PEI1.2-αLA show a silencing of 54% without inducing as much cell death as PEI25 and Turbofect. In cell viability assay and using PEI1.2-αLA, control siRNA treatment showed an initial toxicity but cells recovered from it. In contrast, BCR-ABL siRNA treatment induced cell growth arrest for at least 4 days ($\rho < 0.01$). SiRNA treatment of tumors grown in mice show that GFP siRNA treatment has a slight decrease in tumor volumes after day 10, suggesting a degree of toxicity; conversely, BCR-ABL siRNA treatment was effective in reducing tumor volumes starting from day 3. ddPCR supports this effect by revealing a reduction of the BCR-ABL mRNA expression.

Conclusion

With the aim of balancing out effective transfection with lower cytotoxicity, PEI1.2 was grafted with specific lipid moiety and degree modification. PEI1.2-αLA polymer showed similar effect to PEI25 in terms of transfection but milder effect on the cell numbers. Decrease of BCR-ABL mRNA by siRNA delivery shows a functional effect in restraining cell proliferation in vitro and in vivo. These data demonstrate the potential of PEI1.2-αLA polymer to effectively deliver siRNA and for therapeutic use for CML treatment.

Funded By: NSERC CREATE Program

women & children's health research institute

Abstract #:	175
Presenter:	Manoj Parmar
Supervisor:	Hasan Uludag
Title:	Targeting cell cycle proteins in breast cancer cells by siRNA using lipid-substituted polyethylenimine
Authors:	Manoj B. Parmar, Hamidreza Montazeri Aliabadi, Parvin Mahdipoor, Cezary Kucharski, Robert Maranchuk, Hasan Uludag
Affiliations:	University of Alberta
Research Activity:	Women's Health : Oncology
Investigation Type:	Quantitative Research

Introduction

There are significant limitations (side effects) to all breast cancer chemotherapy regimens, radiation and surgical treatments, which urgently warrant a search for alternative and more effective therapies. Control of breast cancer growth based on RNA interference (RNAi) using small interfering RNA (siRNA) has been a promising approach in recent years. The siRNA-mediated silencing of a unique or over-expressed cell cycle protein that is essential for unregulated cell growth could lead to malignant cell death and, in turn, control tumor growth without affecting the normal tissues.

Methods and Results

To identify the best carrier for siRNA delivery against cell cycle proteins, we screened low molecular weight (2.0 kDa) linoleic acid, caprylic acid and α-linoleic acid substituted polyethylenimines (PEI) with commercially available carriers by inhibition of cell growth assay. The linoleic acid substituted PEI (PEI-LA) has delivered the siRNA most successfully. The uptake of siRNA-carrier complexes was determined by flow cytometry and the up-taken complexes per cell were calculated by confocal microscopy. To explore the potential cell cycle proteins as therapeutic targets, we screened an siRNA library in MDA-MB-231 and MDA-MB-435 cells using PEI-LA as a delivery agent. Out of 169 cell cycle protein targets, the siRNA against cell division cycle protein 20 (CDC20), a recombinase RAD51, and serine-threonine protein kinase CHEK1 diminished the cell growth most significantly in MDA-MB-435 cells. These identified targets with another well-studied cell cycle protein, kinesin spindle protein (KSP), were then evaluated in MDA-MB-435, MDA-MB-231 and MCF7 cells using independently prepared siRNAs. KSP was the most successful target among all identified cell cycle proteins as around 80% MDA-MB-435 cell growth was inhibited by KSP siRNA. However, the significant down-regulation of mRNA transcript of all proteins was found by digital-PCR. The synergistic effect was not seen in the combinational siRNA delivery of cell cycle proteins. We also explored the efficacy of dicer-substrate siRNAs (DsiRNAs) against CDC20, RAD51 and CHEK1. All DsiRNAs decreased the cell growth significantly. However, CDC20 was the most effective DsiRNA since it inhibited MDA-MB-435 and MCF7 cell growth approximately 80%. Currently, we are determining the efficacy of CDC20 DsiRNA *in vivo* over time-period sensitivity.

Conclusion

The identified cell cycle proteins could be promising targets to treat breast cancer by non-viral RNAi therapy. The presented study has enlightened the importance of cell cycle protein targets in cell survival and breast cancer therapy, and has given the safe and nontoxic delivery system (PEI-LA) for the down-regulation of cell cycle proteins.

Funded By: Graduate Studentship

women & children's health research institute

Abstract #:	176
Presenter:	Hoda Soleymani Abyaneh
Supervisor:	Afsaneh Lavasanifar
Title:	Towards development of polymeric micellar nano-carriers for tumor targeted drug delivery: The effect of core forming block on micellar stability
Authors:	Hoda Soleymani Abyaneh, Mohammad Reza Vakili, Fanglin Zhan, Phillip Choi, Afsaneh Lavasanifar
Affiliations:	University of Alberta
Research Activity:	Women's Health : Oncology
Investigation Type:	Mixed Methods

Introduction

The long-term objective of this study is to design polymeric micelles capable of efficient drug loading and targeted delivery to tumor. In this study, the effect of core-forming block on the formation of stereo-complex micelles from a blend of oppositely oriented stereo-active block copolymers and its influence on micellar stability was investigated.

Methods

AB diblock copolymers consisting of methoxy poly(ethylene oxide) (MePEO) as the A block and poly(lactide)s (PLA)s of different stereochemistry as the B block; as well as ABC triblock copolymers of MePEO; PLAs (as A and B block, respectively) and poly(ε-caprolactone) (PCL) or poly(α-benzylcarboxylate-ε-caprolactone) (PBCL) as the C block were synthesized. Block copolymers were characterized for their chemical structure, optical rotation, thermal properties and critical micellar concentration (CMC) by NMR, polarimetry, differential scanning calorimetry and dynamic light scattering. Mixed micelles of either PEO-PLA, PEO-PLA-PCL, or PEO-PLA-PBCL were prepared by blending a 1:1 molar ratio of poly(D-lactide) (PDLA) and poly(L-lactide) (PLLA) containing block copolymers. Micelles were then characterized for their Z average diameter, polydispersity and kinetic stability.

Results

Mixed micelles of PEO-PLLA/PEO-PDLA and PEO-PLLA-PCL/PEO-PDLA-PCL showed a lower CMC and larger average diameter compared to those of PEO-PLLA-PBCL/PEO-PDLA-PBCL. The introduction of the third block (block C) appeared to interfere with the formation of stereo-complex micelles from a blend of block copolymers containing stereo-active PLA as block B. Kinetic stability upon incubation with sodium dodecyl sulfate was the highest for PEO-PLA and the lowest for PEO-PLA-PCL mixed micelles.

Conclusion

Chemical tailoring of the micellar core in mixed micelles from a blend of oppositely oriented stereo-active block copolymers may be used to optimize their size and stability and eventually lead to improved accumulation and drug delivery to solid tumors.

Funded By: Graduate Studentship

women & children's health research institute

Abstract #: 177
Presenter: Deniz Meneksedag
Supervisor: Hasan Uludag
Title: Probing the effect of endogenous molecules on siRNA-PEI Polyplexes
Authors: Deniz Meneksedag, Tian Tang, Hasan Uludag
Affiliations: University of Alberta
Research Activity: Women's Health : Oncology
Investigation Type: Quantitative Research

Introduction

Drug resistance is one of the main causes underlying the failure in cancer chemotherapy; e.g. 50-70% of the breast and ovarian cancer patients were reported to display multidrug resistance (MDR). Silencing of the overexpressed proteins associated with MDR, such as P-glycoprotein (P-gp), with short interfering RNA (siRNA) delivery is a promising approach for the elimination MDR, and hence for the treatment of cancer. Delivery of siRNA is composed of several stages; initiated with the formation of polyplexes from siRNAs and carriers, followed by endocytosis, release into cytosol and dissociation of siRNAs from their carrier vectors. Despite the great amount of research pursued on siRNA therapeutics, the underlying mechanisms of polyplex dissociation and how endogenous molecules may affect the integrity of polyplexes in cytosol are still unclear; which hinder the development of more effective delivery systems. In order to enlighten this gap, we have focused on miRNA-21 and heparin as representative anionic endogenous molecules in this study, and investigated their effects on the integrity of siRNA polyplexes, which are capable of P-gp silencing.

Methods

We have used a combined computational and experimental approach to assess (i) the binding of polymeric carrier, polyethylenimine (PEI), to siRNA and miRNA, and (ii) the effect of miRNA and heparin on the integrity of pre-formed siRNA-PEI polyplexes. For computational studies, simulations were performed with NAMD molecular dynamics (MD) package, and trajectories were analyzed with Visual Molecular Dynamics (VMD) program for structural properties. For experimental studies, PEI binding was investigated with gel electrophoresis mobility shift assay (EMSA) and SYBR Green II dye exclusion assays, while the effect of miRNA and heparin on polyplexes was assessed with EMSA.

Results and Conclusion

Individual complexation simulations along with EMSA and SYBR Green II dye exclusion assays revealed PEI's slightly better binding to miRNA than siRNA. Despite the observed better binding, miRNA introduction into pre-formed siRNA-PEI polyplex failed to break the existing interactions between siRNA and PEI. Instead, the miRNA bound to the pre-formed siRNA polyplex through the electrostatic interactions with the accessible PEIs, and formed an external layer coating the polyplex. This ternary structure reveals some implications, such as layer-by-layer coating of polyplexes, which potentially can be useful for more controlled siRNA loading into polyplexes. On the other hand, heparin introduction resulted in successful dissociation in experiments. Simulations are being performed to examine the molecular details of heparin's effect on polyplexes, which will reveal the key interactions leading to dissociation.

Funded By: NSERC, CIHR, AIHS, AITF, CFI

women & children's health research institute

Abstract #: 178
Presenter: Habib Al Yousef
Supervisor: Roger Leng
Title: Influences of ubiquitin ligases on p53 regulation post-irradiation in ATM-proficient and ATM-deficient cells
Authors: Habib Al Yousef
Affiliations: University of Alberta
Research Activity: Women's Health : Oncology
Investigation Type:

Introduction

The importance of p53 tumor suppressor is reflected by the fact that it is inactivated in more than 50% of all human cancers. The mechanism that controls the tight regulation of p53 has been extensively studied, but not yet fully understood. In unstressed cells, PIRH-2 and UBE4B Ubiquitin ligases degrade p53 and keep it at basal level but their roles in regulating p53 in the DNA damage response remains largely unknown. Following exposure to DNA-damaging agents like ionizing radiation; both ATM (Ataxia Telangiectasia Mutated) and ATR (Ataxia Telangiectasia and Rad3 related) protein kinases activate and stabilize p53 via phosphorylation. The precise contribution of this phosphorylation is uncertain. So, I will examine the expression levels of p53, UBE4B and PIRH-2 and determine the phosphorylation status of p53 in response to gamma radiation in normal and ATM-deficient cells.

Methods

Expression of p53 and its phosphorylated forms (Ser15, Ser 392,Ser 20, Ser37), protein kinases (ATM and ATR) and ubiquitin ligases (PIRH-2 UBE4B) will be analyzed by western blotting using wild type (GM00714B) and ATM-deficient AT-derived) (GM00719B and VKE cells) EBV-transformed lymphoblastoid cell lines (LCLs). This will be executed post-exposure to 2 Gray and 6 Gray of g radiation in 24 hour time course.

Results

In AT cells, UBE4B and PIRH-2 expression was elevated at early times post-irradiation and phosphorylation patterns are similar to normal cells which indicate that p53 activation in AT cells isn't exclusively ATM-dependent.

Conclusion

UBE4B and PIRH-2 may negatively regulate p53 expression in response to ionizing radiation and In ATM-deficient cells; the ATR-signaling is the predominant positive activator of p53 at early times after exposure to gamma radiation.

Funded By: Ministry of Higher Education, SA, CIHR

women & children's health research institute

Abstract #: 179
Presenter: Ghazal Danesh
Supervisor: Manijeh Pasdar

Title: Comprehensive characterization of cell-cell adhesion proteins in ovarian cancer

Authors: Ghazal Danesh, Manijeh Pasdar
Affiliations: University of Alberta

Research Activity: Women's Health : Oncology
Investigation Type: Quantitative Research

Introduction

Ovarian cancer is the most deadly gynaecological cancer. It is often diagnosed at an advanced stage due to difficulties in detection and the elusive mechanisms of ovarian cancer development. Epithelial ovarian cancer is the most common subtype, accounting for 90% of ovarian cancer cases. We hypothesize that different ovarian cancinoma cell lines have different cell-cell adhesion protein complements that may explain differences in their migratory and invasive properties.

Methods

β-catenin, E-cadherin, N-cadherin, desmoglein, desmoplakin, and plakoglobin were selected as cell-cell adhesion proteins of interest, since they are components of adhesive junctional complexes (adherens junctions and desmosomes), which attach epithelial cells together. The IOSE-364 normal ovarian surface epithelium cell line and the A2780CP, A2780S, ES-2, OV-90, OVCAR-3, OVCAR-429, and SKOV-3 ovarian cancinoma cell lines were used in our studies. Western blots were used to detect the presence or absence of cell-cell adhesion proteins and immunofluorescence was used to examine their subcellular localization in various cell lines. Migration and invasion assays were used to compare the migratory properties and metastatic potential of two ovarian cancer cell lines with different cell-cell adhesion protein complements to each other and to the normal ovarian surface epithelium cell line.

Results

The ovarian cancer cell lines used in our studies have different cell-cell adhesion protein complements that also differ from the normal ovarian surface epithelium cell line.

Conclusion

Variations in adhesion proteins can account for disparities in cell migration and invasion. Our study of cell-cell adhesion proteins in ovarian cancer is a step towards the discovery of diagnostic markers for the early detection of this deadly cancer and development of potential therapeutic targets for its treatment.

Funded By: Summer Studentship

women & children's health research institute

Abstract #: 180
Presenter: Jasdeep Mann
Supervisor: Dr. Ing Swie Goping

Title: Proliferative function of bad in breast cancer.

Authors: Jasdeep Mann, Tim Buckland, Rachel Montpetit, Dr. Shairaz Baksh, Dr. Ing Swie Goping
Affiliations: University of Alberta

Research Activity: Women's Health : Oncology
Investigation Type: Mixed Methods

Introduction

Breast cancer is the most common disease diagnosed amongst Canadian women. Currently, taxane-based chemotherapy is provided for early and metastatic breast cancer patients; however, chemotherapeutic resistance is a major clinical problem with an estimated 50-70% of patients withstanding toxic side effects, yet receiving no benefit from treatment. Identification of biomarkers that predict patient response to taxane therapy would be a major advance in the clinical management of breast cancer.

Our lab examines the pro-apoptotic protein Bcl-2-associated death promoter (Bad), a BH3-only protein of the Bcl-2 family and we have identified Bad as a strong, independent prognostic indicator for disease-free and overall survival of breast cancer patients after taxane chemotherapy. Therefore, it is critical to understand the function of Bad in breast cancer.

Bad is a phospho-protein with conserved serine residues, which have been shown to regulate Bad activity. Its pro-apoptotic activity is apparent when the Ser118 site is dephosphorylated and has the ability to bind and inhibit inhibitors of the mitochondrial apoptotic machinery. However, previous data in our lab suggests the Ser118 site, when phosphorylated, causes Bad to exhibit a proliferative function instead. Understanding the novel proliferative function of Bad in breast cancer is the goal of this project.

Methods

Stable cell lines expressing three Bad mutants (S118A, S118D, and S99A/S118D) in the MDA-MB-231 breast cancer cell background were created to directly test the functional role of phosphorylation at S118. These experiments include cell counts and colony formation assays to examine differences in proliferation, co-immunoprecipitation experiments to examine Bad-binding partners, and western blot analysis of the phosphorylation status of Bad. As well, *in vivo* tumor growth assays were performed in the subcutaneous flanks and mammary glands of mice. Immunohistochemistry was performed on the tumors to measure proliferative function, regulated cell death, and the vascularization of the tumors.

Results

Our results indicated that phosphorylation of Ser118 on Bad is important for proliferation, as well as downstream phosphorylation of other conserved serine residues, Ser75 and Ser99. Phosphorylation of S99 is necessary for Bad proliferation and binding to 14-3-3 proteins. 14-3-3 proteins sequester Bad into the cytosol and away from the mitochondria. Also, S118D Bad reveals increased proliferation and vascularization, and decreased cell death *in vivo*.

Conclusion

Understanding the proliferative function of Bad will aid in our understanding of why patients with higher levels of Bad respond better to taxane chemotherapy. Further studies will uncover the molecular mechanism of Bad regulation.

Funded By: Alberta Cancer Foundation

women & children's health research institute

Abstract #:	181
Presenter:	Ning Yang
Supervisor:	Ing Swie Goping
Title:	Characterization of cell death induced by the cyanine dye D112: a potentially selective anti-cancer compound
Authors:	Ning Yang, Paul Gilman, Razmik Mirzayans, Michael Weinfeld, Ing Swie Goping
Affiliations:	University of Alberta
Research Activity:	Women's Health : Oncology
Investigation Type:	Qualitative Research

Chemotherapeutic drugs that are used in anti-cancer treatments often cause the death of both cancerous and noncancerous cells. This non-selective toxicity is the root cause of untoward side effects that limits the effectiveness of therapy. In order to improve chemotherapeutic options for cancer patients, there is a need to identify novel compounds with higher discrimination for cancer cells. In the past, methine dyes that increase the sensitivity of photographic emulsions have been investigated for anti-cancer properties. In the 1970's, Kodak Laboratories initiated a screen of approximately 7000 dye structural variants for selective toxicity. Among these, D112 was identified as the most promising compound with elevated toxicity against a colon cancer cell line in comparison to a non-transformed cell line. Despite those initial promising studies, and probably as a result of changing company priorities, no further work on D112 was conducted. Therefore, we decided to characterize the mechanism of D112-induced toxicity. We identified that in response to D112 treatment, the T-cell leukemia cell line Jurkat showed caspase activation, mitochondrial depolarization, and phosphatidylserine externalization, all of which are hallmarks of apoptosis. Chemical inhibition of caspase enzymatic activity and blockade of the mitochondrial apoptotic pathway through Bcl-2 expression inhibited D112-induced apoptosis. To gain insight into the molecular mechanism of D112 induced mitochondrial dysfunction, we analyzed the intracellular localization of D112, and found that D112 associated with mitochondria. Importantly, we found that D112 was a more effective apoptotic agent against multiple transformed versus non-transformed cell lines, confirming selective cytotoxic properties. Results from this work identify D112 as a potentially relevant clinical drug warranting further investigation.

Funded By: Graduate Studentship

women & children's health research institute

Abstract #:	182
Presenter:	Amanda Cao
Supervisor:	Denise Hemmings
Title:	Regulation of blood brain barrier permeability in posterior cerebral arteries by sphingosine 1-phosphate
Authors:	Amanda Cao, Daniel Kerage, Denise Hemmings
Affiliations:	University of Alberta
Research Activity:	Women's Health : Urology/Gynecology
Investigation Type:	Quantitative Research

Preeclampsia is a pregnancy complication characterized by hypertension and proteinuria. It can develop into life-threatening eclampsia that is associated with stroke and edema. Cerebral arteries possess a tight blood brain barrier that regulates the entry of substances into the brain. As systemic blood pressure rises, these arteries constrict to maintain a constant diameter and prevent fluctuations in blood flow. If the pressure gets too high, this autoregulation fails and increases perfusion of the brain and edema. We recently discovered a novel mechanism to control vascular tone in resistance arteries through the regulation of endothelial permeability by sphingosine 1-phosphate (S1P), a bioactive lipid. Using pressure myography we found that S1P infused inside intact uterine and mesenteric arteries regulated endothelial permeability in a concentration-dependent manner. We hypothesized that greater concentrations of S1P would be needed to increase endothelial permeability in cerebral arteries under normal conditions and this would be further increased in pregnancy as a protective mechanism. Conversely, under pathological conditions, we expected increased permeability at lower S1P concentrations. We isolated posterior cerebral arteries from the following groups of rats: young normal controls (Group 1), pregnant (Group 2) and intrauterine growth restricted offspring fed a high fat diet (Group 3). S1P concentrations similar to those in uterine arteries (0.1-1 µM) increased endothelial permeability in cerebral arteries from Group 3 whereas these same concentrations had no effect on arteries from Group 1 and increased barrier function in arteries from Group 2. These results suggest that S1P is important in maintaining the blood brain barrier under normal conditions and during pregnancy. Pathological conditions could result in S1P-mediated increased permeability and edema.

Funded By: Summer Studentship

women & children's health research institute

Abstract #:	183
Presenter:	Harneet Chahal
Supervisor:	Zubia Mumtaz
Title:	Abortion-seeking behavior among rural women in Chakwal, Pakistan
Authors:	Harneet Chahal, Zubia Mumtaz
Affiliations:	University of Alberta
Research Activity:	Other
Investigation Type:	Qualitative Research

Introduction

Restrictive laws and pro-natalistic religious beliefs have strongly stigmatized abortions in Pakistan. To avoid scrutiny of the public eye and legal repercussions, women often resort to clandestine abortion services which are typically administered by unskilled providers. Complications associated with abortions are magnified in these unsafe settings, elevating high rates of maternal morbidity and mortality persistent in this region. Given the negative consequences of unsafe abortion on maternal health outcomes, this study examines what factors push women to obtain this medical procedure and how they navigate their wish for an abortion within this restrictive setting.

Methods

A focused ethnography was conducted in Chakwal, Pakistan over four months in 2013. Participants were recruited from a clinic run by the Rahnuma Family Planning Association of Pakistan, which provides limited abortion services. Twenty eight in-depth interviews were conducted with women seeking an abortion (inpatients) or that had received an abortion (outpatients). Fifteen in-depth interviews were conducted with facility health service providers. Three focus group discussions were also conducted, two with patients and one with healthcare providers.

Results

Women's decision to have an abortion was heavily driven by a desire to limit fertility. This was rooted in concerns of poverty, family composition and sex of the fetus. Despite an awareness of available contraceptive options, patients chose abortion as a family planning method. The availability of oral misoprostol pills as an abortifacient made this strategy a feasible option. While this allowed unplanned pregnancies to be terminated safely and effectively, provider's personal beliefs emerged as a key barrier in patient's ability to access misoprostol. This forced women into the waiting arms of clandestine providers.

Conclusion

To support women's access to safe abortions we recommend training providers to safely administer misoprostol within women's homes. Education campaigns will also be important to curb the stigma surrounding abortions and reduce women's need to seek clandestine providers in order to obtain this procedure.

Funded By: CIHR

women & children's health research institute

Abstract #:	184
Presenter:	Michelle Chan
Supervisor:	Andrea Neilson
Title:	Short and medium terms effects of dilation and curettage/evacuation of uterus for termination of pregnancy
Authors:	Michelle Chan, Andrea Neilson
Affiliations:	University of Alberta
Research Activity:	Women's Health : Urology/Gynecology
Investigation Type:	Qualitative Research

Introduction

Family planning is a complex process with difficult decisions. Last year, Edmonton cared for approximately 480 second trimester terminations. There are many options such as: intracardiac injections, intra-amniotic instillations, induction of labour or operative management. Presently, the standard of care is to offer women in their second trimester an induction of labour. Currently, there is no Canadian data to refer to in offering patients the safer and/or more efficacious procedure during their second trimester. This study will examine the short and medium term effects of dilation and curettage/evacuation of uterus for termination of pregnancy.

Previous retrospective studies suggest that an induction of labour results in more complications and decreased satisfaction. Women undergoing induction of labour were found to have increased complications such as: retained products, unplanned procedure, blood loss needing transfusion, hospital readmission, and infection needing antibiotics. The purpose of this study is to identify the short and medium term effects of dilation and curettage/evacuation of uterus for termination of pregnancy. The primary outcome will be complication events in dilation and curettage/evacuation.

Methods

This is a prospective study looking at the outcomes dilation and curettage/evacuation. Adult women aged 16 and over will be included to look at adverse events and outcomes. The study will take place over one year looking at 200-300 women. Women will be followed at one month post-operatively and again at three and six months by phone or email survey. Data points collected will include: demographics, medical history, obstetric history, and outcomes such as: estimated blood loss, fever requiring antibiotics, injury, retained products, readmission or admission to critical care, unplanned procedures.

Results

Pending data collection and ethics approval.

Conclusion

Family planning is a complex process with difficult decisions. With study results, we hope to gather Canadian data regarding the outcomes of dilation and curettage/evacuation in the second trimester. With this data future research comparing induction of labour versus dilation and curettage/evacuation for second trimester loss or termination of pregnancy can be compared to offering patients the safer and/or more efficacious procedure during their second trimester.

women & children's health research institute

Abstract #: 185
Presenter: Tasneem Siyam
Supervisor: Nese Yuksel

Title: Assessment of quality of life and breast cancer risk after HT administration in women who underwent BPSO

Authors: Tasneem Siyam, Sue Ross, Sandy Campbell, Nese Yuksel
Affiliations: University of Alberta

Research Activity: Women's Health : Urology/Gynecology
Investigation Type: Qualitative Research

Introduction

Women who are carriers of BRCA mutations are often challenged by the decision to uptake bilateral prophylactic salpingo-oophorectomy (BPSO) due to fear of symptoms associated with surgical menopause, and the subsequent need for hormone therapy (HT), that presumably may further increase their risk of breast cancer. The primary objective of this systematic review is to identify, evaluate and synthesize evidence on the effect of HT on the quality of life and breast cancer risk, after BPSO in carriers of BRCA mutations.

Methods

We searched electronic databases including MEDLINE, EMBASE, CINHAL, and others, from inception to March 21, 2014, to identify randomized controlled trials (RCTs) and observational studies that addressed the effect of HT on the quality of life and breast cancer risk in women who have *BRCA* mutations and who have undergone a BPSO. Data synthesis included written evidence summaries and meta-analyses. When sufficient qualitative homogeneity was demonstrated, outcome data were pooled quantitatively. Continuous outcomes were analyzed using weighted mean differences (WMD) and 95% Confidence interval (CI). DerSimonian-Laird random effects model was used to calculate the pooled Odds ratio (OR) and 95% CI of discreet variables. Statistical heterogeneity was assessed using chi-squared test and I^2 statistic.

Results

Of the 829 records identified, 8 met our inclusion criteria. All studies were observational in nature. Across studies, study populations were mostly comprised of BRCA 1 & 2 mutation carriers (88%) and both pre and post-menopausal women at the time of BPSO (63%). The mean age of women was 42 years (34-78). Of the 8 studies included, 4 assessed the effect on quality of life. All studies demonstrated improvement in quality of life with HT. The pooled estimate of weighted mean difference (WMD) from random effect model = 3.26 (95% CI = 0.96-5.56, P = 0.005). The risk of breast cancer with HT was evaluated in 3 studies. Two studies reported a decreased risk with HT use, and one reported an increased risk. However, none were statistically significant. The pooled OR from generic inverse variance meta-analysis was protective but non-significant (OR = 0.63 (95%CI = 0.28-1.40, p = 0.26). Furthermore, pooled data from 3 studies that looked at other outcomes showed that HT users were less likely to have hot flashes (P = 0.0003), night sweats (P = 0.002) and vaginal dryness (P = 0.02) than non-users.

Conclusion

Evidence from our review suggests that HT is a reasonable approach for mitigating most symptoms induced by BPSO, without counteracting the breast cancer risk-reducing benefits of BPSO, at least in the short term. These findings present a valuable source of information for patients contemplating BPSO, and their clinicians.

women & children's health research institute

Abstract #: 186
Presenter: Rongfang Hu
Supervisor: Kathleen M Hegadoren
Title: Gender differences in sleep quality and memory among ICU patients
Authors: Rongfang Hu, Kathleen M Hegadoren
Affiliations: University of Alberta
Research Activity: Women's Health : Stress Disorders in Women
Investigation Type: Quantitative Research

Introduction

Sleep deprivation and disruption in patients in intensive care units (ICU) have been well recognized as a risk factor for stress-related disorders post-discharge from ICU. A relationship between memories during the ICU experience and stress-related disorders after discharge has also been reported. However, the relationship between patients' perceived sleep quality and memories of ICU after discharge has not been explored. In addition, a large body of evidence support that women are more vulnerable to stress disorders; thus it is important to consider gender as another potential risk factor.

Objectives

This study aimed to identify gender differences in perceived sleep quality and memory of ICU among ICU survivors.

Methods

The study was conducted in two teaching hospitals in China, enrolling 491 recovering, post-ICU adult patients (284 of males, 207 of females). The Richards & Campbell Sleep Questionnaire and ICU Memory Tool were used to evaluate patients' sleep quality and memories of ICU respectively at 1 week after ICU discharge. Gender differences in sleep quality and memories of ICU were examined.

Results

Total sleep score in women was significantly lower than that of men (47.51±25.43 *vs* 52.52±28.01, P= 0.046). A total of 133 (27.1%) patients experienced delusional memories, while 89.2% reported factual memories and 75.2% reported feeling memories. No significant difference was found in rate of delusional memories and rate of feeling memories between gender, but the women had significantly lower rates of factual memories compared with men (85.5% vs 91.9%, P = 0.027). There were significant differences in memories of family, darkness, clock, lights, and ward around between gender (P<0.05). There were also significant differences of four memory experiences between gender (P=0.013). No significant difference was found in personal-related memories and pain memories between gender (P>0.05). Differences in sleep quality were related to different types of memory experience (P<0.05).

Conclusion

The results suggest that perceived sleep quality in ICU is low for both for men and women; however, women report worse perceived sleep quality. Both genders experience delusional memories of ICU. The rate of factual memories is higher in men when compared with women. Future follow-up studies should include longer term assessments of psychological well-being and quality of life, to determine the ongoing consequences of ICU experiences and the associations between sleep quality, memories of ICU and gender in risk modeling to help identify those at higher risk for developing stress disorders post-ICU.

Key words: sleep quality, ICU, memories, gender

women & children's health research institute

Abstract #:	187
Presenter:	Vikas Chadha
Supervisor:	Sue Ross
Title:	Literature Review: Menopausal symptoms and experiences among aboriginal women around the world
Authors:	Vikas Chadha, Neha Chadha, Sue Ross, Beate Sydora
Affiliations:	University of Alberta
Research Activity:	Women's Health : Mature Women's Health
Investigation Type:	Qualitative Research

Introduction

Menopausal symptoms among women can be debilitating and vary widely. In the context of menopause, aboriginal women are an under-studied population and less is known about their experiences and understanding. Therefore, the purpose of this literature review is to collate the research done on aboriginal women globally and come to a greater understanding on their knowledge, perceptions, and attitude towards aging and menopause.

Methods

We conducted a search of 8 medical and psychological science databases (Medline, Pubmed, CINAHL, ScienceDirect, Global Health, Scopus, EMBASE, and PsychInfo) using the search words Aboriginal, Indigenous, Native, Native Americans, Indians, Metis, Inuit, Eskimo, and Tribes in combination with either Menopause or Climacteric Symptoms. This initial search yielded a total of 16,138 articles, mostly (12,268) from ScienceDirect, which prompted a constricted search of this database via pre-set filters. Following duplicate removal, 69 papers were screened and 22 were selected for review. The following criteria were used for inclusion: The paper must study aboriginal women and their menopausal experiences. Aboriginal was defined as being native to the region or country with a characteristic biological, social, psychological, and cultural profile. All literature reviews, as well as those only studying rural or ethnic women were excluded.

Results

The 22 relevant papers presented information about 18 different aboriginal groups. Menopause symptoms or lack of symptoms were not mentioned for 3/18 aboriginal groups. In papers discussing the experience of menopause, vasomotor symptoms (hot flashes and/or night sweats) were common with 11/15 of the aboriginal groups reporting this as the major symptom. Other symptoms such as sexual problems (2/15) and physical discomfort (1/15) are more prevalent than vasomotor symptoms among other groups. Two of 15 of the aboriginal groups reported less or no symptoms at all. Another finding was that some women have an overall lack of knowledge about menopause, which may be due to decreased communication and education. Several aboriginal groups went through menopause at an earlier age than the average age of 51 in the USA.

Conclusion

This literature review has highlighted the importance of understanding the differences in menopausal experiences among women of different aboriginal biological, social, psychological, and cultural background. This knowledge could be helpful to bridge possible gaps between aboriginal women and health care professionals to further enhance an important dialogue about women's healthcare.

Funded By: RAH, LHHW

women & children's health research institute

Abstract #:	188
Presenter:	Jennifer Croden
Supervisor:	Sue Ross
Title:	The availability of natural health products for menopausal symptoms in Canadian pharmacy chains and their regulation by Health Canada
Authors:	Jennifer Croden, Nese Yuksel, Sue Ross, Beate Sydora
Affiliations:	University of Alberta
Research Activity:	Women's Health : Mature Women's Health
Investigation Type:	Mixed Methods

Introduction

Menopause is a natural phase in a woman's aging process, characterized by the cessation of menstruation. Women who are going through the menopause transition can experience physiological symptoms that significantly impact their quality of life. Concern about adverse effects of traditional hormone therapy is causing more women to seek alternative treatments for menopausal symptoms, including herbal remedies often found in over-the-counter natural health products (NHPs). The goal of this study was to investigate over-the-counter NHPs for menopause available to the average Canadian woman, the health claims made by the products' manufacturers, and how these products are assessed by Health Canada.

Methods

Edmonton stores belonging to each of nine Canadian pharmacy chains were visited to identify NHPs marketed specifically for the relief of menopausal symptoms. Details were extracted from the packaging label or product websites: a) cost, b) medically active ingredients, c) any claim(s) of efficacy, d) contra-indications and side effects, and e) regulatory information (i.e. natural product number (NPN)). Data were entered and analyzed using Microsoft Excel.

Results

In total, 20 over-the-counter menopausal supplements were identified. Pharmacies varied in the number of products sold, ranging from 2-12 (mean (SD) 6 (4.1)). Costs per recommended daily dose ranged from $0.08-$1.94 (mean (SD) $0.70 ($0.46)). 20 medically active ingredients were identified in these products, with the most frequently used being black cohosh (in 70% of products) and soy isoflavones (30%). Every NHP made a symptom-specific health claim, with the majority claiming relief from vasomotor symptoms such as hot flashes (75% of products) and night sweats (50%). Every product had a labeled contra-indication for at least one condition (use with breast cancer, gynecological disease, pregnancy, and others), but none had a labeled side effect. For NHPs to be regulated by Health Canada, the manufacturers are required to provide evidence that the product is effective for its advertised use; however, the evidence requirement for NHPs for menopause was found to reflect the low risk nature of these products. Additionally, only 90% of the herbal remedies were found to be properly regulated as determined by the presence of a Natural Product Number (NPN) provided to therapeutics by Health Canada.

Conclusion

Over-the-counter herbal products regulated by Health Canada are widely available for women who wish to self-manage their menopausal symptoms. The next stage of this study is to investigate whether published evidence supports the claims of efficacy, contraindications, and side effects of the herbal ingredients.

Funded By: Summer Studentship

women & children's health research institute

Abstract #:	189
Presenter:	Nicole Veltri
Supervisor:	Sue Ross
Title:	Health and demographics of women attending a specialized menopause clinic and treatment options provided: A chart review
Authors:	Nicole Veltri, Justin Marillier, Christoph Sydora, Hilary Fast, Nese Yuksel, Lori Battochio, Tami Shandro, Sue Ross, Beate Sydora
Affiliations:	University of Alberta
Research Activity:	Women's Health : Mature Women's Health
Investigation Type:	Quantitative Research

Introduction

Menopause is defined as the permanent cessation of menstruation. Although it is a natural stage in the aging process, hormonal changes during the transition period are quite frequently associated with symptoms that can significantly impact a woman's health and quality of life. For severe cases, specialized multidisciplinary menopause clinics offer patient-centered treatment over and above the care provided by their family physician.

We examined the charts of a sample of women who attended the Lois Hole Hospital for Women (LHHW) Menopause Clinic, where clinical care is provided by a range of disciplines (including specialized physician, pharmacist, dietician, nurses). Our goal was to describe the women attending the clinic with regard to their menopause symptoms, other medical problems and the treatment options they were offered.

Methods

This retrospective cohort study was based on a chart review of a convenience sample of 164 patients who attended the LHHW Menopause Clinic during 2008 to 2013. Data from clinic charts were entered into a REDCap database and descriptive statistics were applied to characterize patient demographics, menopause symptoms, medical conditions, and treatments provided. (Ethics approval: HREB (EDM) / Pro00041189)

Results

At initial consult, mean age of the women was 52 years (SD=6.5) ranging from 30 to 68; 4.4% were pre-menopausal, 28.8% peri-menopausal, and 66.9% post-menopausal25.3% had experienced surgical menopause. The most common self-reported menopause symptoms at presentation were sleep dysfunction (46%), hot flashes (35%), and mood symptoms (32%) which correlated well with the physician referral assessment. 31% of women specifically indicated that they were mainly seeking information about hormone therapy. The majority of women (97%) had additional medical problems with 86% presenting with more than one. Specific medical conditions included depression (40%), anxiety (34%), migraines (28%) and high cholesterol (20%). Many women (64.1%) were overweight with a BMI greater than 26. Treatments offered included hormone therapy (78%), vitamin supplements including specifically calcium and vitamin D (61%), and changes to diet (38%) and exercise (12%).

Conclusion

Women seeking help at the LHHW Menopause Clinic present with complex medical issues in addition to a variety of menopause symptoms. A range of treatment modalities was suggested for patients. Further analysis of our data will explore outcomes for specific groups of women to better address their individual needs.

Funded By: Support services

women & children's health research institute

Abstract #:	190
Presenter:	Sangho Choi
Supervisor:	Beate Sydora
Title:	Experience of menopause in women with inflammatory bowel diseases: Lessons from analysis of patient recruitment and data collection
Authors:	Sangho Choi, Vivian Huang, Karen Kroeker, Richard Fedorak
Affiliations:	University of Alberta
Research Activity:	Women's Health : Mature Women's Health
Investigation Type:	

Introduction

Hormonal changes during menopause lead to a variety of physical and psychological symptoms that can be influenced by medical treatment, diet and lifestyle options. Women with chronic illnesses, such as Inflammatory Bowel Diseases (IBD), may experience menopause symptoms in a different way than women without IBD, partly due to surgical and medical interferences. It is not known whether and how IBD and its treatment affects menopause; neither is it clear how hormonal changes during menopause effect the clinical presentation of IBD. The objective of this project was to study the correlation between menopause symptoms and clinical presentation of IBD.

Methods

Women age 30 - 65 with IBD were enrolled and surveyed regarding their experience and feelings of menopause symptoms and symptoms commonly associated with intestinal inflammation using validated questionnaires. Healthy control participants of the same age were enrolled via snowball method using contact through IBD patients to match controls' and patients' age and socioeconomic status. Participant blood samples were collected through local laboratories to correlate levels of menopause-related hormones (estradiol, FSH, progesterone) and inflammatory cytokines (INFg, TNFa, IL-1b, IL-12) with menopause stage and IBD activity. Providing blood samples was voluntary for participants.

Results

Patient recruitment appeared to be more difficult than anticipated due to administrative issues regarding patient access through the recently established clinical database e-clinician, and due to the timing of the project during the summer, i.e. vacation months, with both clinician and scheduled patient absences. In addition, there was a large discrepancy between the actual (25) and our estimated (110) number of eligible patients, who were seen in the clinic where enrollment took place during two summer months. Enrollment of IBD patients' friends or family members as controls was not effective with a response rate of only 6% (1 in 18). Providing blood sample was voluntary for participants with 6 out of 18 patients donating blood although 15 out of 18 agreed to donate blood. Results from 18 IBD patients showed increased severity in menopause symptoms compared to those without IBD.

Conclusion

Taken their limited research time into consideration, summer student should be aware of potential pitfalls and delays in their project in particular when patient recruitment is involved. With regard to this particular project we hope that the knowledge gained from this study will support women with IBD in health choices when coping with hormonal changes and symptoms during menopause.

Funded By: Women and Children Health Research Institute (WCHRI), Royal Alexandra Hospital Foundation, and a Clinical Research and Progress

women & children's health research institute

Abstract #: 191
Presenter: Nadia du Toit
Supervisor: Nese Yuksel
Title: The safety and endometrial protection of levonorgestrel IUS in women on estrogen therapy.
Authors: Nadia du Toit, T Shandro, S Hagen, L Battochio, C Maslanko, N Schuurmans, Nese Yuksel
Affiliations: University of Alberta
Research Activity: Women's Health : Mature Women's Health
Investigation Type:

Introduction

It is essential to provide progestogen in peri-and postmenopausal females who retain their uteri and desire estrogen replacement therapy secondary to climacteric symptoms. This will counteract the proliferative effect of estrogen on the endometrium. However, the oral regime is associated with irregular vaginal bleeding which is burdensome for some women. A subset of women, also do not tolerate the mood side effects such as depression that is associated with progesterone. The levonorgestrel intrauterine system has been studied as an alternative method in women who cannot tolerate oral progestogens. The high endometrial progestin concentrations, accomplish endometrial protective effects, with a minimal amount of adverse effects secondary to its significantly decreased serum concentrations. With our study, we aim to look at the long-term effects of LNG-IUS on endometrial proliferation and the safety profile in continuous use in women on concurrent estrogen therapy for menopausal symptoms.

Objectives

Primary objective:

- To determine if LNG-IUS provides endometrial protection in women on estrogen therapy alone with long-term continuous use.

Secondary objectives:

- To capture reasons for use of the LNG-IUS in perimenopausal and postmenopausal women
- To determine change in bleeding patterns after LNG-IUS treatment was initiated
- To determine tolerability and continuation rates of patients who were started on LNG-IUS
- To determine adverse effects with long term LNG-IUS treatment
- To assess reasons for discontinuation of LNG-IUS.

Methods

This will be a retrospective chart review of peri- and postmenopausal women using LNG-IUS therapy to provide endometrial protection when on estrogen therapy alone for menopausal symptoms. The patients will be identified through a current list of patients who are on the combination of estrogen therapy and LNG-IUS from January 2002 to December 2013 at the menopause clinics at the Grey Nuns Hospital and the Lois Hole Hospital at the Royal Alexandra site. The charts will be reviewed by the obstetric and gynecology resident and considered according to the inclusion and exclusion criteria.

Results

The study proposal was approved by Health Ethics Research Board and data collection started in February 2014.

Conclusion

This study aims to determine if the LNG-IUS provides endometrial protection with long-term continuous use in women on estrogen therapy for menopausal symptoms.

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