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Pain, Suffering, and the Flexible Self

by

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Dedication

This dissertation is dedicated to my partner Dr. Theo De Gagne, who I know is always there for me. He provided me with untiring love and support during the completion of this project.

I am also grateful for the invaluable support of many other people who helped to make this dissertation possible. These include my immediate family members: my father Dr. Irving Ozier; my mother Joyce; my brother David; and my sister Elizabeth. I bear a special debt of graditude to my supervisor, Dr. Bill Whelton, who never stopped believing in me and working to help me fulfill my potential as a researcher and as a human being. I am also very indebted to Dr. Leslie Sherlin, Dr. Horst Mueller, Dr. Chris Westbury, Dr. Don Kuiken, Dr. Marty Mrazik, and Dylan Lampman, who each made an invaluable and unique contribution to my project. I am grateful for the support of many friends including Meris Williams, Martin Gagel, David Beare, Rochelle Major, Michelle Smith, Easter Yassa, Elaine Greidanus, Mandy York, Shelagh Dunn, Sherry Antonucci, Josh Dunn and many other fellow students who supported me and my project. Finally, I am eternally grateful for the generous support of my participants, without whom this project would surely not have been possible.

Abstract

This dissertation is comprised of three articles that use neuropsychological research and technologies to consider the issues of organized flexibility, the self, and pain versus suffering. The first study outlines a theoretical model based on the contention that the human mind emerges in part through the interaction of three, large-scale, neural sub-systems. We describe how rigid patterns of interaction between these neural subsystems putatively lead to rigid modes of self-related processing, and thus contribute to "suffering". The second and third articles describe two studies designed to test the potential of LORETA neurotherapy to ameliorate psychological suffering, in this case by teaching a cohort of chronic pain patients to increase their neural flexibility. There is currently a lack of clarity around the kind of electrophysiological activity that is specifically associated with the suffering aspect of chronic pain. Therefore, the second article describes a study in which a cohort of chronic pain patients entered a state of chronic pain related suffering. LORETA EEG analysis was then used to investigate the electrophysiological activity that was specifically associated with this suffering. This study failed to find statically significant results, however it did produce qualitative support for the hypothesized pattern of neural changes. Finally, the third study directly tested the possible efficacy of LORETA neurotherapy as a chronic pain management intervention. LORETA neurotherapy was used to teach a cohort of eight participants with mixed chronic pain conditions to volitionally down regulate activity in the mPFC, a region that is crucial to for autobiographical self-related processing. Participants in an active

control condition were trained in Autogenics and CBT, a well-established approach to chronic pain management. The neurotherapy group members developed the ability to volitionally regulate their neural activity in the intended manner, improved their phasic pain regulation abilities, and demonstrated statistically significant clinical improvements in mood and functional status. However, the observed phasic pain regulation improvements were not statistically significant, and were not associated with the observed neural changes in the expected manner. These results are interpreted and their implications discussed.

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CHAPTER 1

Extensive research conducted over the last two generations has effectively demonstrated that psychotherapy works (Smith, Glass, & Miller, 1980). However, despite the dedicated efforts of psychotherapy process researchers over this same time span, less progress has been made in tackling the much more complex question of *how* therapy works. In other words, we are still struggling to identify psychotherapy's "active ingredients" or core mechanisms of change (Kazdin, 2007). Making progress on this question promises to offer a range of invaluable benefits including: increased theoretical coherence across therapeutic schools; the ability to train student therapists more effectively; and, ultimately, the ability to provide clients with more targeted, parsimonious, efficacious treatment (Moses & Barlow, 2006).

In the quest to determine how psychotherapy works it is important to differentiate between important facilitative conditions and true mechanisms of change (Kazdin, 2007). For example, there is now ample evidence that a good therapeutic alliance predicts outcome (Truscott, 2009). However, after a successful course of therapy the client should leave the therapeutic relationship and continue to demonstrate improved function. Therefore, it would seem that the co-construction of a positive therapeutic alliance is a key facilitative condition for activating some form of systemic change *within* the client, a change that continues to provide psychological benefit once the relationship is no longer present. Therefore, a seminal question remains: What are the key variables within the client that effective psychotherapy helps to change?

Recent work by Barlow and his colleagues (for example see Brown & Barlow, 2009) offers exciting potential for making progress on this question. Brown and his co-workers argue that two of the most common forms of human psychological suffering, anxiety and depression (meant here to exclude bipolar disorders), can be best understood as superficially different expressions of a common stress-diathesis response. According to Barlow and his co-workers, high levels of the personality variable neuroticism operate as the underlying diathesis. These authors go on to argue that the powerful simplicity of this conceptualization of anxiety and depression has been obscured, in large part, by use of the DSM. Brown and Barlow (2009) have provided convincing evidence that a DSM-type nosology of psychological disorders tends to exaggerate relatively superficial differences between disorders, and therefore to obscure more important commonalities *across* disorders.

The results of a study conducted by Brown (2007) offer compelling support for this parsimonious conceptualization of anxiety and depression. Brown conducted a 2-year longitudinal study with a sample of over 600 outpatients who received treatment for Major Depressive Disorder, Generalized Anxiety Disorder, or Social Phobia. He found that over the two year study period "…*all* of the temporal covariance of the *DSM–IV* disorder constructs was accounted for by change in…" neuroticism scores (Brown & Barlow, 2009, p. 269, italics added for emphasis). This finding points toward a pair of key conclusions. First, neuroticism may be at the very heart of much psychological suffering (Brown & Barlow, 2009; Griffith et al., 2009). Second, "…counter to earlier initial evidence and

conceptualizations…", neuroticism "… may be therapeutically malleable, and that this in fact mediates the extent of change in the emotional disorders …" (Brown & Barlow, 2009, p. 263).

Psychological Heath from the Perspective of Complexity Theory

This dissertation will build upon the work of Barlow and his colleagues to offer a brain-based conceptualization of suffering and of a key pathway through which psychological interventions may lessen it. We will start this project by reframing Barlow et al.'s core argument within the broader paradigm of complexity theory (Siegel, 2009). We believe that grounding our theory of psychological functioning within a broader, trans-disciplinary paradigm helps to lessen the kinds of theoretical confusion that have plagued psychotherapy almost from its inception (Siegel, 2009). At the same time, we believe that compelling arguments have now been made that both human minds (Mahoney, 1991) and brains (Freeman, 1997) can be fruitfully understood as complex, self organizing, dynamic systems. Therefore, a complexity theory perspective is a promising paradigm through which to ground our brain-based conceptualization of psychological suffering and its amelioration.

The first step in reframing the relevant ideas of Barlow et al. from within a complexity theory perspective is to briefly outline what we think it *means* to be psychologically healthy. For us, this understanding starts with a pair of observations. First, human beings have both minds and brains. Second, minds and brains are clearly very different things, so that one cannot be meaningfully reduced to the other. Wilber's (2000) four-quadrant model offers a useful means

of underscoring this latter conclusion. Wilber's model involves a two by two grid (inside vs. outside and individual vs. collective) that generates four quadrants, within which all human knowledge can be meaningfully assigned. Each quadrant has it's own epistemology and own truth claims. Therefore, Wilber's work clearly reminds us that "truth" can be meaningfully debated within, but never *between*, quadrants. For the purposes of this dissertation, it is the contrast between the inside/individual quadrant and the outside/individual quadrant that is of primary importance. Data related to an individual's mind (e.g., a participant's experience of pain during a pain induction) belongs to the former quadrant, while information about the neural correlates of that experience (e.g., the EEG responses exhibited by the participant during the pain induction) belongs in the latter quadrant.

Therefore, while acknowledging the dangers of reducing one into the other, we contend that brains and minds can be best understood as being *parallel* dynamic systems that are highly interdependent, though in some as yet not well understood manner (Siegel, 2009). As such, we believe that, despite their clear differences, minds and brains can both be best understood as being "healthy" to the degree that they each fulfill the criteria that define a well functioning dynamic system as these criteria have been described across a range of scientific disciplines (Siegel, 1999; Gleik, 1987).

In essence, according to complexity theory, an optimally healthy self-organizing dynamic system is one whose composite subsystems relate to each other in such a way that the total system is able to self-organize as flexibly as possible without becoming *so* flexible that it slips into a state of true

disorganization (associated with behavior that lacks any underlying coherence; Gleik, 1987). This kind of internal relationship maximizes each subsystem's ability to fluidly shift its position of relative dominance within the total system. Such flexibility is valuable because it offers the most effective means available for meeting the essential challenge faced by any living system, namely, successfully adapting to a constantly changing external environment while *simultaneously* maintaining enough internal stability to preserve integrity as an entity that exists across time (Siegel, 2009).

Rigid, Self-focused Processing and Psychopathology

Researchers have explored the relationships between neuroticism and two prevalent forms of repetitive, rigid, cognitive processing that have been strongly linked to psychopathology: rumination and worry. Rumination can be defined as "unproductive, repetitive thought" (Muris, Roelofs, Rassin, Franken, & Meyer, 2005, p. 1110). Worry, on the other hand, can be defined as an "apprehensive expectation of possible negative outcomes in future events" (Muris et al., 2005, p. 1110). Both worry and rumination tend to be *non-present* focused and highly *self*-focused.

Muris et al. (2005) looked at the associations between neuroticism, worry, rumination, depression and anxiety in a cohort of undergraduate students. Echoing earlier findings (Lam, Smith, Checkley, Rijsdijk, & Sham, 2003; Roberts, Gilboa, & Gotlib, 1998), Muris et al. found that that neuroticism was strongly correlated with both rumination and worry. These authors also found evidence that worry and rumination *mediated* the effects of neuroticism on both anxiety and

depression. Muris et al. conclude that "…rumination and worry can best be considered as psychopathology-related unproductive, repetitive thought, which seems to be a cognitive concomitant of neuroticism…" and that "… when confronted with stress or threat, rumination and worry are activated in individuals characterized by high levels of neuroticism, which in turn enhances symptoms of anxiety and depression" (2005, p. 1110).

Worry involves thoughts of the future, while rumination more often involves thoughts of the past. Despite these content related differences, worry and rumination share two fundamental traits. First, they both involve mental projection of the "autobiographical self" (Damasio, 1999) into negatively valenced, imagined realties that exist outside the realm of the present moment. Second, as pointed out by Muris et al. in the quote above, worry and rumination are both strongly defined by the quality of *repetitiveness*, which is a form of rigidity.

In partial summation, there is evidence that neuroticism lies at the heart of anxiety and depression (Brown & Barlow, 2009; Griffith et al., 2009), two of the most common forms of human suffering. Further, neuroticism operates as the diathesis for anxiety and depression, at least in part, because a person high in neuroticism responds to perceived threat by engaging in repetitive, non-present focused, self focused forms of mental elaboration. Finally, from the perspective of complexity theory, these forms of self-focused processing are detrimental to health because their *rigidity* lessens the person's ability to self-organize in a dynamic, flexible manner.

Self Related Processing from a Neural Perspective

The self has received considerable attention from cognitive neuroscientists in the last decade. Damasio's (1999) neural model of the self has had a profound influence on this emerging area of research. Damasio's model will be outlined in the chapters that follow, as it serves as a cornerstone for the ideas developed in this dissertation. In brief, Damasio suggests that human beings possess two distinct, nested, modes of self-awareness. The first, evolutionarily much older, mode of self is called the core self. The core self is an ephemeral, constantly regenerating, present-focused sense of self that emerges from awareness of the ever-changing homeostatic state of the body as it interacts with its environment. The second level of consciousness, the autobiographical self, is what is more commonly meant by "a self". The autobiographical self emerges from rich sets of self-defining memories, has a sense of identity that bridges moments in time, and is strongly dependent on linguistic construction. Further, unlike the core self that is always bound through the body to the present moment, the autobiographical self is able to imaginatively project itself through space and time.

As will be outlined in subsequent chapters, neuroimaging has started to reveal the neural correlates of self-referential processing. In brief, evidence exists that activity in a set of older brain regions including the anterior insula is strongly associated with generation of the core self (Farb et al., 2007). On the other hand, processes of autobiographical self reflection and projection appear to be strongly supported by a diverse set of brain regions called the Default Mode Network

(DMN; Northoff, Heinzel, De Greck, Bermphol, Dobrowolny, & Panksepp, 2006; Buckner, Andrews-Hanna, & Schacter, 2008).

Psychopathology and Rigid Neural Processing

There is now strong evidence that the brain is organized into a relatively small number of large, resting state networks (Fox, Snyder, Vincent, Corbetta, Van Essen, and Raichle, 2005). The DMN and the "task positive network" appear to be two of the most important of these networks. The DMN is considered the brain's "task negative" network because it shows high levels of activity in the absence of explicit task demands (e.g., when the person is at so called "rest") while showing reductions in activity at the initiation of a task (Gusnard & Raichle, 2001). The exception to this general pattern is that DMN activity levels remain high, or even increase, if the relevant task involves autobiographical self-reflection or projection (Buckner et al., 2008). On the other hand, the "task positive network" shows the opposite pattern of activation, increasing its levels of activity during external task demands. In other words, these two large-scale networks seem to typically operate in an anti-correlated fashion. This finding suggests that an important neural correlate of psychological health may be the ability to flexibly activate the DMN when it is adaptive to engage in autobiographical self-reflection or projection, and to *de*activate the DMN when it is maladaptive to do so.

There is growing evidence that people suffering from forms of psychological disturbance marked by rigid patterns of non-present and self-focused thought manifest disturbed patterns of DMN activation. Specifically,

people with Major Depressive Disorder (Sheline, Barch, Price, Rundle, Vaishnavi, Snyder et al., 2009) and Social Anxiety Disorder (Gentili et al., 2009) have been found to manifest maladaptively high levels of DMN activity, while people with chronic pain have been found to have an impaired ability to adaptively deactivate the DMN (Baliki, Geha, Apkarian, & Chialvo1, 2008).

These emerging findings linking psychological suffering and DMN hyperactivity are consistent with a key idea alluded to at the outset. Namely, while brains and minds are clearly different, degrees of rigidity/flexibility at the levels of mind and brain should reflect each other, albeit each from within their distinct epistemological "quadrants" (Wilber, 2000).

Rationale for the Current Research

The ideas presented thus far imply that psychological interventions may work to decrease suffering by helping clients to become more flexible in their modes of processing, particularly in learning how to shift adaptively out of rigid, autobiographical self focused, modes of processing (Teasdale, 1999). In fact, an emerging wave of psychotherapies make facilitating this kind of increased flexibility a primary clinical focus, and these therapies have shown considerable clinical potential (e.g., Hayes, Strosahl, & Wilson, 1999; Papageorgiou, & Wells, 2000; Segal, Williams, & Teasdale, 2002).

However, the ideas thus far also suggest an alternative possibility, namely, that offering clients direct feedback about the activity of their brains could help them to learn how to become more psychologically flexible, thereby helping them

to self-regulate their suffering more effectively. In general terms, the feasibility of this possibility is consistent with an extensive body of literature showing that, when people are provided with feedback about their neural activity, they can learn to self–regulate it successfully (Heinrich, Gevensleben, & Strehl, 2007; Levesque, Beauregard, & Mensour, 2006).

Goals of the Dissertation

In this light, this dissertation was conducted with three overarching, interrelated goals.

The first goal was to develop a large-scale, neurally grounded, theoretical model that elaborates and refines the core ideas outlined in this introduction. This neural model posits three large scale, interacting neural systems. It then describes how we believe the interactions between these three systems correlate with changes in one's mode of self-related processing.

The second goal was to test the feasibility and clinical impact of using LORETA neurofeedback to teach a cohort of clinical participants how to down regulate their DMN activity more effectively. More specifically, we trained a cohort of people with heterogeneous chronic pain conditions to down-train activity in the mPFC, a key node in the DMN (Buckner et al., 2008). Our key hypotheses were that this training would be achievable and that successful training effects would be associated with improved pain regulation.

The choice to work with people with chronic pain was made for several reasons. First, effective new approaches to chronic pain management are needed

because chronic pain is very prevalent condition that continues to cause tremendous suffering and disability (Veillette, Dion, Altier, & Choiniere, 2004). Second, chronic pain was selected because the suffering aspect of chronic pain has been associated with hyperactivity in the mPFC (Baliki et al., 2006; Schweinhardt, Kalk, Wartolowska, Chessell, Wordsworth, & Tracey, 2008). Third, an earlier study using fMRI neurofeedback (DeCharms et al., 2005) produced promising results in teaching the self-regulation of chronic pain. The results of DeCharms et al. (2005) suggested the potential value of adapting this basic methodology to use with an alternate, more accessibly priced neurofeedback modality. Finally, chronic pain was selected because, in theoretical terms, it exemplifies psychological suffering in general. This is because: it involves a strong tendency to engage in a form of rigid, ruminative, autobiographical self-focused processing called catastrophizing (Sullivan, Sullivan, & Adams, 2002); much like the worry and rumination that are so closely associated with anxiety and depression, chronic pain related catastrophizing appears to be a pain related cognitive expression of an underlying diathesis of neuroticism (Goubert, Crombez, & Van Damme, 2003); and degree of catastrophizing has been consistently correlated with the degrees of disability and suffering caused by a chronic pain condition (Sullivan, Sullivan, & Adams, 2002).

The third goal of the dissertation was to conduct an initial empirical test of selected aspects of our neural model. Namely, if we found that chronic pain related suffering was related to activity within the mPFC, and also that the lessening of this neural activity was associated with lessened degrees of suffering,

this would provide initial validation of a key theoretical contention underlying our neural model.

Format of the Dissertation

This dissertation is written in a paper format consisting of five chapters. Chapter one consists of the present introduction to the dissertation. This introduction has briefly introduced several issues that underlie the chapters to follow. These issues have included psychological suffering as conceptualized from the perspective of complexity theory; the association between suffering and rigid, repetitive, negatively valenced, self referential forms of processing; and the neural correlates of self referential processing. The rationale and overarching goals of the dissertation were then presented.

Chapter two offers the theoretical model alluded to earlier. Again, in brief, this neural model describes three large scale, interacting neural systems. It then explains how we believe the interactions between these three large scale systems correlate with changes in levels of a variable called *experiencing* (Gendlin, 1996). Varying depths of client experiencing have been found to correlate with degree of success in psychotherapy outcome (Whelton, 2004). These changes are also associated with profound shifts in the client's *mode* of self-related processing.

Chapters three and four present two separate, yet related empirical investigations that were designed to test the feasibility and clinical impact of using LORETA neurotherapy to decrease neural rigidity and thereby help to lessen the suffering associated with chronic pain. The format for each of these

chapters consists of a review of relevant literature, methods, results, and discussion sections.

Chapter three details a study that was conducted with a cohort of seven adults living with heterogeneous chronic pain conditions. This study involved a contrast between two behavioral tasks, one designed to induce a state of chronic pain related suffering and the other designed to lessen this suffering. The central goal of this study was to use LORETA EEG analysis to identify the electrophysiological correlates of chronic pain related suffering with the mPFC.

Chapter four details a study that was conducted following the study described immediately above. This latter study involved a cohort of 15 adults with heterogeneous chronic pain conditions. Eight of these participants were randomly assigned to receive a course of LORETA neurotherapy. The remaining participants were randomly assigned to participate in an active control involving training in Autogenics/Cognitive Behavioral Therapy based chronic pain management training. Both within and between group, pre-to post training changes were determined and interpreted.

Finally, in Chapter 5, the findings from each of the previous chapters are briefly reviewed. Overall theoretical and clinical implications are then provided.

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CHAPTER 2

EXPERIENCING, PSYCHOPATHOLGY AND THE TRI-PARTITE MIND[1]

In this chapter we will develop a neurologically grounded model of what happens within a client when psychotherapy successfully restores or enhances the client's sense of mental health. As a first step we will offer a brief definition of what we think it *means* to be psychologically healthy.

For us, assembling this definition starts with a pair of observations. First, human beings have both minds and brains. Second, minds and brains are clearly not the same things, so that one cannot be meaningfully reduced to the other (Wilber, 2000). However, we contend that minds and brains can be best understood as being *parallel* dynamic systems that are highly interdependent, though in some as yet not well understood manner (Siegel, 2009). Therefore, we believe that, despite their clear differences, minds and brains can therefore both be best understood as being "healthy" to the degree that they each fulfill the criteria that define of a well functioning dynamic system, as these criteria have been described across a range of scientific disciplines (Gleik, 1987; Siegel, 1999).

In essence, an optimally healthy self organizing dynamic system is one whose composite subsystems relate to each other in such a way that the total system is able to be as flexible as possible without becoming *so* flexible that it slips into a state of true disorganization (associated with behavior that lacks any underlying coherence; Gleik, 1987). This kind of sub-system to sub-system relationship maximizes each subsystem's ability to fluidly shift its position of

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[1] A version of this chapter has been submitted for publication. Ozier & Westbury, 2011. *Consiousness and Cognition.*

relative dominance within the total system. This ability is valuable because it[2] offers the most effective means available of meeting the essential challenge faced by any living system, namely, adapting to a constantly changing external environment while *simultaneously* maintaining enough internal stability to preserve integrity as an entity that exists across time (Seigel, 2009).

Psychotherapy, Experiencing, and Adaptive Flexibility

Starting from this definition of health, we will now begin our consideration of how psychotherapy works to enhance mental health. Our consideration will focus on a client process variable called *experiencing*. Depth of client experiencing has been consistently linked to the success of psychotherapy (Greenberg, Korman & Pavio, 2002). Though depth of experiencing exists on a continuum, we use the heuristic of a tripartite model of experiencing, distinguishing between low, medium, and high level modes of experiencing. We view each of these modes as a distinctive form of processing that is invaluable to human beings in particular contexts. Consistent with our definition of health as organized flexibility, we contend that a key determinant of health is the ability to shift flexibly into the mode of experiencing that is most appropriate to the task demands of any specific situation.

Research shows that low level experiencing, relative to deepened experiencing (e.g., mid to high level) is not well suited to resolving the kinds of complex challenges that people typically confront in psychotherapy (Hendricks, 2002). It therefore follows that an individual course of psychotherapy will tend to

be successful to the extent that it facilitates deepened client experiencing. However, on a more global level, we contend that a key cause of human psychological suffering is the tendency to stay rigidly stuck in a low level of experiencing, regardless of current task demands. From this perspective, an overarching goal of psychotherapy is therefore to increase clients' overall levels of flexibility by strengthening their abilities to switch adaptively between levels of experiencing.

We contend that, at a neural level, low, mid, and high level experiencing are associated with the differential engagement of three, large-scale neural systems. We will argue that, at the level of the brain, rigid over adherence to low level experiencing is reflected in maladaptive over-activation of the neural system that supports this form of phenomenological processing. As a client learns to become more flexible by learning to switch between modes of experiencing, this is reflected at the level of the brain by adaptive increases in neural flexibility within the three, large-scale neural systems in question.

The chapter will move through several sections. First, we will offer background by briefly reviewing relevant psychotherapy process and process/outcome research. Next, we will offer a detailed explanation of our tripartite conceptualization of experiencing. After that we will outline a tripartite model of neural subsystems that we believe to interact differentially in order to support low, medium and high levels of experiencing. Following this we will offer selected neuroscientific support for this neural model. We will then offer a detailed consideration of the implications of our model for conceptualizations of

psychopathology. Finally, we will briefly consider the implications of our model for the practice of psychotherapy.

Experiencing as a Common Factor in Psychotherapy

Although the psychological and behavioral manifestations of symptoms that bring people into psychotherapy may be of many different kinds, in every case in which therapy is a feasible treatment option, the common feature is that the client wishes to alter the significance of distress producing aspects of her experience. While schools of psychotherapy continue to multiply, there has long been opinion (Seligman, 1995; Boisvert & Faust, 2003) and more recently much empirical evidence (reviewed below) suggesting that there are common factors underlying all psychotherapeutic processes, regardless of their theoretical underpinnings. This topic was first broached by Rosenzweig (1936), whose paper is often cited for the quotation from Lewis Carroll's (1865) *Alice in Wonderland* that he used to open his discussion of common factors in psychotherapy: "At last the Dodo said, 'Everybody has won, and all must have prizes'". Rosenzweig's claim that effective psychotherapeutic encounters are effective because they share common elements has been referred to as "the Dodo Bird Verdict" (Luborsky, Singer, & Luborsky, 1975).

Perhaps the most compelling evidence in favor of the Dodo Bird verdict is that many impartial meta-analyses of psychotherapy outcome studies have found that all common schools of psychotherapy have approximately equal effect sizes (Robinson, Berman, & Neimeyer, 1990; Smith, Glass, & Miller, 1980; Wampold, Mondin, Moody, Stich, Benson & Ahn, 1997-- for discussions of the role of bias

in studies that conclude otherwise, see Luborsky, 1995; Luborsky, Diguer et al., 1999; Messer & Wampold, 2002). This conclusion does not mean that psychotherapy is ineffective; the effect sizes are not equal because they are very low. The average psychotherapy effect size found by Smith, Glass, & Miller (1980) in their meta-analysis of 475 outcome studies was 0.875. The average effect size found by Robinson, Berman, & Neimeyer (1990) in their meta-analysis of 58 outcome studies (of therapy for depression only) was 0.869. These are unquestionably large effect sizes.

Given the strength of the evidence for common factors in successful psychotherapy, a great deal of psychotherapy process/outcome research has been devoted to trying to understand what those common factors might be. Some of the earliest of this process/outcome research was conducted in the early 1960's under the direction of Eugene Gendlin. Gendlin was originally trained as a phenomenological philosopher. Gendlin investigated the processes through which human beings use language to generate fresh ideas in a creative, emergent manner; processes that allow for the resolution of complex, ill defined problems. Gendlin began studying the process of psychotherapy because doing so provided him with an ideal means of investigating his phenomenon of interest (Hendricks, 2002).

In their early process/outcome work, Gendlin and his colleagues collected hundreds of hours of audiotapes from completed therapies (Hendricks, 2002). Each of the therapies was rated for degree of outcome success. The researchers analyzed the tapes to try to identify in-session behaviors that predicted therapeutic

success. Gendlin hypothesized that there would be specific therapist behaviors and/or certain topics of discussion that would predict therapeutic outcome. However, no such mediator variables were identified. Instead, Gendlin eventually noticed that there was something about *how* the clients talked that seemed to differentiate successful from non-successful therapies. The successful clients seemed to routinely speak in a distinctive, slow, tentative, halting manner, as if they were frequently confirming the "rightness" of what they had just said against some kind of inchoate, background sense of what they *meant* to say (though they hadn't actually said it yet).

In response to these observations, Gendlin developed a theory of human cognitive function centered on the distinctive mode of processing that he labeled "experiencing". Since that time, a substantial body of empirical evidence has emerged to support the claim that depth of experiencing does play a key role in psychotherapeutic success. Depth of client experiencing is one of the few process variables that correlates consistently with positive therapy outcome (Greenberg, Korman & Pavio, 2002; Klein, Mathieu-Coughlan, & Kiesler, 1986; Whelton, 2004).

Most of the therapy process/outcome studies looking at the experiencing variable have used the EXP Scale (Klein, Mathieu, Gendlin, & Kiesler, 1969). Pascual-Leone (2009, p. 117) writes that "The Experiencing Scale is widely considered to be the gold standard of good experiential process and remains one of the most extensively studied and validated measures of productive in session process in psychotherapy research…". He notes that high EXP scores have

"…been shown to be predictive of good treatment outcome across most major schools of psychotherapy, including client-centered therapy, CBT, psychodynamic therapy, and emotion-focused psychotherapy" (p.117). Strikingly, one study (Goldman, 1997) found that depth of client experiencing was a better predictor of success than the strength of the therapeutic alliance, a robust and widely cited mediating variable. Depth of client experiencing therefore qualifies as one of a handful of mediating variables that have been shown to be psychotherapeutic common factors.

While evidence suggests that deepened experiencing is crucial to psychotherapeutic change, this form of processing is not limited to psychotherapy. Instead, deepened experiencing is a widely prevalent, innate form of cognitive processing that is well suited to helping human beings reason through complex, ill-defined, personally salient problems.

A Tripartite Model of Experiencing

Lane & McRae (2003) have developed taxonomy of emotions. We will briefly outline this taxonomy here, so that we can then use it to describe the experiencing construct more cogently. Lane & McRae's vocabulary is particularly valuable to our current purposes because the *felt sense*, the construct upon which high level experiencing fundamentally depends, is notoriously difficult to describe with commonly used English words.

Lane's taxonomy draws a fundamental distinction between *emotions* and *feelings*. *Emotions* are defined as non-conscious, implicitly generated visceral activations and/or actions tendencies that arise in response to a stimulus. Lane

distinguishes two basic classes of emotions. One class consists of discrete foundational emotional states such as anger or sadness. The other class consists of "background emotions" that are "bodily states … generated by internal regulators as well as external stimuli and [that] provide information about one's current state of well being" (Lane & McRae, 2003, p. 100).

In contrast to emotions, *feelings* are defined as cognitions that arise through the explicit awareness of emotions. Lane subdivides feelings into different classes: focal, reflective, and background. *Focal feelings* arise through attending to foundational emotions such as fear or anger. *Reflective feelings* involve the conscious reflection upon focal feelings and therefore involve a significant meta-cognitive component. *Background feelings* arise through attending to background emotional states. Because background emotions are more diffuse than focal emotions, background feelings typically arise on the periphery of awareness as relatively diffuse conscious experiences such as "feeling lousy" (Lane and McRae, 2003, p. 103). However, crucially for the model we will develop, Lane and McRae (2003) postulate that when background emotional states are given adequate attention it is possible for them to give rise to subtle, nuanced, consciously accessible background feelings. We hold that, in Lane's terms, a felt sense can be understood as comprising *the background feeling that arises through consciously attending to the background emotion of a particular "situation, problem, or aspect of one's life"* (Gendlin, 1996, p. 20). The felt sense will be explained in more detail during our description of high level experiencing.

Three Levels of Experiencing

The experiencing process is commonly addressed within the literature as a continuous variable, with higher levels of experiencing associated with more productive therapy outcome. However, we make a heuristic and qualitative distinction between low, medium, and high levels of experiencing, and we particularly highlight the distinctive qualities of mid level experiencing. We believe that adopting this tripartite model of experiencing is valuable for two reasons. First, doing so usefully informs clinical practice in ways we will describe below. Second, we believe that this tripartite model of experiencing is consistent with the neural systems that support the experiencing process, a contention that will become a central focus of the later sections of the paper.

Low Level Experiencing

During low level experiencing (approximately equivalent to levels 1-3 on the 7 point EXP Scale; Klein, Mathieu, Gendlin, & Kiesler, 1969) the client speaks largely in a conceptual manner. She spends much of her time projecting herself into remembered pasts or imagined futures, simulated realities that are decoupled from the "here and now'" (Buckner, Andrews-Hanna, & Schacter, 2008). In this mode the client also tends to spend a lot of time standing outside herself and treating herself as an object of deductive inquiry, trying to deduce what she "must" want in her life, how she "must" be feeling about her situation, and therefore what steps she "should" take next to resolve her presenting issue. This conceptual mode of processing is reflected in the client's predominant use of *Externalizing Voice* (Rice, Koke, Greenberg, & Wagstaff, 1979), which is defined

by an externalizing vocal quality. A speaker exhibiting this quality speaks at a regular, fast, even pace, indicating "…that energy is being invested in recounting rather than exploring" (Wiseman and Rice, 1989, p. 282).

While low level experiencing is most easily recognized by the presence of an externalized tone, this does not imply that low level experiencing must be devoid of emotional arousal or focal feelings. Instead, when emotions/feelings do arise, they emerge out of and recede back into a conceptualized map of the terrain under discussion, rather than emerging from an embodied, background *sense* of that terrain (as in deepened experiencing).

Low level experiencing is a valuable mode of processing for human beings. Its primary advantages are the rapidity and ease with which space and time can be imaginatively traversed. These qualities make it very well suited for solving problems efficiently in domains of relative certainty by rapidly generating possible future events and then thinking them through (see related discussion in Damasio, 1994). However, it is notably ill suited to resolving the kinds of complex, value laden life challenges that usually bring people into psychotherapy. As such, low level experiencing is correlated with unproductive psychotherapeutic process (Hendricks, 2002). Externalizing voice, which is strongly correlated with low level experiencing, is also predictive of therapeutic failure (Greenberg and Malcolm, 2002). Findings around the experience of intense focal feelings in therapy are more nuanced. In contrast to popular notions of effective therapy, intense focal feeling is not necessarily predictive of successful outcome (Greenberg and Malcolm, 2002). Instead, when intense focal

feelings arise in the context of low level experiencing this constitutes a form of "mindless emoting" (Teasdale, 1999) that tends to predict failure. In contrast, when intense focal feelings arise in the context of deepened experiencing they tend to predict therapeutic success.

Medium Level Experiencing

A client who is processing at medium levels of experiencing (approximately equivalent to a rating of four on the EXP Scale) will typically demonstrate substantial variability in manner of processing. He will tend to have extended periods in which his processing is strongly reminiscent of low level experiencing, as described above. However, a background emotion of the overall situation has now become tacitly active within the client. Therefore, the client begins to implicitly *refer to* this background emotion. The background emotion of the overall situation, though strongly activated, has not yet become an object of focal attention, thereby preventing it from being transformed into a felt sense (as occurs during high level experiencing).

Guiding, continuous scale somatic feelings of rightness or wrongness now begin to emerge as the client tactility attempts to speak *from* the relevant background emotion. Feelings of rightness are experienced as subtle, somatic feelings of easing, while feelings of wrongness arise as subtle sensations of somatic tension (Dreyfus, 2002). These sensations most commonly arise within the sternum, chest or throat areas (Ozier & James, 2005). Dreyfus explains the role of feelings of rightness or wrongness in his discussion of Merleau-Ponty and the development of expertise. Dreyfus (2002) argues that these feelings guide

behaviour by helping one to maintain a state of "maximal grip" (Merleau-Ponty, 1962, p. 302) in one's relation to the task at hand. Dreyfus makes an analogy to the children's game "colder…warm…warmer" in which behaviour is guided through feedback that offers subsequent approximations toward a goal. However, in this case the ideal end goal state itself is not explicitly represented in *any way* but instead evolves through the process of continually readjusting one's behaviour to maintain the sense of an "optimal gestalt" (Dreyfus, 2002, p. 413) with one's situation. According to Merleau-Ponty (1962) and Dreyfus (2002), it is to a significant extent by unconsciously responding to these subtly embodied cues that experts within a given domain achieve skilful coping.

During medium level experiencing the client will frequently speak for extended periods in Externalizing Voice until an emerging feeling of wrongness tells him that he is beginning to veer off course from what he is implicitly trying to say. This will typically initiate transition to a period of *Focused Voice* (Rice et al., 1979), which has a tentative, inwardly searching quality, indicating a "turning inward of attentional energy toward tracking inner experience" (Wiseman and Rice, 1989, p. 282). Focused Voice tends to be slow and halting, with frequent starts and stops as possible next steps are inwardly checked for "rightness" against the implicit sense of what needs to be said next (Rice et al., 1979). Typically, when an increasing feeling of rightness eventually tells the client that he has found the thread again, this will transition back to another phase of Externalizing Voice.

Focused Voice has been found to be associated with productive therapeutic process (Greenberg & Malcolm, 2002). Medium level experiencing, combined with occasional periods of high level experiencing, is typically the most productive mode of information processing during psychotherapy.

High Level Experiencing

As alluded to earlier, high level experiencing (approximately EXP Scale levels 5 to 7) is based on the generation of a *felt sense*, the product of a non-consciously controlled yet highly sophisticated level of human information processing system. Just as the emotional system generates emotions, and the cognitive system generates cognitions, the felt sense processing system generates felt senses. A specific felt sense is a "bodily sense of some situation, problem, or aspect of one's life…" (Gendlin, 1996, p. 20). Felt senses are "implicit higher level meanings […involving…] the sense of something that includes thoughts, feelings, perceptions, internal actions, and context." (Greenberg, Rice, & Elliot, 1993, p.165). Once a felt sense has become the focus of awareness, specific focal emotions, memories, images, or ideas that are associated with particular aspects of the overall situation in question can emerge *out of* the background tapestry of the felt sense. These specific phenomena can then become figural against the ground of the felt sense. However, the discrete and tangible phenomena evoked by attending to the felt sense are not themselves the felt sense.

Equating a felt sense with a focal feeling such as anger or sadness is a common error. There are two related differences between a felt sense and a focal feeling. First, as a form of background feeling, a felt sense initially manifests less

distinctly and less intensely than a focal feeling. Second, the meaning of a focal feeling is explicit while the meaning of a felt sense is implicit. A generic symbol (such as the word ‘sad’ or ‘angry’) is able to describe a given focal feeling each time we feel it. A felt sense, in contrast, is difficult to symbolize. Each felt sense is a rich and complex mosaic of implicit meanings. High level experiencing can be understood as the act of symbolizing the next step toward healing or problem resolution that will typically be implicitly contained within a felt sense.

At high levels of experiencing the client senses her situation as a lived whole and can then experientially work, step by step, through her issue from *inside* that felt sense. In contrast to mid-level experiencing, the felt sense is now symbolized in focal awareness and can therefore be used in a deliberate, intentional manner as the client moves back and forth between the implicit meanings contained within the felt sense and the explicit meanings contained within potential symbols (Gendlin, 1996; Mathieu-Coughlan & Klein, 1984).

The client’s verbal patterns tend to be extremely slow and irregular with frequent periods of very long silence. When it does occur, speech is largely in the previously described Focused Voice (Rice et al., 1979). As with medium level experiencing, continuous scale feelings of rightness and wrongness continue to guide the process of meaning making and problem resolution. However, unlike with medium level experiencing, the correctness of possible steps can now also be overtly checked in a *binary* yes/no fashion. This step is achieved in psychotherapy by making a checking statement and then waiting for the felt sense system to respond by either producing, or failing to produce, a distinctive form of sensation

called a "*felt give" (*Gendlin, Beebe, Cassens, Klein & Oberlander, 1968, p. 231). Gendlin describes the felt give as a subtle, pleasant, stirring sensation that is usually experienced in the stomach, chest or throat (Gendlin, 1996). When a felt give arises in response to a checking statement, this is taken is confirmation that the felt sense system has assessed the proffered symbol or potential next step to be a right match or a good next step.

During the iterative movement between a felt sense and symbolizing possible next steps, the felt sense's responses must be given priority (Gendlin, 1996). No matter how correct an idea, theory, or potential next step may appear *conceptually*, it should only be considered to be pointing in a useful therapeutic direction if it evokes a felt give when a checking statement is used to confirm its potential rightness. For example, imagine that, after reflection, a client has the surprising realization that he is not only deeply sad at the recent death of his wife but he also feels angry at her for leaving him. As the client says this a felt give emerges within him, thereby indicating the likely experiential rightness of this step. The therapist might then confirm the rightness of this potential step by reflecting back to the client: "So a part of you is angry at her for leaving you alone". If a second felt give emerged within the client in response to this checking statement then this would serve as an experiential confirmation that what had just emerged was a "right" next step forward for the client.

High level experiencing is not easy for many people to engage in (Gendlin, 1996). It often requires significant guidance. This is one disadvantage of higher-level experiencing in many problem-solving contexts. However, as we

will argue at the close of this paper, in the context of psychotherapy we see high level experiencing ability as necessary for success. The most important advantage of high level experiencing is that it can help to turn implicit meanings into explicit meanings so they may to be worked with more fruitfully.

From Clinical Psychology to Neuropsychology

A client comes to psychotherapy in order to resolve issues that are usually not only complex and ill defined, but that are also highly salient within his sense of narrative or "autobiographical self" (Damasio, 1999, p.17). Regardless of the level of experiencing involved, psychotherapy can therefore be understood as a guided exploration of the client's sense of self. For this reason, to be credible, our neural model of self-referential processing during psychotherapy must be consistent with current neuroscientific understandings of how self-referential processing occurs more generally. In this section, we will briefly review neuro-imaging studies on self-referential processing. However, the indivisible relationship between consciousness and the sense of self means that addressing self referencing from a neural perspective first requires access to a neurally grounded model of human consciousness. We therefore start by offering a synopsis of Damasio's (1999) model of consciousness so that it can then serve as a foundation for the ideas that follow.

Damasio's Theory of Consciousness

Damasio (1999) argues that the process of constructing the self starts with the generation of two separate neural maps. The first is a map of the stimuli with which a person is currently interacting. The second map represents the changing

state of that person's own body as she interacts with those stimuli. This latter map of the changing state of the body, which forms the basis for what Damasio calls *the proto-self*, is putatively neurally encoded by a number of structures that are devoted to mapping and regulating the internal state of the body, including brain stem nuclei, the hypothalamus, and the insula.

According to Damasio, there is no sense of consciousness attached to the functioning of the proto-self because it is a process of unfolding without any sense that the unfolding *belongs* to anyone in particular. Consciousness arises when both of these first order maps get remapped into a single second order map, which thereby encodes a complete record of the proto-self changing itself as it interacts with the world. As this second order map arises it produces an ephemeral, background feeling that the changes occurring to the proxy, proto-self are happening to a self. It is as if the core self watches the changes that are occurring to the proto-self while constantly regenerating a fresh background feeling of identification with the experience of the proxy, proto-self. This background sense of a watching self is *the core self*. The core self generates core consciousness, which is transient and is constantly being regenerated.

Damasio suggests that the second order map that is essential to core consciousness is likely generated by the coordinated activity of a limited number of brain centers. In the most recent (2003) version of his model, Damasio stresses the importance of the anterior cingulate cortex (ACC) and the insula in supporting generation of the core self, arguing that the insula may be "involved more

significantly than any other structure" (p. 105) in the subjective feeling processes that underpin self-awareness.

In Damasio's model of consciousness, over time we generate rich networks of self-defining memories. These networks allow for the emergence of extended consciousness and the related autobiographical sense of self. This sense of self becomes richly elaborated and extended through time. However, the autobiographical self always relies on the feeling of the core self to become activated in a meaningful way. It is the continuous, background activity of the core self that allows your self-defining autobiographical memories to feel like *your* memories. Without a constantly emerging background "feeling of what is happening" (Damasio, 1999) there can be no extended consciousness.

The Neurology of Self-Related Processing

Recent research extends Damasio's model of the neural representation of the self by providing evidence that our self has a complex neural representation composed of several interacting processes. Northoff, Heinzel, De Greck, Bermphol, Dobrowolny, & Panskeep, (2006) performed a meta-analysis of 27 PET and fMRI studies that involved self-related tasks. This analysis involved performing a hierarchical cluster analysis upon the 324 peak activations that were reported in the included studies. This analysis revealed the presence of three reliable clusters (shown in Figure 1) that emerged regardless of the sensory mode of stimulus presentation.

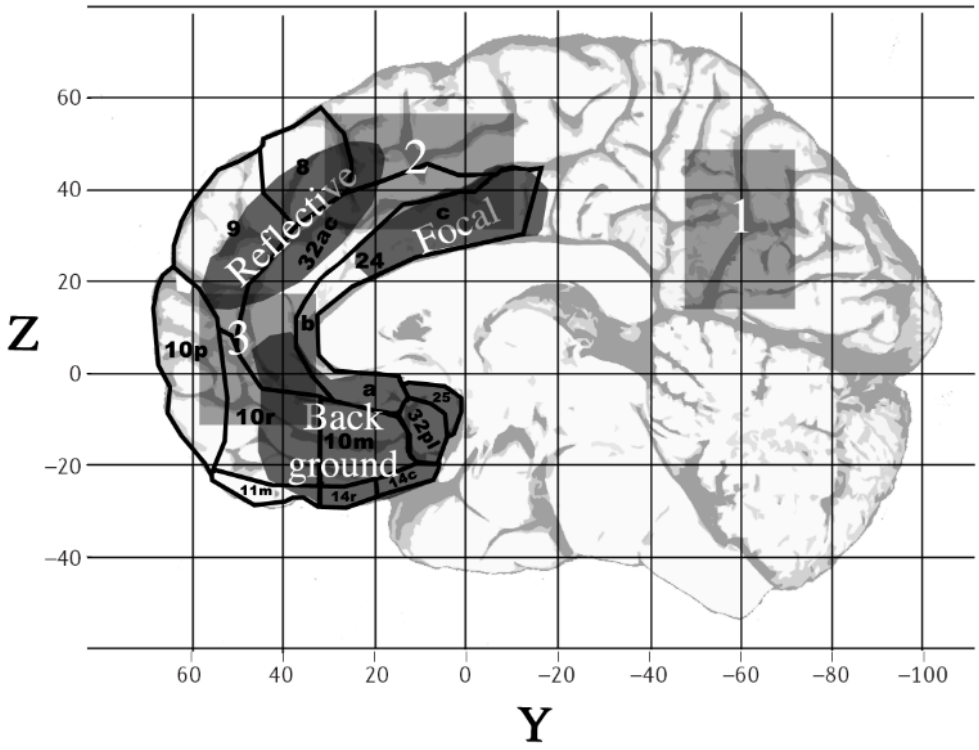

Figure 2-1: Summary of regions implicated in self-related tasks. The three rectangular regions are re-drawn from Northoff et. al.'s (2006a) meta-analysis of 27 imaging studies of self-referential processing, which found three modality-insensitive activation clusters. The extent in either dimension represent the standard deviation of the cluster. Region 1 is involved in autobiographical memory. Region 2 is involved in explicit cognizing about self-related stimuli. Region 3 is implicated in non-symbolic, self-related affective processing. The three regions labeled with names are re-drawn from Lane & MacCrae's (2003) summary of the neural substrates of conscious emotional experience, and are associated with the three types of emotion they identify. The area labeled 'reflective' is associated with conscious reflection on experienced feelings. The area labeled 'focal' is implicated in direct conscious awareness of basic emotional states such as fear or anger. The area labeled 'background' is implicated in generating background states that are not noticed unless they are attended to. See also Figure 2.

Region 1 is centered in the posterior parietal cortex. This region is implicated in the access of episodic, autobiographical memories (Buckner, Andrews-Hanna, & Schacter, 2008). Region 2 falls within the dorsomedial prefrontal cortex (dmPFC). Region 3 falls within the orbital medial prefrontal cortex (omPFC). Northoff et. al. (2006) suggest that that the omPFC cluster is implicated in non-symbolic self-related affective processing while the dmPFC cluster is implicated in re-representation of this information in a symbolically accessible manner.

Related research has generally supported the conclusions of the Northoff et al. (2006) meta-analysis. However, recent work suggests that refinement is necessary to the conclusion that there is a single cluster in the omPFC that supports the "non-symbolic, affective" aspects of self-referential processing. Andrews-Hanna, Reidler, Sepulcre, Poulin, & Buckner (2010) used MRI to investigate the neural correlates of self-referential processing. They produced evidence that that there are three neural sub-systems that operate together to support autobiographical self -reflection and projection of the autobiographical self. Projection of the autobiographical self is understood here to mean "mentally transporting oneself into alternate times, locations, or perspectives" (McVay and Kane, 2010, p. 193). These systems include dissociable clusters of activation within the PFC (see Figure 2). One of these subsystems had activation centered in BA 9 (0, 52, 26). Andrews-Hanna et al. (2010) suggest that this subsystem (like the more dorsal cluster in BA 8 identified by Northoff et al. (2006) is involved in the meta-cognitive processes of reflecting upon one's own state of mind. A

second subsystem had omPFC activation centered in ventral BA 10 (0, 26, -18). This subsystem plays a key role in mental scene construction, a process that is vital to allowing the autobiographical self to mentally project through space and time. A third subsystem, also with omPFC activation, lies between the activation of the other two subsystems, in dorsal BA 10r (-6, 52, -2). Activation in this region was found to be strongly associated with task variables related to "personal significance, introspection about one's own mental state, and evoked emotion" (Andrews-Hanna et al., 2010, p. 558). The authors suggest that this middle subsystem is fundamentally devoted to "evaluating aspects of personal significance" (Andrews-Hanna et al., 2010, p. 559) and that, of the three subsystems, it constitutes the core subsystem for self related processing.

The conclusion that self related processing is supported by three distinct PFC regions is consistent with the results of a recent resting state connectivity study that was designed to identify large, distinct functional networks within the human brain (Liao et al., 2010; see Figure 2). Liao et al. (2010) used simultaneous EEG-MRI in order to help overcome the difficulties that MRI has had with distinguishing resting state networks that lie close to each other. They identified components of three distinct resting state brain networks within the medial PFC. These authors argue that the three distinct networks they identified have traditionally, mistakenly, been subsumed within a single, large, frontal component of the "default mode network". The first of these putative networks (see gray area in Figure 2A) is anterior, involving clusters in the dmPFC (BA 9 [centred at 9, 69, 15]), and the OFC (BA 10p [at 0, 63, -6] and ventral BA 10 [at 9, 63, -18]). The

second putative resting state network identified by Liao et al. (2010) . is centered in the mOFC (BAs 11 and ventral BA 10: example peak at 9, 54, -21) and overlapped the mOFC centered sub system identified by Andrews-Hanna et al. (2010; see Figure 2B). Finally, Liao et al. identified a network that lies between these two networks, centered in dorsal BA 10r and in neighboring BA 32 ac (see Figure 2C). As shown on Figures 2 A-C, all three networks overlap with the core self-processing sub-system (labeled C in Figure 2) identified by Andrew–Hanna et al. (2010).

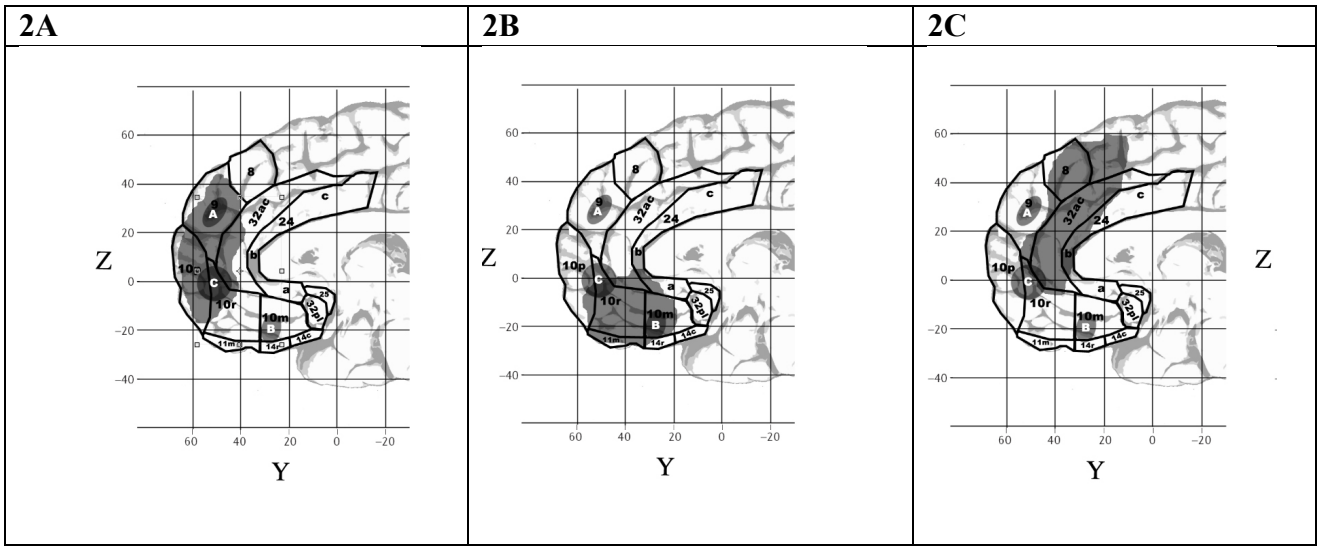

Figure 2-2: Frontal regions associated by resting state connectivity and with self-related processing.

Grey Areas: Frontal components of the three distinct medial subsystems identified by resting state connectivity (Liao et al, 2010).

Regions A,B, & C: Default network medial frontal activation for systems associated with narrative self-reflection and self-projection, as identified by Andrews-Hanna et al. (2010). The region in Figure 2A (the dorsal medial prefrontal cortex subsystem) shows functional connectivity with the temporoparietal cortex, lateral temporal cortex, and the temporal pole and is associated with meta-cognitive processes of reflecting on one's own state of mind. The region in 2B (the medial temporal lobe system) shows functional connectivity with the posterior inferior parietal lobe, retrosplenial cortex, and hippocampal and parahippocampal regions, and is associated with mental scene construction. The region in 2C, considered part of the core subsystem for self-related processing, is a common 'hub' for the other two subsystems, comprised of the medial prefrontal region shown and posterior cingulate cortex, associated with introspection and evaluating aspects of personal significance.

Note that all three subsystems overlap with Andrews-Hanna et al. (2010)'s common hub for self-related processing, marked with a C.

The Neurology of Self-Related Reasoning

In this section we will build on the ideas presented thus far to offer our systems level model of human, self-referential reasoning, which is summarized diagrammatically in Figure 3. We conceive of this model as involving interaction between three neural systems. In brief, we conceptualize our three functional systems as a more strongly emotional, ventral "hot cognitive system" (Goel & Dolan, 2003); a more strongly cognitive, emotionally neutral, dorsal "cold cognitive system" (Goel & Dolan, 2003); and a middle mediation system that supports middle to high level experiencing. Ultimately, we will outline the systems level interactions *between* these three large scale systems and how we believe these neural changes impact depth of experiencing. In advance of this we will describe the key components of each of our three systems independently.

We conceptualize each subsystem as involving a specific set of contextualizing neural processes (some of which also contextualize each other), where 'contextualized' means that the content and output of the process is modulated (its valence and/or meaning modified) by input from another source. Each subsystem has an evolutionarily nested form, with phylogenetically older components interacting with newer analogues that perform similar functions in more complex and integrative ways. In the case of each system we will discuss these processes in phylogenetic order, first addressing the evolutionarily older components, and then their more recent analogues.

'Hot' Cognition System: The BLA of the amygdala & inferior prefrontal cortex

Evolutionarily Older Hot Cognition Subsystem: The BLA of the amygdala

The lowest level of our hot cognition system is formed by the basolateral complex of the amygdala (BLA, made up of the lateral, basal, and accessory basal nuclei). The amygdala is a complex, heterogeneous, and phylogenetically ancient system. For the purposes of our model (following Etkin, Egner, Peraza, Kandel, and Hirsch, 2006), we consider a simplified model of the amygdala consisting of the BLA and of the central nucleus (CNA).

The CNA has extensive connections to the brainstem, hypothalamus, basal forebrain, and the ventral insula, as discussed below. It appears to play crucial roles in determining general affective responses to both appetitive and aversive stimuli and in initiating species-specific behaviors in response to those stimuli (Bechara et al., 1999; Balleine and Killcross, 2006). The BLA has strong cortical connections by which it receives extensive multi-modal sensory input, and plays a crucial role in associative learning by encoding memories related to sensory stimuli (Etkin, Keller, Schatzberg, Menon, & Greicius, 2010). In turn, this allows the BLA to modulate the "… memory encoding and sensory processing in other regions… [by broadcasting its memory-informed assessment of] the threat value of a stimulus" (Etkin, Keller, Schatzberg, Menon, & Greicius, 2010, p. 1362). Chief among these modulated regions is the CNA itself, to which the BLA sends output. In our terms, the BLA *contextualizes* the output of the CNA.

Evolutionarily Newer Hot Cognition Subsystem: mOFC and vmPFC

As illustrated in Figure 3, the BLA is itself contextualized by the medial orbital PFC, to which it has strong bidirectional connections **(**Ongur & Price, 2000). Acting in concert with adjacent vmPFC, medial orbital PFC (BA 11) may be important for using input from the amygdala to represent the pleasant or unpleasant affective value of a stimulus (Davidson & Irwin, 1999; Knutson, Fong, Adams, varner, & Hommer, 2001; O'Doherty, Kringelbach, Rolls, Hornak, & Andrews, 2001) in a flexible format that is sensitive to momentary changes in social and motivational context (Bechara, Damasio, & Damasio, 2000; Ochsner & Feldmann Barrett, 2001; Rolls, 2000). This allows for a richer encoding of the affective properties of stimuli than the amygdala alone would be capable of computing (Bechara, Damasio, Damasio, & Lee, 1999; Schoenbaum, Chiba, & Gallagher, 1999). We believe that it is useful to conceptualize medial BA11 as an evolutionarily new analogue of the amygdala's BLA, since it also integrates emotional memory and guides appropriate behavior to encountered stimuli.

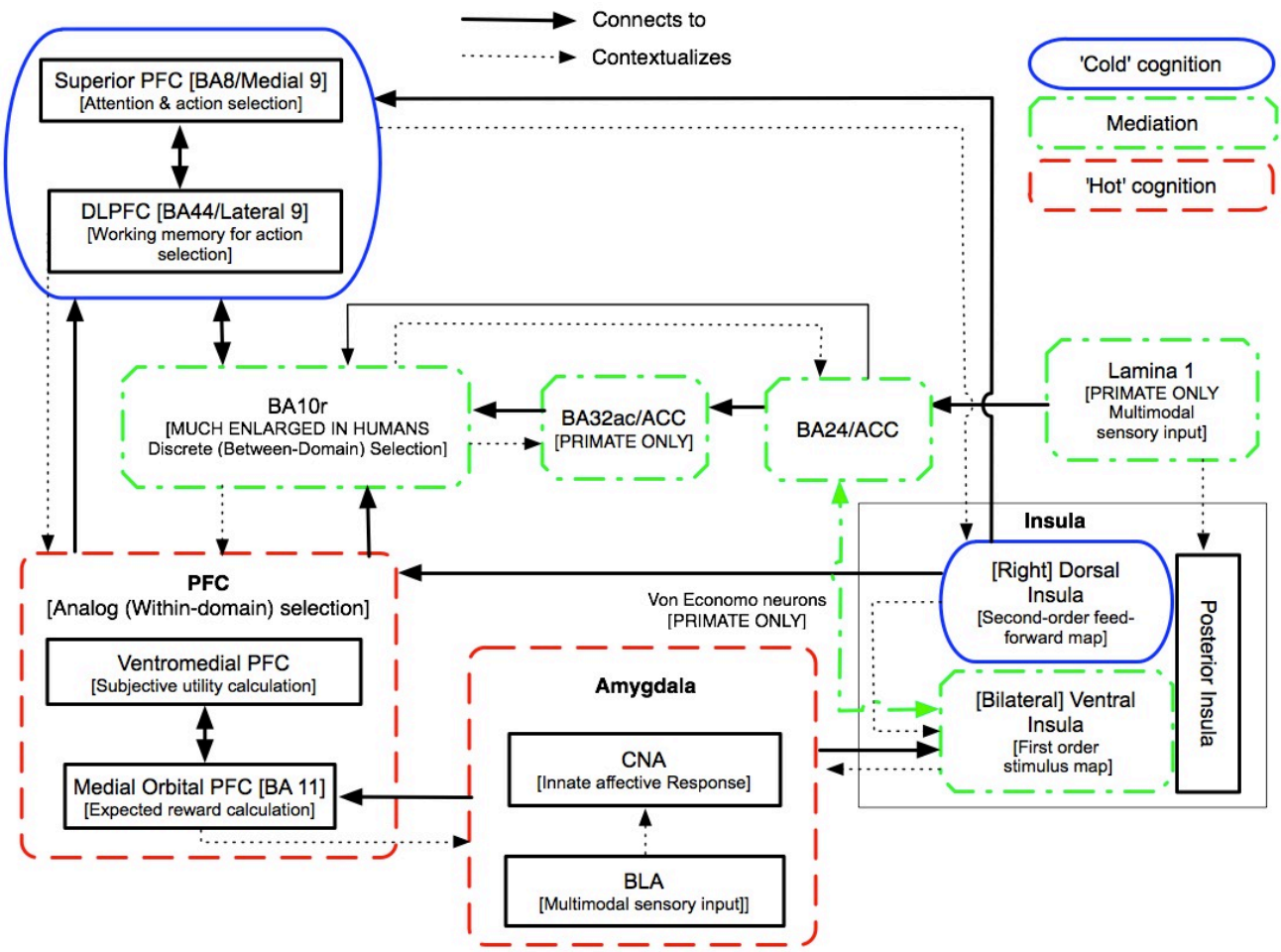

Figure 2-3: Outline diagram of the tripartite model of the human mind

Rolls (2009, p. 114) has argued that orbital/ventro-medial PFC complex is the "computer of reward magnitude and expected reward value…", tracking the ongoing, homeostatically contextualized, dynamic reward value of encountered stimuli. One piece of evidence cited in support of this claim is that neurons in this region fire faster in response to food when a person is hungry than when he is not. In the orbital PFC, reward valuations are integrated with other relevant information to generate representations of "expected value", defined as probability times reward value (Rolls, 2009). These expected value representations are then fed more dorsally, this time into the vmPFC. There they are processed into representations of *subjective utility* (Rolls, 2009, p. 114). Subjective utility integrates the expected reward value of a stimulus with broader contextual information such as the person's degree of risk aversion and other related personality and/or internally mediated factors. Rolls (2009) argues that reward value, expected value, and subjective utility judgments are all neurally coded in a continuous fashion, based in part on the finding that there is a linear correlation between assessed value and the firing rate of the coding neurons.

Neuroimaging (Li, Lu, D'Argembeau, Ng, & Bechara, 2009) and neuropsychological evidence (Naqvi, Shiv, & Bechara, 2006) suggests that a medial OFC/vmPFC subsystem generates *somatic markers* in order to communicate its predicted value of potential rewards (see Figure 4). Somatic markers are a form of "gut feeling" (Damaio, 2003, p. 148) through which vmPFC subsystem (in particular) is able to guide both behavior and conscious cognitive processing (Damasio, 1994).

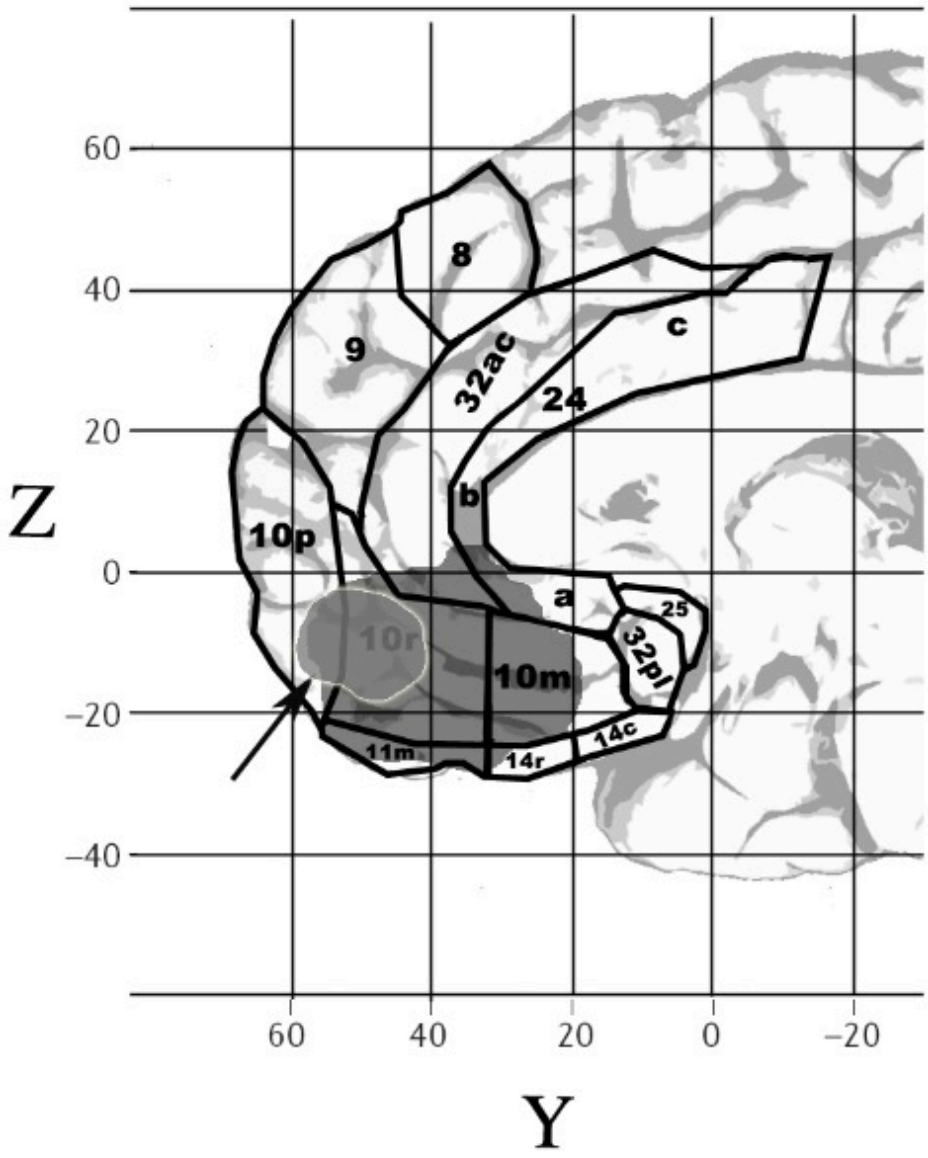

Figure 2-4: Arrow points to medial BOLD activation in the region that was positively correlated with *successful learning* during completion of the Iowa Gambling task (from Li et al., 2009, p. 481). Note the overlap between this putative "somatic marking region" and the center of the ventral medial subsystem identified by resting state connectivity (Liao et al, 2010, as in Figure 2B).

As this description makes clear, somatic markers are both functionally and phenomenologically similar to the previously described "feelings of rightness/wrongness" that we posit to be crucial to high, and particularly mid level, experiencing. Functionally, both of these classes of embodied responses can either overtly or covertly guide behavior and/or conscious cognitive processing. However, while somatic markers are typically associated with "the gut" (Damasio, 2003), feelings of "rightness/wrongness" seem to be more frequently experienced higher up in the chest or sternum area (Ozier & James, 2005). Further, Damasio presents the somatic marker as a kind of biasing "alarm signal" (Damasio, 2003, p. 147) suggesting a relatively crude form of assessment (e.g., good vs. bad). Alternately, along with Dreyfus (2002), we conceive of feelings of rightness and wrongness as capable of reflecting subtle, dynamic variations of felt "rightness".

'Cold Cognition System: Right dorsal insula & superior prefrontal cortex

Although cold cognition is underlain by many posterior cortical regions, for purposes of simplicity and clarity of exposition we focus on its synthesis in dorsolateral PFC (dlPFC, BA 9, 45, and 46; see Vincent, Kahn, Snyder, Raichle, and Buckner, 2008) and on the specific contribution of the right dorsal anterior insula (AI).

Evolutionarily Older Cold Cognition Subsystem: Lamina 1/Dorsal Anterior Insula

Craig (2002, 2004) has produced neuroanatomical and experimental evidence of the existence of a previously unrecognized afferent neural system

called lamina 1 that has crucial implications for our model. Lamina 1 only exists within human beings and other primates. This system collects afferent information from *all* the tissues of the body and then systematically integrates and re-represents this information. Lamina 1 terminates in three cortical locations (Craig, 2007): somatosensory cortex (BA 3a), dorsal ACC (BA 24c) (Strigo, Simmons, Matthews, Craig, & Paulus, 2008), and the posterior insula (Craig, 2002; 2007). Within the insula, lamina 1 continues to feed forward until termination in the anterior insula.

The insula has been assigned a diverse range of functions. Among these have been roles in learning and memory, perception of temporal sequence, pain perception, language, autonomic arousal, and integration of emotional and motivational factors (Flynn, Benson, & Ardila, 1999). As shown in Figure 3, the insula will be presented in a simplified manner as being composed of three functional zones: the dorsal AI, the ventral AI, and the posterior insula. We will focus almost exclusively on the anterior insula here.

Emerging evidence suggests that it is crucial to distinguish between ventral and dorsal components of the AI. As illustrated in Figure 5, these two regions have markedly different resting state connections with the PFC (Nelson, Dosenbach, Cohen, Schlaggar, & Petersen, 2010). The ventral AI (with a right ventral AI seed at 30, 23, -11) shows very limited resting stated connectivity with the lateral PFC. It does show strong resting state connectivity with the medial PFC, including with the inferior ACC (BAs 24 and 32 ac) and medial PFC (BA 10). The dorsal AI (with a right seed identified at 34, 29, 4) has strong

connections with lateral PFC, including an epicenter of connectivity in the dlPFC. The dorsal AI shows strong resting state connectivity with one just medial PFC region (0, 36, 46). This falls in a region that was identified by Seeley et al. (2007) as being the *only* medial PFC centered node within their *Executive Network*, a network of brain regions that is centered in the dlPFC (with bilateral epicenters in both BAs 46 and lateral BA 9) and implicated in attentional control and conscious response selection. Seeley et al.'s Executive Network has strong parallels to what we are calling the cold cognition system.

A recent meta-analysis (Kurth, Zilles, Fox, Paird, & Eickoff, 2010) provides further evidence of a functional distinction between the ventral and dorsal components of the AI. These authors looked at the results of over 1,700 neuroimaging studies to investigate the involvement of different insular regions within four broad functional domains. The ventral AI was implicated *only* in processing tasks that required social or emotional valuation. The dorsal AI was implicated in processing tasks in the same social-emotional domain but also to be strongly and broadly activated by tasks in the cognitive domain (e.g., language, attention, memory).

These findings support our key contention that, along with the dlPFC and dmPFC, the dorsal AI is a part of the brain's cold cognition system. However, unlike the dlPFC and/or dmPFC, the right dorsal AI serves as the key interchange *between* this system and the brain's ventral AI centered mediation system, as will be discussed below.

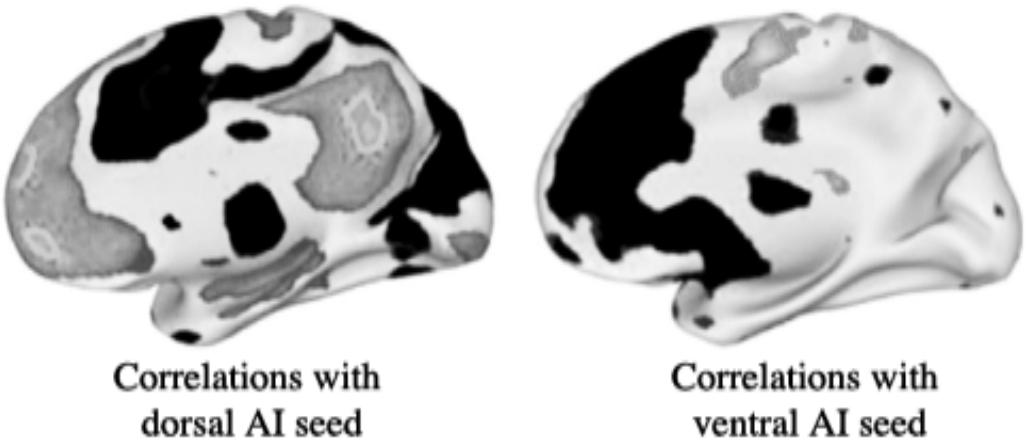

Figure 2-5: The dorsal (left) and ventral (right) AI show markedly different patterns of resting state connectivity with left medial cortex (Figure adapted from Nelson et al., 2010, p. 676). Black regions are positive correlations with seed regions in the dorsal versus ventral AI; light great regions are negative correlations with each seed.

Craig (2004) argues that, as a key terminus for the lamina 1 information, a consciously accessible "meta-representation" (p. 239) of the current state of the entire body is generated within the right *dorsal* anterior insula. According to Craig, this representation provides a person with a background sense of self as an integrated, embodied entity and is "the material me" (Craig, 2004, p. 241). This right dorsal anterior insula meta-representation therefore constitutes a *second order map* in Damasio's (1999) terms, providing a contextual, homeostatic ground against which ongoing first order maps (representations of the proto-self responding to salient stimuli) can become figural. We contend that first order, proto-self related maps are *also* represented in the insula (Damasio, 1999), but bilaterally in the *ventral* AI.

The ventral AI directly receives rudimentary salience assessments about encountered stimuli from the CNA (Seeley, Menon, Schatzberg, Keler, Glover, Kenna, Reiss, & Greicius, 2007) (see Figure 3). Via lamina 1, fast amygdala-driven assessments of the salience of an encountered stimulus can be contextualized, given greater or lesser weight. During this process, first order neural maps that include information from lamina 1 about the organism's overall homeostatic state contextualize the CNA's salience assessments. These maps (supported by ventral AI) can then be immediately *re*-contextualized by second order maps (supported by right dorsal AI). We believe these latter maps to be based on lamina 1 information (as will be discussed below). The ventral/dorsal AI figure–ground relationship makes it possible for homeostatic meaning to be

quickly and cogently assigned to whatever internal or external stimulus is encoded in the first order body map in question.

As a concrete illustration of this process, Craig (2007) asks us to compare the experience of drinking a cool glass of water on a warm, summer day with this same experience on a rainy day when we are chilled to the bone. This example makes clear that it is not possible to ascribe homeostatic meaning to *a stimulus in itself*: A stimulus must always be considered against the homeostatic context of the organism's current state. During daily life this necessity is strongly obscured by the human tendency to project the meaning of things onto the things themselves (Craig, 2007). It is also only through this crossing of the part (contextualized encoding of the body's action response to a specific stimulus) against the whole (enhanced awareness of the body's current, overall homeostatic state) that both homeostatic meaning *and* self-awareness of that meaning become possible (Damasio, 1999; Craig, 2004).

The existence of lamina 1 only in primates is suggestive evidence that primates may have evolved a unique ability to refine the CNA's preliminary salience assessment. The described process may allow primates to quickly get both a "first opinion" (supported by ventral AI) and a "second opinion" (supported by right dorsal AI) about the CNA's original interpretations. An evocative, concrete demonstration of this capability was recently offered by a study conducted by Björnsdotter, Löken, Olausson, Vallbo, and Wessberg (2009), who showed that lamina 1 responds specifically to *gentle* touch. When people are allowed to have a loved one hold their hand during a pain induction they rate their

experience of pain unpleasantness as significantly lower (Master, Eisenberger, Taylor, Naliboff, Shiriyan, & Lieberman, 2009). Lamina 1 re-contextualization allows the meaning, or threat value, of the pain stimuli to be "tuned" by factoring in a background context that includes the presence of social support.

Evolutionarily Newer Cold Cognition Subsystem: dlPFC/dmPFC

Findings cited in the section above have led us to designate the dlPFC (BAs 9/46) and more dorsal, medial PFC regions (BAs 8/9) as components of our evolutionarily new cold cognition system. We will focus in detail only on the dlPFC here.

The dlPFC has been implicated by human imaging and animal lesion studies in a wide range of higher cognitive functions, including evaluation of expected reward; response and goal selection, initiation, and inhibition; word and random response generation; attentional shifting; sensitivity to the demands of a changing context; and selective retrieval from a set of items held in short-term memory. Several commentators have tried to generalize across these tasks. Miller & Cohen (2001) argue that the prefrontal cortex in general is critical "when we need to use the 'rules of the game,' internal representations of goals and the means to achieve them" (p. 168). Petrides (1996) argued that dlPFC in particular is active when "several pieces of information in working memory need to be monitored and manipulated on the basis of the requirements of the task or the subject's current plans" (p. 61). Kapur et al. (1994) proposed that the region's role may be characterized as "manipulation of the representation in context of the instructions and mapping the response onto an output system" (p. 2195).

Likewise, Leon & Shadlen (1999) suggest that the dlPFC plays "a role in guiding behavior that does not ensue immediately, but is to be enacted seconds after the acquisition of a sensory instruction" (p. 415). Deacon (1998) has argued that all tasks modulated by dlPFC "have to do with using information about something you've just done or seen against itself, so to speak, to inhibit the tendency to follow up that correlation and instead shift attention and direct action to alternative associations." (p. 263). These descriptions all capture the fact that the role played by the dlPFC involves modulating the nature of imminent behavior in response to changing task demands. An elegant phrase for the role has been proposed by Frith (2000); 'sculpting the response space'. Although Frith's pithy description over-emphasizes the dlPFC's role as an autonomous entity while under-emphasizing the neurological context upon which it is dependent, it does capture the idea that cold cognition is in large part devoted to the slow selection of action, especially under the guidance of memory.

As we have mentioned earlier, a key element of our model is our contention that the right dorsal AI –dlPFC relationship is strongly *bi*-directional. In other words, it is not only that the right dorsal AI provides the dlPFC with the homeostatic background against which its cognitive operations can become figural, though this is required if these operations are to occur within conscious awareness. We posit that the dlPFC also feeds *back* to the right dorsal AI, thereby allowing the evolutionarily new cold cognition system to directly influence the contents of the brain's crucial second order body map (see Figure 3). In other words, we believe that the right dorsal AI continually and dynamically integrates

real-time lamina 1 information with top-down, memory-based predictions of what that the person's overall, homeostatic context *will* be like in the very near future. We posit that these top-down alterations are generated unconsciously and are experienced as being completely real by the person generating them (Damasio, 1994; Paulus & Stein, 2006). In short, the right dorsal AI meta-representation is a *feed-forward model of the embodied sense of self* (Critchley, 2005).

Though the right dorsal AI is always integrating lamina 1 real time information with top down predictions, the *relative balance* between these two forms of input is variable. As will be discussed at length in the final section of this paper, this balance is a key factor in determining depth of experiencing.

The top down mechanism just described strongly echoes the "as-if-body loop" construct posited by Damasio (1994; 1999). Damasio claims that higher order brain centers can distort the contents of the neural maps that underlie core consciousness. These top down simulations are very fast because they are enacted entirely within the brain and do not rely on the much slower process of monitoring actual changes going on within the body proper (Damasio, 1994), such as the ones that are reflected in lamina 1 output. This "as-if-body loop" element has two important implications. First, the integration of both lamina 1 information *and* top down predictions greatly increases the sophistication and speed with which the right dorsal AI can tune the ventral AI's salience assessments. Second, top down input into right dorsal AI can at times be much stronger than lamina 1 input. The resulting cognitive mode would allow for the fastest possible generation of the "embodied" backgrounds considered necessary

for consciousness (Damasio, 1994), thereby allowing the cold cognition system to imaginatively move through space and time with tremendous speed. This concept is essential to our conceptualizations of both low level experiencing and psychopathology and will be discussed in the final sections of this paper.

Mediation System: Lamina 1,Ventral Insula,VENs,BA 24,BA32ac and BA10r

The third system in our model (Figure 3) is a mediation system that helps integrate the hot and cold cognition systems considered above. As with the hot and cold systems, we identify two mediation network sub-systems, one evolutionarily newer than the other.

Evolutionarily Older Mediation Network: CNA/Lamina 1/Ventral Insula/ /VENs/BA 24

In addition to identifying an "executive system", Seeley et al. (2007) also identified a large scale "salience network" within the brain. Their "salience network" is devoted to determining which stimuli are the "most homeostatically relevant" from among the endless range of "internal and extra-personal" stimuli that bombard the nervous system (Seeley et al., 2007, p. 2354). The center of the salience network falls in the bilateral ventral AI (42,10,-12 and -40,18,-12). It also has key nodes in the CNA (20, 4, -20), anterior ACC (throughout BA 24 A and B), and the medial PFC (BA 10r; -24,56,10) (Seeley et al., 2007, Supplemental Table 2). These maxima clearly illustrate that what we have termed the "mediation network" closely follows Seeley's "Salience Network" not only in terms of function, but also in terms of brain region membership (see Figure 3).

Following Seeley et al., the lowest level of the old mediation system is the amygdala's CNA. As described earlier, the CNA plays a crucial role in determining general affective responses to both appetitive and aversive stimuli (Balleine and Killcross, 2006) and in initiating species-specific behaviors in response to those stimuli (Li et al., 2010). In other words, the CNA helps organisms recognize what matters on a basic level and also helps to generate the embodied action tendencies needed to act effectively in response. The CNA sends its assessments to the ventral AI for further refinement as needed (Seeley et al., 2007).

Recall that lamina 1 terminates in the posterior insula. As a result the ventral and dorsal AI are both ideally positioned to receive input from lamina 1. The ventral AI is also strongly connected to diverse limbic and paralimbic structures including the ACC (Wager & Feldman-Barrett, 2004). This allows ventral AI to contextualize the CNA's salience assessments and to initiate homeostatic changes as needed in response. These geographical considerations are consistent with earlier cited evidence that the ventral AI shows strongly preferential involvement during tasks that require social or emotional valuation (which we take to be akin to salience assessment); with Lamm and Singer's (2010) recent conclusion that the ventral AI appears to be "predominantly engaged in internal and bodily homeostatic regulation" (p. 586); and with the fact that the ventral AI forms the center of Seeley's et al.'s (2007) "salience network".

We contend that among the ventral AI's key functions are to contextualize the earlier salience assessments of the CNA through the use of lamina 1

information; to initiate appropriate homeostatic and behavioral changes in response to these assessments (primarily in partnership with the ACC, as discussed below); and, finally, to make the contents of the first body order map that it helps to represent available to the right dorsal AI for re-contextualization, thereby allowing conscious behavioral control when required.

Voluminous evidence links the anterior insula and the ACC in emotional processing and in core self level functioning (Craig, 2002). Craig (2007) stresses that the ACC plays a key role in generating motivational drive and behavioral initiative. However, like the AI, the ACC is a highly heterogeneous structure (Paus, 2001). Therefore, we will address the functions of the specific sectors of the ACC with which the ventral AI has evolved to work most closely, namely, BA 24b.

Our contention that the ventral AI has a close functional partnership with BA 24b is predicated on the existence of a special class of very large, spindle shaped cells called Von Economo neurons (VENs). Within the human brain, VENs are found almost exclusively linking the *ventral* AI (Allman et al., 2010) and BA 24 (Allman, Watson, Tetrault & Hakeem, 2005; Frith and Frith, 2003; see Figure 6). Human beings have by far the highest density of VENs of any species studied to date. Further, "within the hominoid species, the group comprising humans and apes, the density of spindle cells declines with approximately the phylogenic distance from humans" (Allman, Hakeem & Watson, 2001, p. 335).

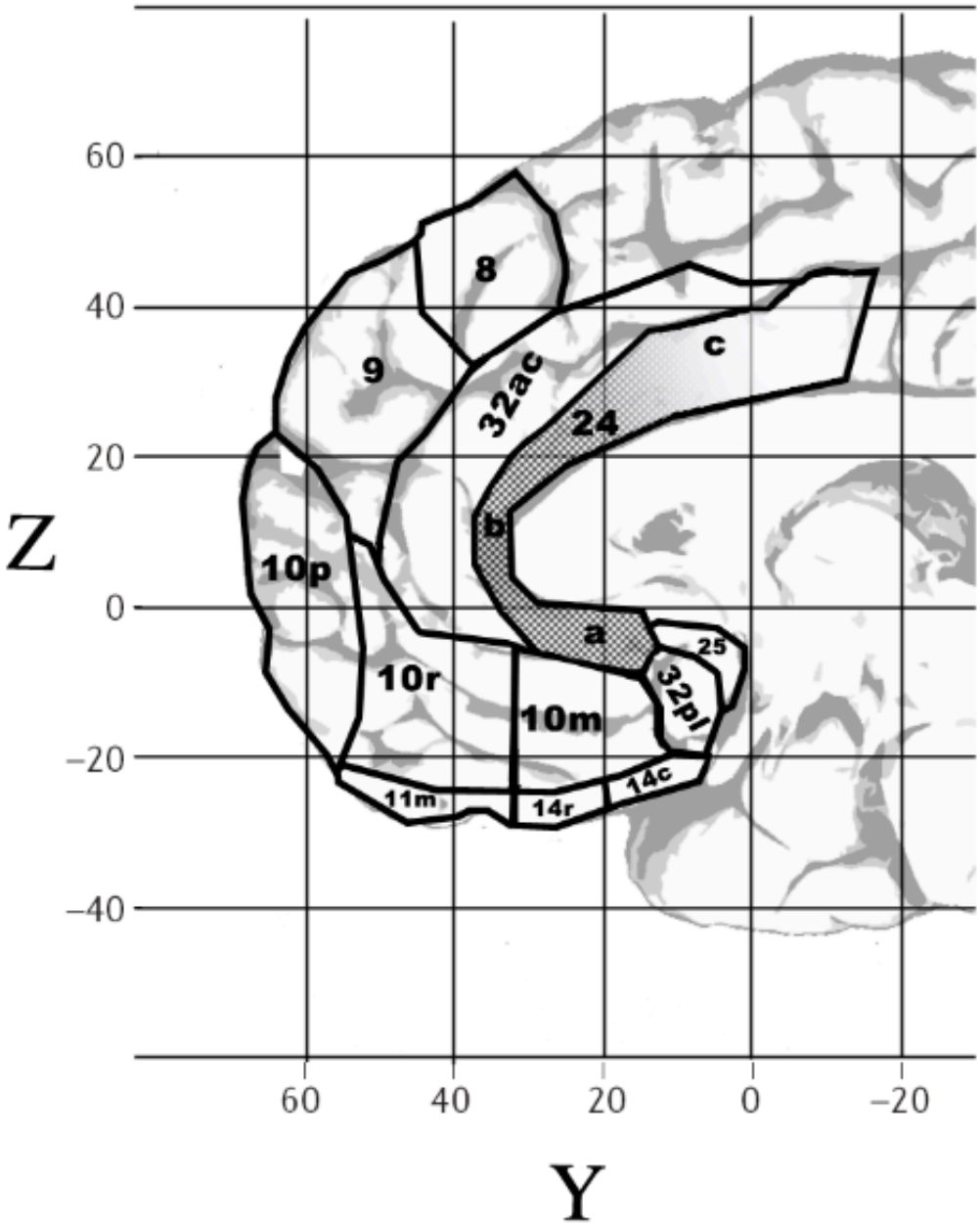

Figure 2-6: As illustrated with the halftone gradient in this figure, the main concentration of Von Economo neurons in the human brain is found in BA24, with a decreasing density moving dorsally (Allman et al. 2010)

The existence of VENs supports our contention that there is a strong link between the ventral AI and BA24b/BA10r region whose connectivity was shown in Seeley's et al.'s (2007) "salience network". Two functions that have been ascribed to this latter region are of particular importance for emotional processing, psychotherapy, and high level experiencing: the pre-conscious resolution of emotional conflicts and the assessment of the expected utility of possible actions.

In regard to the pre-conscious resolution of emotional conflicts, the work of Etkin and his colleagues has strong relevance. Enger, Etkin, Gale, and Hirsch (2008) studied conflict resolution with a sample of healthy participants. This fMRI-based study involved two tasks. The first was a traditional cognitive Stroop task. The second was a modified emotional Stroop task. Successful conflict resolution during the cognitive Stroop test was associated with activity in the dlPFC (centered at 38,16,54), the core component of our evolutionarily newer cold cognition system. On the other hand, successful conflict resolution during the emotional Stroop test was associated with activity in posterior BA 10r (-12,44,-2). Using the same experimental paradigm, Etkin, Egner, Peraza, Kandel, & Hirsch (2006) have also shown that this region achieves resolution of emotional conflict by down-regulating activation of the CNA. Finally, these authors very recently used their paradigm to demonstrate that the described form of emotion regulation is implicit, occurring beneath conscious awareness (Etkin, Prater, Hoeft, Menon, & Schatzberg, 2010).

In regard to the issue of assessing the reward value of potential actions, the work of Rolls (2009) is again of strong relevance. Rolls (2009) claims that while

the orbital and ventromedial prefrontal cortices (parts of the evolutionarily new hot cognition system) are crucial to assessing the expected utility value of possible *rewards*, they do not judge the expected utility value of possible *actions*. Rolls ascribes this role to BA 10r.

Evolutionarily Newer Mediation Network: BA10r and BA32 ac

We believe that the evolutionarily newer mediation network supports high level experiencing. Although this process is supported by many different posterior cortical regions, for purposes of clarity of exposition we focus here on the most important roles played by BA 10r and BA32a.

In addition to making their output accessible to right dorsal AI, evidence suggests that the bilateral ventral AIs *also* feed their output directly into anterior BA 10r (Seeley et al., 2007). Once in anterior BA 10r, this information derived from lamina 1 is integrated into a single meta-representation of the body's overall homeostatic state. We contend that access to this meta-representation helps BA 10r to resolve salience-oriented problems that are beyond the processing capacities of the evolutionarily older mediation system. In other words, the bilateral ventral anterior insula and anterior BA 10r are the penultimate and ultimate convergence zones in a processing hierarchy that is primarily devoted to establishing the homeostatic meaning of stimuli and to resolving conflicts between different meaningful stimuli.

As with the ventral AI, BA 10r's salience related functions are usually performed outside of focal awareness. However, unlike the ventral AI representations, attention can be focused onto this BA 10r meta-representation in

such a way that it *can* emerge fully into focal awareness (Lane & McCrae, 2003). We suggest that this requires the engagement of BA 32ac. BA 32ac is not only involved in attentional control processes (Hölzel et al., 2007), it is also paired with BA 10r in the resting state network under consideration here (Liao et al., 2010; see Figure 2C). Gaining conscious access to this meta-representation means that BA 10r's salience related processing can be performed under the guidance of conscious control. In short, we hold that this class of background feeling equates with a felt sense, and that the process of consciously working with this background feeling equates with high level experiencing.

We will offer a detailed neurally grounded conceptualization of high level experiencing in the next section. At this stage we will offer selected connectivity, phylogenic, and functional evidence to support the plausibility of our basic claim that BAs 10r and 32ac can support a felt sense type, background feeling.

In terms of connectivity, support for our model comes from the finding (cited earlier) of strong resting state linkages between bilateral, agranular/ ventral AI and the BA 10r (peak at -24, 56, 10; Seeley et al., 2007). Connectivity support also comes from the earlier cited findings of Nelson et al. (2010) that show the ventral AI is functionally connected to BA 10r and 32ac (see Figure 4).

Phylogenetically, BA 10 has distinctions that suggest that its role in human neural processing may be distinct from its role in other primates. Humans have by far the largest BA 10 of any hominoid species. BA 10 is proportionally much larger within the human brain than it is in the macaque brain. BA 10 may be the only area of prefrontal cortex that is much larger in human beings than it is in

other primates (Allman, Hakeem & Watson, 2001). Phylogenic evidence also suggests that the other putative core component of the evolutionarily newer mediation system, BA 32ac, is also very recent and relatively much more developed in human beings. For example, macaques have only have one BA 32, while humans have evolved two functionally distinct BA 32s (Ongur, Ferry & Price, 2003), one section (32ac/ anterior cingulate) dorsal to the other (32pl/ paralimbic). Both regions are marked on Figures 1, 2, 6 and 7.

Functionally oriented research also offers support for the role that we ascribe to BA 10r. Gilbert et al. (2006) conducted a meta-analysis in which they considered the results of 104 neuroimaging studies that had reported activation in BA 10. BAs 10 r/p showed a very specific pattern of activation, only preferentially activating during tasks that involved *both* mentalizing and emotion. The average peak for these tasks centered in a focused area with peak coordinates and standard deviations: x: -3 (6.8); y: 53.5 (3.9); and y: 9.3 (9.5)) These findings suggest that the BA 10 region in question is preferentially involved in *embodied forms of mentalizing*, exactly as would be expected if it supported the consciously accessible, felt sense type representation that we posit it does.

Further work by Rolls and his colleagues offers support for another aspect of the functional role that we ascribe to BA 10r. Recall that during high level experiencing, behavior is guided through both continuous scale feelings of rightness and wrongness (as in mid level experiencing) *and* by binary, yes/no "felt give" responses. In this regard, there is strong significance to Rolls (2009) claims that the OFC-vmPFC based stimulus evaluation system is only capable of

directing goal related activity as long as this can be achieved on a continuous rating scale basis. However, as Rolls notes, it is also sometimes necessary to make *binary* decisions and that this cannot be effectively achieved with a continuous scale. When a binary (choice) decision must be reached an additional tier of decision-making must be performed through the activation of a neural system "…that does not continuously represent the affective value of the stimulus, but which instead falls into a binary state…" [with] … the settling of an attractor network into one of its two…attractor states each representing a choice…" (p. 235). Rolls contends that these higher order, binary decisions are made in the anterior medial BA 10r region. A study conducted by Grabenhorst, Rolls and Paris (2008) is among the experiments that Rolls (2009) uses to substantiate his claim about the primary role of BA 10r in making binary decisions. In this fMRI study a sample of healthy participants were exposed to water at varying degrees of warmth. During half of the trials participants were asked to rate the pleasantness of the stimuli on a continuous scale (e.g., from very pleasant to very unpleasant). During the other half of the trials participants were asked to make a binary, Yes/No decision as to whether or not they would want to have each stimulus repeated. The authors found that across all trials a region spanning the posterior ACC (BA 24b), the inferior area 32ac, and posterior 10r (which we will refer to as 'the continuous rating region') tracked the subjective pleasantness (or reward value) of the stimuli in a continuous manner (see Figure 7), regardless of whether it was a "decide" or "rate trial". An anterior medial BA 10r region and the *ventral* anterior insula were the only two brain regions to preferentially

activate during the Yes/No decision trials, as compared to the rating trials. This region precisely overlaps with the region identified by Andrews-Hanna et al. (2010) and Liao et al. (2010) as the common region for the different self-related processing networks (Figures 2 and 7).

As well as supporting our contention that BA 10r can support binary "felt give" decisions, this study also offers support for two other key claims. The first is that that the there is a posterior medial region that uses continuous scale rating to guide behavior, consistent with our assignation of this region a role in supporting continuous scale feelings of rightness and wrongness. The second is that there is a key functional hierarchical relationship between the bilateral ventral AI and anterior BA 10r.

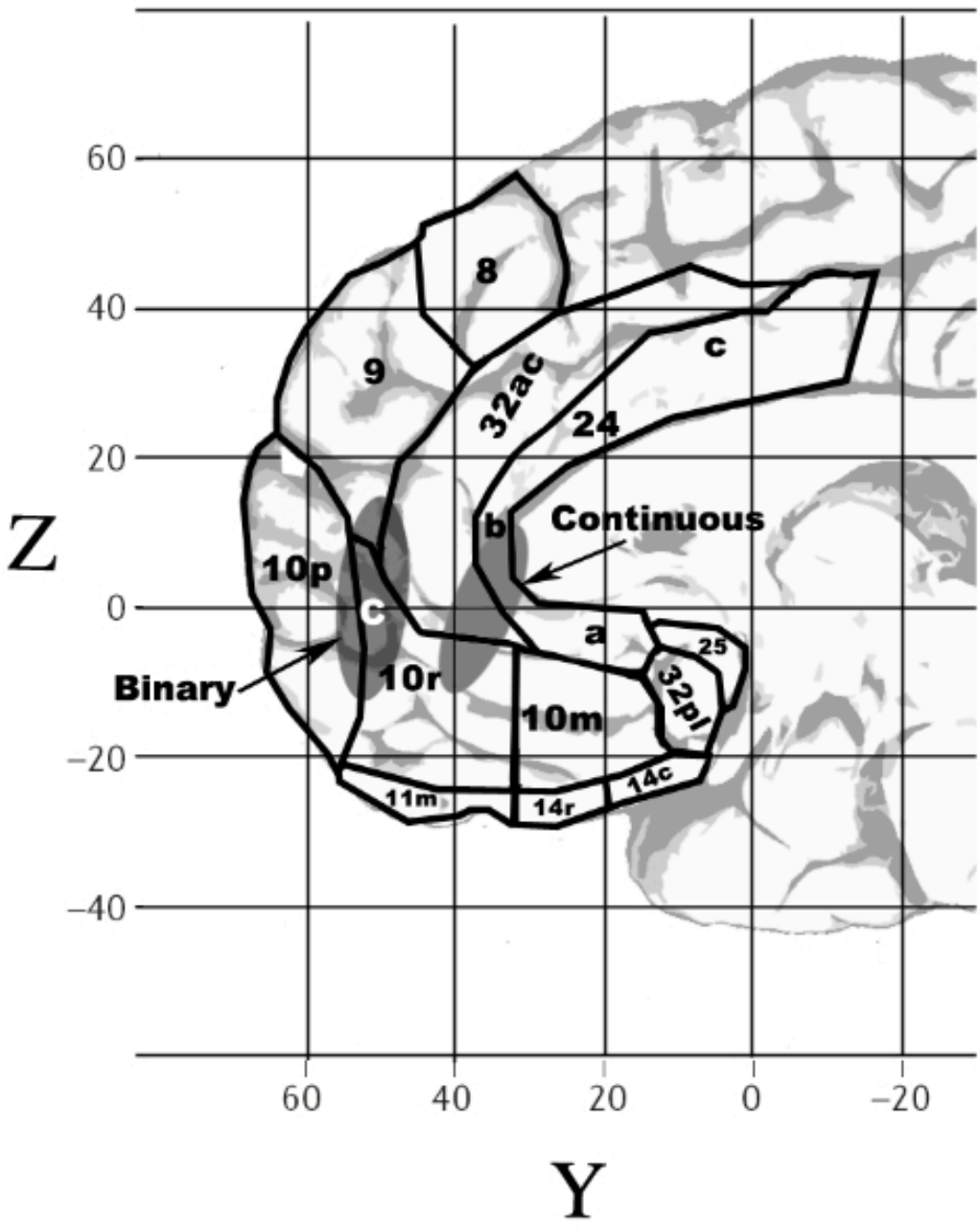

Figure 2-7: Regions associated by Rolls (2009) with continuous and binary decision making. Note that the region associated with binary decision-making is centered precisely on the common region for self-related processing networks found by both Andrews-Hanna et al. (2010) and Liao et al. (2010) (marked in both Figure 2 and this diagram with the letter 'c'). See also Figure 3.

Another aspect of Rolls' model supports the contention that this brain region performs binary decisions. Namely, Rolls (2009) points out that human beings have a broad diversity of homeostatic needs (e.g. food, shelter, social contact), all of which are active to greater and lesser extents at any one time. It would be very inefficient or impossible to attempt to satisfy all of our homeostatic needs all at once. Rolls argues that the brain must therefore support ongoing meta-representations of all of our basic needs *as domains.* He identifies the orbital medial PFC (BA 11) as the key area for supporting these kinds of meta-representations (Rolls, 2009) (example peak: BA 11; 2, 52, -18). Grabenhorst and Rolls (2009) argue that within this orbital medial PFC region there is an ongoing neural competition between these need domain meta-representations. This allows whichever need domain is the most salient at any specific time to be selected for preferential processing by the mOFC and vmPFC.

However, Rolls (2009) goes on to claim that when there is *equal* activity between two or more goal domain meta-representations, the medial orbital frontal cortex (BA 11) calls on the anterior medial BA 10r to resolve the conflict. BA 10r achieves this by allowing the relevant domains to directly compete with each other in a binary fashion until one 'wins', thereby allowing the attractor landscape to settle into a stable basis of attraction. In turn, this settling down of the attractor landscape allows the winning domain to send its current needs into the previously described continuous rating system so that these needs can begin to be addressed in a focused, efficient manner.

The issue of resolving between-domain conflicts has strong relevance for psychotherapy, and particularly for high level experiencing. We will return to this issue at the end of the article.

The Neurology of Experiencing

We will now draw on the ideas expressed thus far to present portraits of how we believe low, medium, and high level experiencing are instantiated in the brain.

Low Level Experiencing

Our conceptualization of low level experiencing is analogous to the Somatic Marker Hypothesis (SMH) (Damasio, 1994) that was briefly alluded to earlier. We will begin by summarizing the SMH before interpreting it specifically from the perspective of our neural model.

Damasio's SMH is based on the contention that when similar kinds of stimuli are experienced, similar body state/cognitive processing changes are enacted in response. When a particular stimulus has been paired consistently enough with a particular set of internal changes (especially in early development) that stimulus can automatically and unconsciously cause the nervous system to generate the internal changes that have become associated with it (Damasio, 1994; Damasio, 1999). Damasio argues that, during our lives, each human being develops an individualized palate of these automatic reactions, which he refers to as "secondary emotional responses".

Damasio (1994) suggests that reasoning can be understood as the process of sequentially making a series of related decisions. In line with the traditional understanding of decision-making, he argues that when we make a decision we mentally generate a range of response/outcome scenarios. However, *before* those scenarios are processed through a laborious cost/benefit analysis, they are evaluated through the use of secondary emotions. The imagined outcomes in

scenarios that produce negative "secondary emotions" are marked as being negative by the mOFC/vmPFC subsystem (Li et al. 2010) through the use of the previously described "somatic markers". As Damasio says "…when the bad outcome connected with a given response option comes to mind, however fleetingly, you experience an unpleasant…response in your…gut…" (Damasio, 1994, p. 173). These possible outcomes can be quickly rejected, often beneath conscious awareness. Conversely, the imagined outcomes that produce pleasant secondary emotions are marked as being worthy of conceptual cost/benefit analysis. The use of fast acting "hot cognition" in this way allows us to focus the operation of our limited "cold" cognitive resources on considering a manageable number of options during cost/benefit analysis.

In line with the SMH, we therefore argue that low level experiencing essentially involves operation of the cold cognition system operating under the (often covert) biasing operations of "somatic markers" generated by the hot cognition system (Goel and Dolan, 2003). We contend that, in this mode, the mediation system is relatively un-activated and running entirely in the background.

A final contention around the neural dynamics of low level experiencing emerges in response to two factors. The first involves the finding that, in a phenomenological state analogous to low level experiencing, the mOFC (centered in BA 11 at -4,56, 24) showed very strong connectivity with the right anterior insula (Farb et al., 2007). This was interpreted to mean that, in this phenomenological mode, mOFC continually references the body maps in the right

anterior insula so that it can evaluate whether encountered stimuli should be viewed as "being good or bad…[for] the 'self'" (p.8). The second factor involves our contention that during low level experiencing top down input into the right dorsal AI is stronger than lamina 1 input. In combination, these two factors lead us to the following contention: that during low level experiencing the mOFC/vmPFC subsystem performs the two functions that are of primary relevance to our model (somatic marker generation and regulation of the amgdala's CNA via the BLA) while using a largely *simulated* touchstone with which to ground its assessments and reactions (see Figure 8).

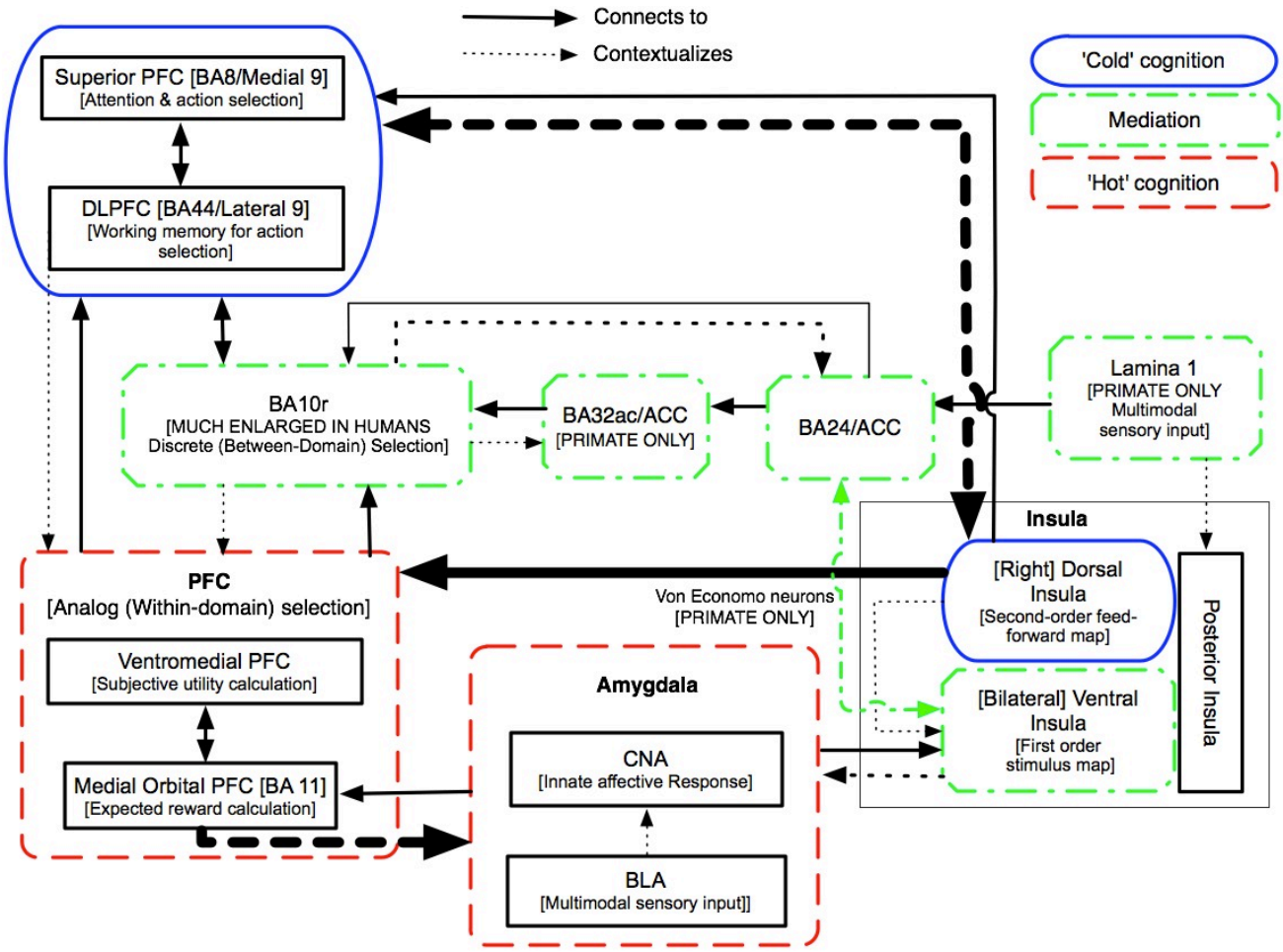

Figure 2-8: The main pathways implicated in Low Level processing are shown with a bolded lines. Because of the strong emphasis on top-down regulation of the dorsal insula, the PFC 'hot cognition' system functions in a 'simulated environment', with the PFC regulating the innate emotional response system not based on real world information, so much as on stored ideas about that world. The mediation system is 'locked out' by the stronger top down processes, and thus has relatively little influence.

As a concrete example of low level experiencing, imagine a psychotherapy client named Tom who has entered therapy in order to resolve vague, distressing feelings of dissatisfaction that he has been having at work. He began having these feelings several months ago, soon after winning a long desired promotion. Imagine that Tom spends his first session engaged in low level experiencing, analyzing his behavior from the outside in an effort to discover what "must" be causing his mysterious feelings of dissatisfaction. With his cold cognitive system strongly engaged, Tom generates tentative hypotheses around what could be causing his problematic feelings (see Figure 8). During this brainstorming his hot cognitive system is also running strongly in the background, producing somatic markers in response to each possible hypothesis (see Figure 8). When a possible hypothesis is somatically marked as holding potential value, this biases Tom to consider it more closely. In this way Tom generates a list of several plausible causes of his feelings. Once he has identified several possible explanations, Tom engages in memory and/or future oriented mental simulations to order to determine the relative plausibility and importance of each one. For example, one of Tom's theories is that he may be feeling de-motivated at work because he might actually be feeling more "insecure" around his new boss than he is consciously acknowledging. Tom tests this theory out by recalling and analyzing his own behaviour during their recent interactions. He also assess the strength of his feelings by generating imaginary scenarios and then speculating on how he would respond in them. For example, he generates a mental scene in which his boss is asking for his input on an upcoming strategic plan. Tom then

speculates as to whether or not he would feel confident enough to offer his honest views on the topic, even though he knows that these views run counter to his boss's. Tom goes on to assess the relative importance of his other possible explanations in a similar way, untimely trying to decide which explanation is the "right" one to address.

Mid Level Experiencing

Our conceptualization of mid level experiencing involves two key alterations from the scenario described above (Figure 9). This lessening of top down input lowers the dorsal AI's level of overall activation. Reduced top down input also allows authentic, real time, Lamina 1 derived information to more strongly influence the right dorsal AI's computations. These changes slow the process of salience assessment. However, they also bring these assessments, along with the associated activity of the mOFC/vmPFC system (Farb et al., 2007), more closely into line with the current homeostatic contexts. Second, the evolutionarily older mediation network is now more strongly engaged. The lamina 1informed ventral AI and the mPFC based, continuous rating region can now participate more strongly during salience assessment and during the resolution of emotional conflicts (Etkin et al., 2006). The continuous scale feelings of rightness and wrongness that these regions generate begin to operate in *parallel* with the cold cognition /somatic marker based mechanisms. Reference to these emergent feelings of rightness and wrongness becomes an alternate means of guiding both cold cognition and behavior.

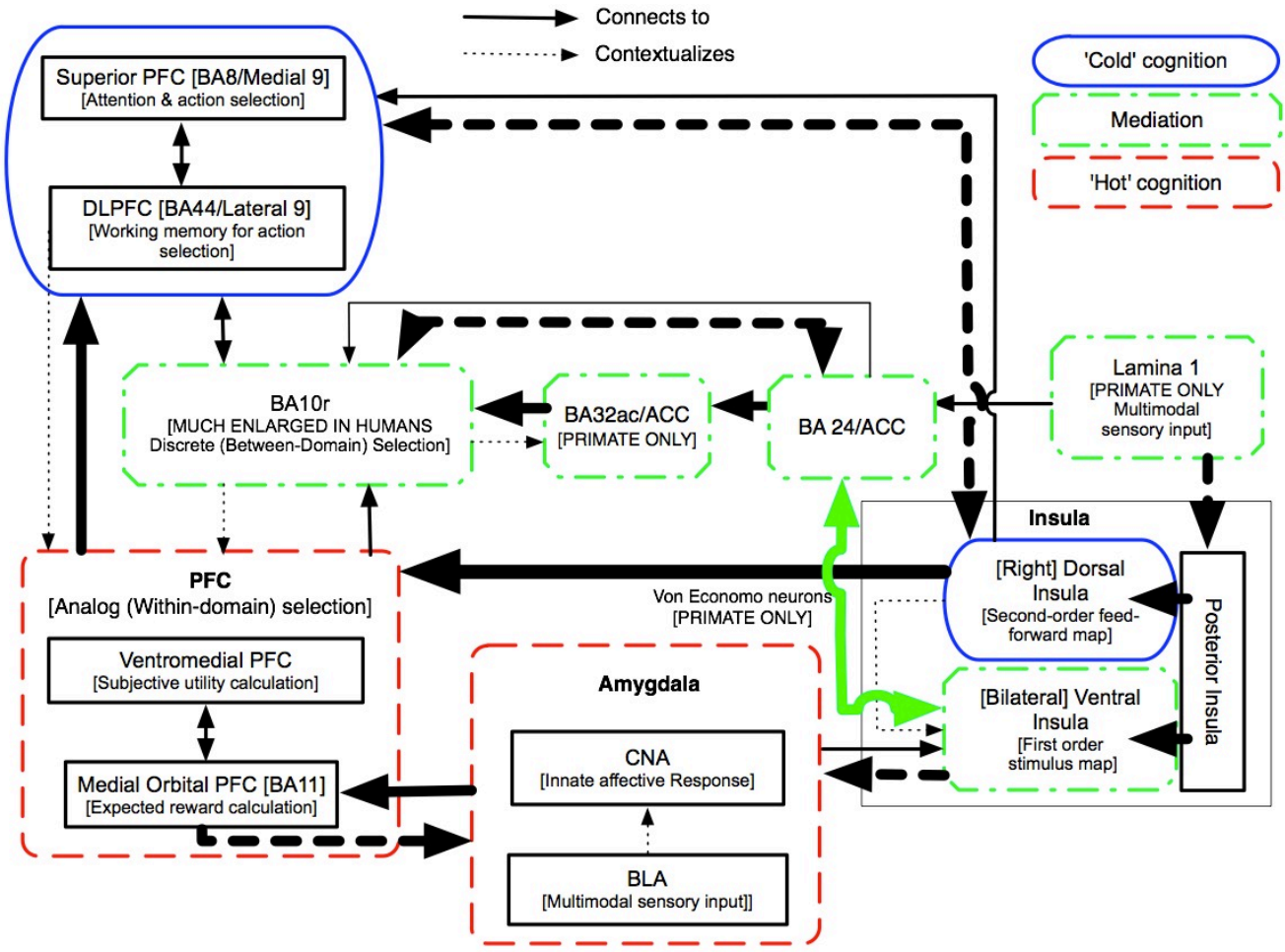

Figure 2-9: The main pathways implicated in Mid Level Experiencing are shown with a bolded lines. The influence of top-down 'simulated' input is weaker than in Low Level Experiencing, allowing a more salient role for the first-order body map of current homeostatic states in ventral anterior insula. In concert with the older mediation network in the ACC, the ventral insula generates continuous-scale feelings of rightness/wrongness that can influence the cold cognition system (operating in parallel) in a bottom-up way

As a concrete illustration of mid-level experiencing, we will return to the case of Tom. Imagine that Tom begins his second therapy session where he ended his first. He has identified a handful of possible sources for his recent feelings of dissatisfaction and is continuing in his efforts to conceptually decide which one is his "real problem". In response, the therapist uses empathic attunement and experiential process directions in order to help Tom to slow down and to begin focusing on his inner, embodied experience (Greenberg, Rice & Elliot, 1993). As this occurs Tom gradually moves into a mid-level of experiencing. This shift correlates with the activation of evolutionarily older mediation network, now running strongly along side his hot and cold cognition systems (see fig. 9). As the session continues, emergent feelings of rightness and wrongness help guide Tom to the recognition, from *the inside,* of how unsafe he has been feeling with his new boss. This exploration leads Tom to the word "bullied". As he sits with this word, Tom realizes that he has been feeling bullied by his new boss, not simply "a little insecure" around him. Once the nature of his feelings about his boss has been clarified, Tom begins to search for the "right next steps forward" through which to resolve this conflict so that he can continue with his successful movement up the corporate ladder. Various options emerge including consulting with a colleague, discussing his concerns openly with his boss, and asking for a transfer to a different department. However, this solution generation process looks quite different from the low level experiencing "brainstorming" that was conducted in session one, as it now has a much slower, more tentative, step-by-step quality.

High Level Experiencing

In order to invite a state of high level experiencing, the client intentionally generates a mental image of the life situation that she wishes to address as a *whole,* as if she is mentally standing back to look at large mural of the overall situation (Gendlin, 1996). While holding this image in her mind's eye, the client focuses on the background feeling that gradually emerges in response to this mental image, typically taking between 90-120 seconds. The therapist asks guiding questions in order to *draw out* the most salient elements that are implicitly contained within it. Once these elements have been drawn out, they can then be re-symbolized within the evolutionarily newer cold cognition system, so that they can help to guide the process of problem resolution.

We now offer a detailed description of how we believe this process is neurally instantiated (see Figure 10). First, the construction of a "mental mural" of the overall situation activates relevant memories. The posterior parietal cortex plays a key role in this memory related processing (see Figure 1). Next, the hot and cold cognition systems work together to reprocess these memories into a consciously accessible mental scene. Attention to this "mental mural" stimulates changes within the body proper (Damasio, 1994). These somatic changes are then *read back* by lamina 1 and strongly represented in the ventral AI. At this stage during high level experiencing, BA 32ac helps to focus conscious attention onto the output of the anterior BA 10r region, where lamina 1derived information is being re-represented into a single meta-representation. As a result, the felt sense of the overall situation emerges into conscious awareness. The tremendous

richness of the homeostatic information being fed forward from lamina 1 means that this background feeling can only be consciously represented at a low resolution, accounting for the inchoate, ephemeral quality of a felt sense.

Once the felt sense has formed in this way, the use of guiding questions (such as "What is the worst part of this whole situation?"; Gendlin, 1996) intensifies the *most salient possibility* from among the tremendous number of possibilities that are weakly activated by considering the relevant life situation and that are all therefore*, implicitly*, part of the background feeling. When that particular possibility is intensified, the activity of its associated *somatic profile* also intensifies automatically. Information about the somatic profile of the dominant activated representation is captured by lamina 1 and can then represented in the ventral AI body maps.

When the most salient possibility in question is activated strongly enough, *its associated somatic profile will stand out from the background of the felt sense*. For example, a somatic sensation such as a tightness in the throat will often begin to emerge from the client's background awareness. When this occurs, the client is encouraged to shift her focal attention from the background felt sense to the physical sensation. This focus of attention can eventually trigger the emergence of an associated conscious "mental image" within the evolutionarily new cold cognition system. Such a "mental image" (Damasio, 1994) most commonly emerges in the form of a relevant visual image, memory, and/or focal emotion. In other words, in high level experiencing the brain to body relationship is worked *in reverse*: focusing attention onto *the somatic profile* has been used as a means of

making *a mental imag*e more salient so it can be conceptualized and communicated. During this process, the "rightness" of each emergent mental image can be confirmed by proposing a binary checking statement and awaiting a felt give response.

For purposes of illustration, we will now return one final time to the case of Tom. During his third session Tom continues to focus on the question of how to address the feeling of being bullied by his boss. However, after twenty minutes of processing at a medium level of experiencing, Tom has failed to find a potential next step that has generated a strong feeling of rightness. The therapist therefore invites Tom to form a felt sense of the whole issue at work, thereby activating the client's evolutionarily new mediation system (see fig. 10). Through the use of guiding questions Tom becomes aware of a feeling of heaviness in his chest that gradually emerges out of the felt sense. After patiently focusing on this sensation for some time, an image of his young children suddenly emerges into his mind's eye, alongside a strong focal feeling of sadness. This is very surprising to Tom because he had been so focused on trying to improve his situation at work he hadn't recognized how sad he had been feeling about having less time with his children since his recent promotion. After confirming the rightness of this step with a checking statement, the client could then profitably return to a medium level of experiencing in order to begin addressing this previously implicit conflict between his desire to excel in his career and his desire to be more present as a father. By harnessing the strengths of the client's evolutionarily new mediation system, the therapist has helped Tom to identify that his very real challenges with

his new boss have been implicitly embedded within a larger values conflict that will also need to be addressed.

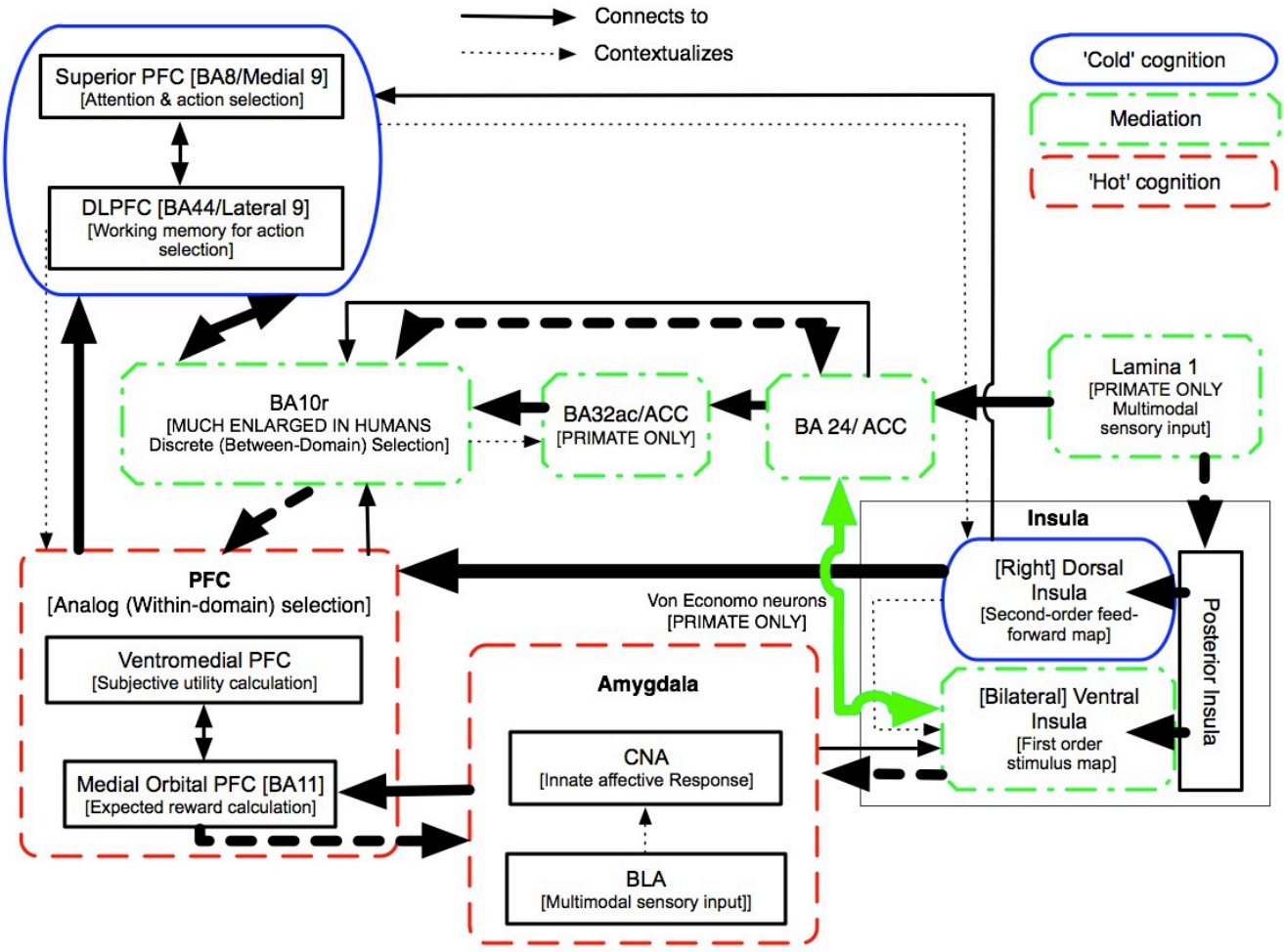

Figure 2-10: The main pathways implicated in High Level Experiencing are shown with a bolded lines. The main characteristic of High Level Experiencing is the activation of the recent, human-only mediation system, and the consequent ability to provide the cold cognition system with a much richer, more fluid, and more consciously accessible (though still inchoate) homeostatic representation of the present situation than is possible in Mid or Low Experiencing. Lamina 1 input from the body mapping provides an additional meta-representation that is more directly accessible to consciousness than the insula maps, and that has 'privileged access' to BA10r. BA10r has the potential to use this somatic mapping information to 'shift the perspective' of the whole system, bringing new possibilities into play rather than limiting the system to a single dimension of analysis.

Implications of the Model for Conceptualization of Psychopathology

We believe that our tri-partite model allows for a useful re-conceptualization of psychopathology as essentially equating with an overly rigid, inflexible relationship *between* the three subsystems we have described (Teasdale, 1999; Siegel, 2009). In order to communicate this over-all conceptualization, we will now use our model to conceptualize three distinct routes into psychopathology.

Problems of Emotional Over and/or Under Regulation

We will begin by addressing two linked forms of psychopathology that typically lead to more severe dysfunction and thus to more frequent DSM diagnoses. The first occurs when people become stuck in a "conceptualizing/doing" (Teasdale, 1999) mode in which cold cognition systems are over-dominant. These people lose touch with their innate emotional responses and action tendencies and tend to experience symptoms related to the experiential emptiness caused by living as ideas rather than as embodied processes. Diagnoses of Generalized Anxiety Disorder and Dysthymia are perhaps most typical for such people.

The second of these basic routes into psychopathology appears when people lack the self-regulation abilities necessary to avoid becoming stuck in a "mindless emoting" (Teasdale, 1999) mode of processing. People who are stuck in this mode suffer the interpersonal and intrapersonal effects of living in a state of unregulated impulsivity and emotional reactivity. Because they cannot regulate their innate emotional responses, they experience the self as *something that*

happens to them, rather than as an integrated guidance system. Diagnoses of the impulse control and substance abuse related disorders are perhaps most typical.

We believe that, despite appearances to the contrary, these apparently opposing forms of psychological dysfunction stem from a *common cause*: that people are living their lives rigidly stuck in a low level of experiencing. This leads to a maladaptive, *systemic dominance* of the evolutionarily new cold cognition system over the mediation system. We believe that this has deleterious effects of psychological health for two basic reasons.

First, in low level experiencing, the top down, 'as-if' body loop is strongly engaged. We contend that this maladaptively up-regulates the right dorsal AI, with the effect that salience assessments flowing up from ventral AI will be brought more continually and more intensely into conscious awareness. This contention is consistent with findings that hyperactivity in the right dorsal AI (centered at 27, 22, 3) has been associated with "Anxiety Sensitivity" (Stein, Simmons, Feinstein, & Paulus, 2007), a fear of anxiety related *sensations*. Anxiety sensitivity is associated with a tendency to become hyper-vigilant toward one's embodied responses and is also a vulnerability factor for the development of clinically significant anxiety and mood disorders (Schmidt, Zvolensky and Maner, 2006).

Second, continual engagement of the "as-if-body-loop" means that cold cognition is no longer strongly constrained by a core self embedded within a particular place and time. Further, over time (following Damasio, 1994), a stimulus can become paired with particular as-if-body-loop simulations so that

encountering that stimulus automatically triggers the associated simulated sense of self-in-world. We believe that this is a critical factor for the development of psychopathology because it can lead to the generation of what Greenberg, Rice & Elliot (1993) have referred to as "maladaptive core schemas". Maladaptive core schemas are typically based in shame or fear, often involving a background sense of the self as bad or weak (Greenberg, 2002). Greenberg, Rice, & Elliot (1993) advise that such maladaptive core schemas can be clinically distinguished from generative (even if possibly aversive) real experiential states because they have a stale, unchanging quality, a quality of stuckness. Ultimately, clinically diagnosable psychopathology emerges when a "maladaptive core schema" of this kind becomes automatically paired to the activation of a basic, adaptive (typically attachment related) need (Greenberg, Rice & Elliot, 1993).

For example, imagine a client who, as a child, was beaten by his father whenever he expressed a desire for nurturance. As a result, in adulthood, experiencing a desire for nurture and intimacy would be likely to pre-consciously generate a strong simulated background body state based in shame and fear, assuming that the client is in a low level experiencing mode of processing at the time. Any potential rejection related cues that the client experienced while attempting to express a desire for closeness (such as a momentarily furrowed brow in the person he was approaching) would then tend to be mistakenly interpreted as being threatening while being contextualized by his memory based right dorsal AI background. Further, as discussed earlier, hyperactivity of the right dorsal AI would also mean that these distorted threat related feelings would

emerge into conscious awareness particularly intensely, therefore causing them to be experienced as even more threatening. In such circumstances, this client would be likely to develop what has been called an "affect phobia" (McCullough, Kuhn, Andrews, Kaplan, Wolf, & Harley, 2003) to social rejection. As with any other phobia, the client would engage in behavioral strategies (such as avoidance of intimacy) and cognitive strategies (such as worry) designed to avoid this shame/fear based feeling (Hayes et al., 2004). If his affect phobia was sufficiently intense, denial of his basic attachment needs could also lead him to begin alternating between states of emotional over and under regulation. In other words, if his loneliness-based sadness becomes severe enough he could begin occasionally acting out his warded off attachment needs in an unregulated fashion by reaching out for intimacy in maladaptive ways. Other people would be likely to experience these unregulated advances as overwhelming or threatening. The pain of the ensuing social rejections might reify the client's felt sense of danger around experiencing and/or expressing a desire for closeness.

In this way, we see the problems of emotional over-control and under-control as both arising from a maladaptive dominance of the evolutionarily new cold cognition system. We believe that as long as this client is only capable of meeting his needs in at low level of experiencing that he will remain "gridlocked" (Teasdale, 1999): his evolutionarily new cold and hot cognition systems will continue jointly over-controlling the adaptive output of his evolutionarily old mediation network (as manifest in innate emotional responses such as his adaptive sadness at social isolation), rendering him incapable of self organizing in such a

way that he can effectively meet his homeostatic needs. A clinically diagnosable psychopathology is likely to be the end result.

Figure 9 illustrates how we believe this client's psychopathology could be ameliorated if he becomes capable of fulfilling his attachment needs while in a mid level of experiencing. For reasons that were described earlier, processing his attachment related needs in this more present focused neural mode should lead to: lessened exaggeration of potentially threatening threat related social cues; lessened hyper-awareness of the emotions that arise in response to potentially threatening social cues; an improved ability to use feelings of rightness and wrongness to guide his approach behaviour; and improved emotional conflict resolution abilities. In turn, these changes should help him to overcome experiential avoidance by expressing his attachment related action tendencies despite the continued presence of now moderated levels of fear and arousal (Hayes, Strosahl, & Wilson, 1999). In turn, the accrual of positive attachment related experiences gained during these interactions should gradually allow him to begin neurally linking the emergence of his adaptive, attachment related emotions to new, positively valenced memories. Over time, this co-activation of his attachment related emotions and these new memories should gradually lessen the psychopathological influence of his maladaptive core schema (Greenberg, Rice, & Elliot, 1993).

Psychopathology Emerging from Impaired High Experiencing Ability

The final form of dysfunction that we will consider from the perspective of our model involves a subtler, more common psychopathology, in which clients

who have well functioning evolutionarily older mediation systems are unable to use their evolutionarily new mediation system effectively enough to enter high level experiencing when it would be adaptive to do so. People with this processing pattern will tend to remain psychologically functional and will receive DSM diagnoses less frequently. However, they will also tend to experience distress at points in their lives when two valued goal domains come strongly, and typically implicitly, into conflict (Rolls, 2009) because they will struggle to consciously identify the true source of their stuckness. This deficit can make it more difficult to resolve conflicts of this kind in a flexible and self-compassionate way, leaving those who suffer from it feeling depleted and less fulfilled than, on the surface, it seems they 'should'.

Support for the Model of Psychopathology

We will now offer selected neuroimaging support for this conceptualization of psychopathology.

Neuroimaging Research into Neuroticism

The personality construct of Neuroticism can be defined as "a trait disposition to experience Negative Affect" (Griffith, Zinbarg, Craske, Mineka, Rose, Waters, & Sutton, 2010, p.1126). Brown (2007) conducted a 2-year longitudinal study with a sample of over 600 outpatients who received treatment for MDD, GAD, or Social Phobia. Over the two year study period "…*all* of the temporal covariance of the *DSM–IV* disorder constructs was accounted for by change in…[Neuroticism scores]" (Brown & Barlow, 2009, p. 269; emphasis added). These results point toward a pair of key conclusions. First, Neuroticism

may be at the very heart of much Psychological dysfunction (Brown & Barlow, 2009; Griffith et al., 2010). Second, Neuroticism "… may be therapeutically malleable, and that this in fact mediates the extent of change in the emotional disorders …" (Brown & Barlow, 2009, p. 263).

In this light, it becomes significant that neuroimaging studies involving measures of neuroticism appear to be consistent with our proffered model of psychopathology. Paulus, Rogalsky, & Simmons (2003) conducted an fMRI experiment involving a sample of healthy participants engaging in a gambling task that involved choosing between risky or safe gambling choices. The risky bets involved the possibility of larger payouts but also of being punished with large losses. This study produced a pair of key findings. First, degree of activation in the right dorsal AI following a punished risky choice correlated significantly ($r = 0.72$) with NEO neuroticism scores. Second, degree of right dorsal AI activity (centered at 32, 18, 7) following a punished risky choice predicted the likelihood that the participant would opt for a safe gamble on the following trial. In other words, the more neurotic a participant was the more they activated the right dorsal AI during a negative experience, and the more likely they were to subsequently let a desire to avoid that experience inform their subsequent behavior, as occurs in the development of affect phobia.

Using PET, Deckersbach, Dougherty, and Rauch (2006) found that Neuroticism was negatively correlated with resting state metabolism ($r = -.63$) levels in the dorsal, posterior insula (-32,-22, 16); that is in the lamina 1 entry point into the insula (Craig, 2007). This finding is therefore consistent with our

claim that a hallmark of psychopathology is a tonic under representation of lamina 1 input, relative to top down input, into the insula.

Cremers et al. (2010) recently conducted an fMRI study using affective pictures. They found that immediately following the presentation of angry and fearful faces, neuroticism was negatively correlated with connectivity between BA 24b (12, 36, 12, in the continuous rating region) and the CNA ($p < 0.01$). This provides support for our contention that psychopathology is associated with weakened functional integrity within the mediation network, and with reduced abilities of the ventral AI and the continuous rating region to regulate the CNA adequately during salience assessment.

Finally, Kim, Hwang, Park, & Kim (2008), again using PET, found that neuroticism was inversely correlated with resting state metabolism in a BA 10/32ac centered cluster. This finding offers further support for our contention that weakened functional integrity within the mediation network is strongly associated with Psychopathology. This finding also offers support for our inclusion of BA 10/32ac as a component of the mediation network.

Neuroimaging Research into Anxiety and Depression

Depression has been associated with dmPFC hyperactivity (Grimm et al., 2009). Alternately, resting state levels of activity in the BA 24b have recently found to be *negatively* correlated with anhedonia scores (Wacker, Dillon, & Pizzagalli, 2009). Increased resting state levels of activity in the same region have also repeatedly been found to predict *improved* outcome response in the treatment of depression (Mayberg et al., 1997; Korb, Hunter, Cook, & Leuchter, 2009).

Hyperactivity in dmPFC has also recently been associated with anxiety arising from a sense of social threat (Wager, van Ast, Hughes Davidson, Lindquist, & Ochsner, 2009*)*. Finally, Mohlman et al. (2009) reported a positive association between left mOFC volume and worry scores in a cohort of older adults with Generalized Anxiety Disorder (GAD). They interpret this finding as support for a model of GAD as rooted in maladaptive, frontal over-control of limbic activity. In GAD, this may occur largely through the use of worry, putatively associated with medial OFC activity, as a maladaptive means of down-regulating the CNA (via the BLA).

Implications for Psychotherapy

Emotion has made an impressive resurgence in psychotherapeutic theory and practice in recent years. Partly through the advent of neuroimaging, there has been a growing appreciation of the profoundly important roles played by emotional processes in both sustaining health and in engendering dysfunction. However, during these advances, emotion has been almost exclusively understood as *focal* emotion. We suggest that the time is now ripe for the field to begin appreciating, both theoretically and clinically, the distinctions that we have highlighted between cold cognition and different *classes* of emotion.

Cold cognition, somatic markers, focal emotion, feelings of rightness/wrongness, and felt senses/felt gives all appear to play vital roles in human information processing. However, based on the model we have presented, we believe that ameliorating psychopathology essentially involves helping clients to strengthen their mediation systems. This, in turn, involves helping them

strengthen their abilities to make adaptive use of the later three classes of response. For this to occur, clinicians need to capable of assessing when the client is unproductively stuck in low level experiencing; of helping the client deepen into a more productive medium level experiencing; of assessing when the client has been successfully processing at a medium level of experiencing for some time yet has still failed to find a "right" next step forward (typically because of implicit, between goal-domain conflict); and finally, of helping the client get "unstuck" if she does fail in this way, by helping her to shift into high level experiencing until the elusive next step has emerged.

Gendlin (1996) has written extensively about how the value of a clinician's ability to assess and help deepen a client's level of experiencing transcends any theoretical model of psychotherapy. This contention is consistent with evidence cited earlier that experiencing has "…been shown to be predictive of good treatment outcome across most major schools of psychotherapy, including client-centered therapy, CBT, psychodynamic therapy, and emotion-focused psychotherapy." (p.117). Because of its essential role in psychotherapy, training student therapists how to work skillfully with the experiencing variable, a trainable skill (Hendricks, 2002), should be as ubiquitous in training programs as teaching students how to form positive therapeutic alliances with their clients.

Conclusion

In this paper we have grounded the process of experiencing in neural processes. Our hope is that the effort to begin putting the modes of cognition he has described on a sound neurological basis will have indirect benefits to the

psychotherapist, by situating a process that seems to be a-rational in sound empirical science that is accessible to rational cold cognition. When we understand how our very structure forces us to live as a dynamic system in interplay between different modes of processing, it may be easier for us inclined too far to using one mode over the others to access the range of these modes in a skillful, flexible way that maximizes our behavioral adaptivity in our environment.

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CHAPTER 3

THE ELECTROPHYSIOLOGICAL CORRELATES OF CHRONIC PAIN RELATED SUFFERING

INTRODUCTION

Chronic pain causes tremendous suffering. Defined as pain that has lasted for more than six months, various studies have found that between 4,000,000 and 7,000,000 Canadians are currently living with this chronic condition (Veillette, Dion, Altier, & Choiniere, 2004). In addition to the personal suffering it causes, the economic impact of chronic pain and chronic pain related disabilities are also immense. In the United States, it has been estimated that $125 billion US is lost every year through direct medical costs and reduced worker productivity (Turk, 2002). The development of efficacious new pain management alternatives is therefore a crucial research priority.

Recent neuro-scientific advances hold strong promise for stimulating the development of brain-based, chronic pain management interventions. To date, this promise has been best illustrated in an fMRI neurofeedback study conducted by DeCharms et al. (2005). Taking advantage of MRI's very strong spatial localization abilities, these authors used fMRI neurofeedback to teach a group of chronic pain patients how to volitionally reduce neural activity in a small, circumscribed, pain related region of the dorsal Anterior Cingulate Cortex (dACC) (BA 24a; centred at x: 2; y; 16, z: 33). DeCharms et al. found that, with less than an hour of training, the majority of the experimental participants successfully learned to voluntarily down-regulate the targeted region. Crucially,

the degree to which participants successfully lessened dACC activity was significantly correlated with pre-post training pain reductions. These participants also reported an average pre-post training drop in pain ratings that was three times larger ($p < .02$) than the equivalent drop reported by control participants. Control participants were trained in autonomic biofeedback, a standard chronic pain intervention.

These results hold evident clinical potential. However, the prohibitive cost of MRI technology will likely make widespread use of this modality untenable for the foreseeable future. In response, our team became curious if it might be possible to adapt DeCharms et al.'s basic approach to use with an alternate, accessibly priced neurofeedback modality that would still allow for the successful training of discrete cortical regions. The current study took a first step toward his goal.

LORETA Neurotherapy

Traditional EEG analysis is not capable of deducing the activity of regions within the cortex. However, a newer form of EEG analysis called Low Resolution Electromagnetic Tomography (LORETA) can achieve this. LORETA is an inverse solution (Pascual-Marqui, 1999) that utilizes EEG data obtained from surface electrodes. Through the use of algorithms best estimates are then made as to the cortical generators of the observed neuronal activity. LORETA has demonstrated relatively strong spatial localization abilities within the cortex (Pascual-Marqui, Esslen, Kochi, & Lehmann, 2002). The ability to localize effectively within the cortex suggests that LORETA based neurotherapy could

potentially be used to successfully adapt the DeCharms et al. (2005) methodology.

To date, four LORETA neurofeedback studies have been identified in the literature. Three of these studies used small, non-clinical samples and trained a single, discrete brain region (Cannon, Congedo, Lubar, & Hutchens, 2009; Cannon, Lubar, Congedo & Thorton, 2007; Congedo, Lubar & Joffe, 2004). The trained regions in these studies ranged in size from 13 cm/3 (Congedo et. al., 2004) to 1 cm/3 (Cannon et. al., 2009). Recently, Cannon, Sokhadze, Lubar, & Baldwin (2008) also reported on a single patient case study in which they used LORETA neurotherapy where the participant had a history of heroin and alcohol dependence.

Crucially, all four of the identified LORETA neurofeedback studies have produced evidence of successful training effects. Further, commercially available LORETA neurofeedback systems are currently on the market for approximately $8,000 (Nova Tech EEG; Mesa, Arizona). These considerations led our team to conduct the current study and a companion study (Ozier, Sherlin, Mueller, Lampman, & Whelton, 2011) that were jointly devoted to investigating LORETA-based neurofeedback as a chronic pain management tool. The current study was conducted, in part, to help clarify the neurotherapy protocol that was later implemented in the companion study.

Cortical Region Targeted for Training

In adapting the DeCharms et al. (2005) methodology to use with LORETA neurofeedback, we switched our training site from the dACC to the Orbital

Medial PFC (OMPFC). We will now offer a detailed rationale for this methodological adaptation.

A Three Tiered Model of Pain

Price (2002) offers a three-tiered model of pain. The first tier involves the "sensory" aspects of pain, including pain location and intensity. The second tier involves feelings of "immediate pain unpleasantness", which can be defined as the coarse, aversive feelings associated with the affective/motivational aspects of pain. The final tier involves feelings of "suffering", which involve "… reflection related to what one remembers or imagines, and includes perceived interference with one's life, difficulties in enduring pain over time, and implications for the future" (Price, 2002, p. 394).

It is clear that these three aspects of pain are highly intertwined, such that activity within any one tier can have important impacts on how the other two tiers are experienced. For example, there is evidence that the chronic pain suffering oriented variable of "catastrophizing" (Thorn, Boothby, & Sullivan, 2002) tends to be positively correlated with both the sensory (Tripp, Nickel, Wang, Litwin, et al., 2006) and also with the "unpleasantness" aspects of pain (Geisser, Robinson, Keefe, & Weiner, 1994).

However, there is also compelling evidence that these three distinct aspects of pain related phenomenology are processed by distinct neural networks (Price, 2002). We will focus our consideration on differences in the neural processing of pain unpleasantness, which was regulated by DeCharms et al. (2005), and

suffering, which we elected to target for down-regulation (Ozier, Sherlin, Mueller, Lampman, & Whelton, 2011).

The Neural Correlates of Pain Unpleasantness versus Suffering

Baliki et al. (2006) compared the patterns of brain activation that occurred when: healthy volunteers experienced induced acute pain; when chronic back pain patients experienced induced acute pain; and when these *same* patients experienced their spontaneous, chronic back pain. Induced, acute pain primarily correlated with increased activation in the Anterior Insula (AI) and the ACC in both the patients and the healthy controls. The AI and the ACC are the two key brain regions in supporting the previously defined, second tier feelings of "pain unpleasantness" (Price, 2002), feelings that are integral to the phenomenology of acute pain. The relevant dACC region lies close to the region that was targeted for down training in the DeCharms et al. (2005) fMRI neurofeedback study.

Alternately, the patients' spontaneous chronic back pain was associated primarily with increased activation in the OMPFC, involving peaks in the medial aspects of BA 24, 32, 8/9,10 and 11 (see Table 1). In other words, the brain regions activated by the experiences of acute and chronic back pain were *entirely* non-overlapping. While striking, this finding is fully consistent with evidence from meta-analysis, which indicates that the PFC plays a much more important role in chronic pain than it does in acute pain (Apkarian, Bushnell, Treede, & Zubieta, 2005).

Table 3-1: Regions specifically associated with Chronic Back Pain

(taken from Baliki et al. 2006, Supplemental Table S4)

Structure	Brodmann Area	Peak Correlates (x, y ,z)
DMPFC	8/9	-10,34,42
mid ACC	24	-6, 24, 24
mPFC	10	-12,58,20 12,60,22
rACC	24/32	0, 32, -6
vmPFC	11	0,36,-12
Supermarginal Area	39/40	-50,-60,30
Inferior Parietal	39/19	-48,-70,-2

Suffering as an Implicit Form of Self Referential Processing

In order to appreciate the implications of Baliki et al's (2006) results, it is important to recognize that chronic pain related "suffering" (Price, 2002) is only possible in reference to a sense of *identity* that exists across time. In this light, it is significant that the MPFC regions identified by Baliki et al. (2006) have also been shown to be essential to self-referential processing. Evidence to this effect comes from a meta-analysis performed by Northoff, Heinzel, De Greck, Bermphol, Dobrowolny, & Panskeep, 2006. Figure 1 shows the three neural regions that are most consistently activated during self-referential processing. All three are medial (x: 25 to –25) (Northoff et al, 2006). One cluster is located in the Dorso-medial PFC (DMPFC) (labelled 1 in fig. 1), one in the Posterior Cingulate Cortex/Precuneus (labelled 2), and one in the OMPFC (labelled 3).

Comparison of Table 1 with Figure 1 reveals that, of the brain regions identified by Baliki et al. (2006) as being specifically related to chronic back pain, the strong majority (6 of 8 reported activity peaks in table 1) fell either within the OMPFC or the DMPFC centred regions that are also essential to self referential processing. More specifically, four of the relevant peaks identified by Baliki et al. (2006) (-12,58,20; 12,60,22; 0,32,-6; 0,36,-12) fell within Northoff et al.'s OMPFC cluster, while the remaining pair of relevant peaks (-10,34,42; -6, 24, 24) fell within Northoff et al.'s DMPFC cluster.

It was in light of these understandings of MPFC function that Baliki et al. (2006) addressed the question, "What is chronic back pain?" by proposing that, "…chronic back pain engages the emotional-mentalizing region of the brain into a

state of continued negative emotions (suffering) regarding the self, punctuated by occasional nociceptive inputs that perpetuate the state" (Baliki et al., 2006, p. 12171).

This conceptualization of chronic pain related suffering has since received support through the findings of another MRI study that was designed to identify the neural correlates of the "emotional augmentation" of chronic Rheumatoid Arthritis pain (Schweinhardt et al., 2008). These authors found that, as expected, there was a positive correlation between depressive symptoms and pain severity. More crucially, they found that this correlation was significantly mediated by activity levels in a single OMPFC region (BA 10 p; centered at -4,66,8) (see the blackened region in Figures 1 and 2 B). The relevant region fell very close to the most strongly activated cluster of the several MPFC sub-regions identified by Baliki et al. (2006) (also in BA 10 p; with maxima at -12,58,20 and 12,60,22).

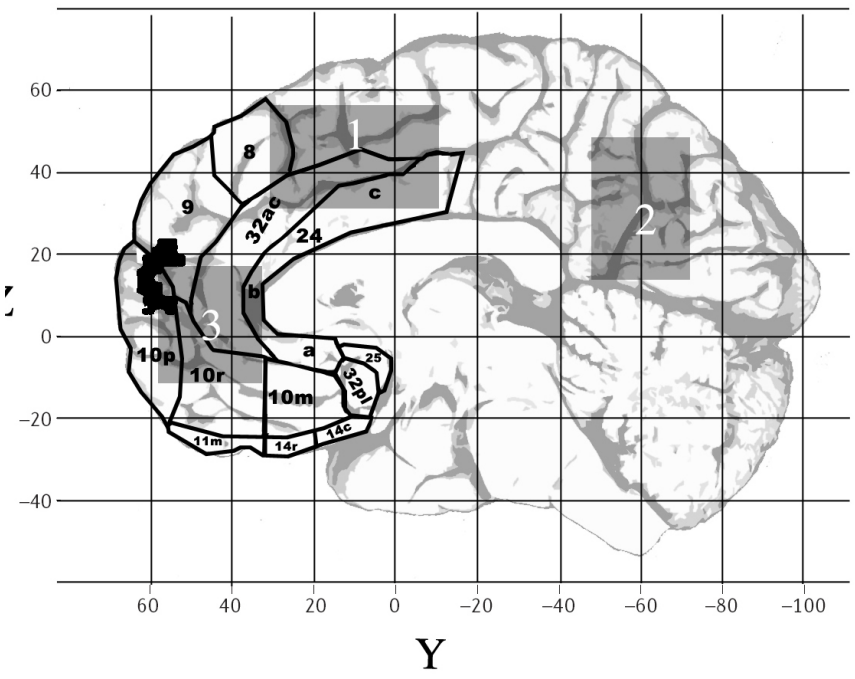


Figure 3-1: Neural Correlates of Self-referential Processing

The three rectangular regions are re-drawn from Northoff et. al.'s (2006) meta-analysis of 27 imaging studies of self-referential processing, which found three modality-insensitive activation clusters. The extent in either dimension represent the standard deviation of the cluster. (The Brodmann area background image is adapted from Öngür, Ferry, & Price, 2003, p. 430).

The Default Mode Network in Self-Referential Processing

The default mode hypothesis (Gusnard & Raichle, 2001) is a final issue that must be accounted for when considering the intersection of self-referential processing, MPFC activity, and the suffering element of chronic pain. The default mode hypothesis arose in response to the existence of the default mode network (DMN), a network of brain regions that show consistently high levels of activation in the absence of any externally directed task. These regions also show high levels of activity during activities that require reflection upon, or projection of, one's sense of autobiographical self (Buckner, Andrews-Hanna, & Schacter, 2008).

Alternately, the DMN consistently *de*activates during externally oriented tasks that require attentional focus to be placed away from the self. This distinctive pattern of activation has led to the widely cited "default mode hypothesis", which argues that the DMN is devoted to the ongoing process of supporting a "stable, unified perspective of the organism relative to its environment (a 'self')" (Gusnard & Raichle, 2001, p. 692). Given this putative functionality, it is not surprising that the DMN strongly overlaps with the set of mid-line brain regions that have been shown to activate preferentially during self-related processing (see Figure 1).

The default mode hypothesis suggests that a feature of psychological health may be the attentional flexibility to focus upon the self when there is nothing more pressing to do, and to *stop* focusing on the self when attention should be deployed elsewhere. This suggestion is consistent with the contentions

of an emerging paradigm within the field of psychology that is grounded in complexity theory. This paradigm contends that the core attribute of mental health is a state of *organized flexibility*, and that this flexibility manifests on *both* the neural and psychological levels (Siegel, 2009; Ozier & Westbury, 2011).

In this light, the finding of Baliki, Geha, Apkarian, & Chialvo1 (2008) become strongly salient. These authors hypothesized that the experience of persistent pain leads to structural changes in the brain (e.g., brain atrophy of the DLPFC) that disrupt the DMN's ability to adaptively *de*activate, thereby lessening the chronic pain patient's ability to shift her focus away from herself when it would be adaptive to do so. In order to explore this hypothesis, Baliki et al. (2008) conducted an fMRI study that compared the neural responses of participants with chronic back pain to those of healthy controls during a visual attention task, the kind of externally directed task that typically leads to DMN deactivation. Consistent with their hypothesis, Baliki et al. found that, relative to resting baseline, during the visual task the healthy controls demonstrated a pattern of more intense and more pervasive DMN deactivation than the chronic back pain patients did. These differences were most strongly focused in the OMPFC (a large medial cluster centred in BAs 10, 11, 32; maxima at 0,48,-18).

Baliki et al.'s (2008) proposal that there is a crucial association between chronic pain related suffering and DMN hyperactivity is further supported by related research into two other forms of psychopathology that also involve maladaptively high levels of self-focused rumination. Both Social Anxiety

Disorder (Gentili et al., 2009) and Depression (Sheline et al., 2009) have also both been found to be associated with DMN hyperactivity.

As a partial summation, we formed our hypotheses for the current study in light of the following list of propositions. First, that suffering plays a vital role in exacerbating the pain-suffering cycle that defines chronic pain. Second, that suffering is correlated with hyperactivity in the identified, self-referencing related sectors of the MPFC/frontal DMN. Third, that learning to volitionally down-regulate neural activity in these regions could offer an effective means of helping chronic pain patients to lessen their suffering, thereby helping to counteract the negative cycle of chronic pain. Finally, that LORETA neurofeedback could be a financially accessible means of helping chronic pain sufferers to develop this kind of volitional control.

The Electrophysiological Correlates of Chronic Pain Related Suffering

Exploration of this latter possibility is, however, complicated by the fact that, unlike MRI neurofeedback, LORETA neurofeedback requires that specific electrophysiological bandwidths be identified for training. Based on the consulted literature, the electrophysiological correlates of chronic pain related suffering have yet to identified. Therefore, we designed the current experiment with this goal in mind. In brief, we used full cap EEG to monitor the brain activity of a cohort of chronic pain patients while they ruminated on the interference caused by chronic pain in their lives (SUFFER condition). We contrasted this task with a cognitive task that was designed to deactivate the relevant OMPFC regions (SOCIAL condition). We had two broad predictions. First, that the SUFFER

minus SOCIAL contrast would reveal significant electrophysiological differences in the same OMPFC regions identified by Baliki et. al. (2006). Second, that these electrophysiological changes would be consistent with greater neural activation in the SUFFER condition.

The nature of the relationship between homodynamic and electrophysiological activity is a complex and highly contested issue. However, simultaneous EGG-fMRI research has produced evidence that frontal DMN activity appears to be *negatively* correlated with frontal midline Theta activity (4-8 Hz) (Scheeringa et al., 2008) and *positively* correlated with activity within the High Alpha (10.5-12.5 Hz) (Jann et al., 2009), Beta (13- 30 Hz) (Mantini, Perrucci, Del Gratta, Romani, & Corbetta, 2007) and Gamma bands (30-50 Hz) (Mantini et al., 2007). These findings are consistent with evidence that, in broader terms, there is "… a systematic relation between frequency and direction of the BOLD response…" such that "… increased neural activity should lead to decrease in low frequency power (e.g. delta and theta) and an increase in high frequency power (e.g. beta and gamma) " (Scheeringa et al., 2009, p. 1237).

In light of all of the above, we hypothesized that the SUFFER condition would be associated with: increased suffering; therefore with increased autobiographical self-referencing; therefore with increased DMN activity; therefore with relative decreases in Theta and/or relative increases in High Alpha, Beta, and/or Gamma within those frontal DMN regions (Fox et al., 2005) that were identified by Baliki et al. (2006) as being preferentially associated with the

suffering aspect of chronic pain. Consequently, within a region comprising the medial (x: 25 to -25; Northoff et al., 2006) aspects of BAs 24, 32, 8/9,10 and 11.

METHODS

Participants

Participants were recruited through posters at a local pain clinic, through a commercial on local television, and through a newspaper story in the local newspaper. In order to be considered for inclusion the participants had to have experienced persistent pain for at least the previous six months. Screening questions were used to exclude potential participants who: had suffered a traumatic brain injury; were actively abusing alcohol or drugs; had been diagnosed with a cerbrovascular disease; had been diagnosed with epilepsy or suffered a seizure of any kind; had been formally diagnosed with a sleep disorder; or who were actively suicidal (see Appendix G). Seven participants (5 females, 2 males, mean age 47.1 years) took part in the current study. All seven subjects were Canadian, Caucasian, and right-handed (see appendix A and appendix B). An eighth participant was recruited for the current study but elected not to participate in the SUFFER task and therefore her data are not reported here. The seven participants were used as their own controls in comparing the two conditions in this study.

Prior to inclusion in the study all participants were given a thorough explanation of the study and had written informed consent was obtained from all of them. Participants were offered an hourly wage of $15/hour for their

participation. The Ethical Committee of the University of Alberta approved the study.

Measures

Four measures were used during completion of the study. These measures were the Pain Disability Index (PDI; Pollard, 1981), the Short Form- McGill Pain Questionnaire (SF-MPQ; Melzak, 1987), the Center for Epidemiological Studies Depression Scale (CED-S; Radloff, 1977), and Numerical Rating Scales (NRS; Jensen & Karoly, 1992).

PDI

The PDI is a seven item self-report measure designed to assess subjective perceptions of how strongly pain impacts levels of daily functioning. Tait and Chibnall (2005) report that the PDI has been used with diverse forms of pain including both chronic and acute and that it has demonstrated strong psychometric properties, including showing good evidence of validity, reliability, and change sensitivity. Tait and Chibnall (2005), for example, assessed four theoretically related variables (i.e., fear-avoidance beliefs) and then attempted to predict scores related to the two factors of the PDI (voluntary activity disability and obligatory activity disability). Using this procedure these authors successfully accounted for 62% of the variance on the voluntary activity sub-scale and 47% of the variance on the obligatory activity sub-scale, thereby providing evidence of the PDI's construct validity.

Short Form- McGill Pain Questionnaire (SF-MPQ)

The SF-MPQ is a 15-item questionnaire that measures the extent to which a variety of sensory (e.g., "shooting") and affective ("sickening") pain descriptors are being experienced. Numerous researchers have found that the SF-MPQ's scores correlate very strongly (Melzack, 2005) with scores on the well validated McGill Pain Questionnaire (Melzack, 1975) even though the SF-MPQ takes much less time to complete. A specific source of factorial validity evidence comes from a study conducted by Wright, Asmundson, & McReary (2001). These authors used confirmatory factor analysis to investigate the SF-MPQ responses of a large group of participants with chronic back pain. Wright et al. found consistency estimates of .78 and .76 for a sensory factor and an affective factor respectively, thereby offering support for the validity of the two-factor structure that had been theoretically proposed by Melzack (1987).

The Center for Epidemiological Studies Depression Scale (CED-S)

The CED-S is a 20-item self report measure that is designed to screen for depressive symptomotology. It has been used widely and numerous investigations has been found to have good internal consistency, acceptable test-retest relaibilty, and a high correlation with the provision of clinical depression diagnoses (Wong, 2000). Of particular relevance to the current study, Turk & Okifukji (1994) investigated the CED-S's performance with a sample of 100 chronic pain patients. The participants had a structured clinical interview with a psychologist and also completed the CED-S. Using an adjusted cut score of 19, Turk & Okifukji (1994) found that the CED-S identified 82% of depressed participants as

being depressed while correctly classifying 62% of non-depressed participants as being non-depressed.

Numerical Rating Scales (NRS)

The NRS is a commonly used method of measuring pain intensity and unpleasantness. The NRS intensity scales used in the current study were broken into 11 equal units (0-10). NRSs are standardized, easy to administer, and easy to understand measures that have demonstrated strong reliability and validity in chronic pain research (Dworkin et. al. 2005). One example of convergent evidence comes from a study conducted by Bijur, Latimer, & Gallagher (2003). In this study 103 patients reporting to a hospital emergency ward with acute pain rated their pain levels three times over the course of an hour. Across the three time points Bijur et. al. (2003) found that verbally administered NRS ratings correlated very strongly (r = .94) with analogous written pain ratings made on the visual analogue scale (VAS), another very commonly used and well validated self-report pain measure (Dworkin et. al., 2005).

Procedures

All participants met with the lead author for four separate sessions of sixty minutes each. During the first meeting the participants filled out the psychometric measures for descriptive purposes, the results of which are outlined in Appendix B. The remainder of the first session was devoted to instructing the participants how to minimize ocular, muscular, and movement artifacts during recording. Sessions two and three involved the completion of related tasks that are not

reported here. Data collection relevant to the current article occurred during the fourth meeting.

Task Procedure

At the start of the fourth meeting the participants were seated in a recliner in a small, dimly lit room. The recliner offered head and neck support to minimize head movement. The participant's ears and foreheads were then cleaned with a mildly abrasive gel. An appropriately sized, 19 channel full cap EEG acquisition device (Electro-cap International Inc, USA) was then fitted on the participants' heads. Prior to beginning of data collection the impedances between each ear and each electrode were checked in order to ensure that they were in an acceptable range.

Following this, participants were instructed to remain relaxed with eyes closed for four minutes while baseline EEG data was collected. Next, the SUFFER and SOCIAL tasks were conducted (see appendix O for task instructions). Each of these tasks involved the completion of two, two-minute blocks. These blocks were randomized to occur in either the order SUFFER-SOCIAL-SUFFER-SOCIAL or SOCIAL-SUFFER-SOCIAL-SUFFER. During each SOC block the participants were instructed to select and then to think about one of the following three social issues: the effects of globalization of trade; the effects of NAFTA; or the right to vote. The specific instructions for the SOC task were to "Think about this topic in a dispassionate way, simply considering the various issues that the topic raises". Alternately, during the SUF blocks participants were given the following instructions: "During the next two minutes I

would like you to ruminate about the role of chronic pain in your life. During this time please ruminate about the way that pain interferes with your life, the suffering it causes, and the obstacles it presents for you". The SUF condition did not involve overt instructions for the participants to directly exacerbate their currently experienced pain as was done in DeCharms et al. (2005). Following each SOC and each SUF block the participants were asked to verbally rate the degree of pain intensity and pain unpleasantness they had experienced in the preceding block on a 0-10 NRS. Two-minute rest periods were taken between the data collection blocks.

EEG Recording

Nineteen -channel EEG was recorded with a Mitsar 201 EEG data acquisition system (Mitsar Corp., Russia). The 19 electrodes were applied according to the International 10/20 system with the following locations: F P1/2, F7/8, F3/4, Fz,, C3/4, Cz, T3/4, T6/8, P3/4, Pz, and O1/2. Data was sampled at a rate of 250 samples per second with low and high pass filters set at .32 and 70 Hz respectively. Impedances between each ear and each electrode were maintained at between 3-5 k Ohms (Congedo et al., 2004).

Data Analysis

Planned Analysis

Behavioral Results

Paired t tests were performed on the behavioral results in order to investigate phenomenological differences between the two task conditions.

EEG Analysis

Preliminary EGG analysis. In the first stage of EEG data analysis, all recorded EEG epochs were carefully and individually checked for artifacts (e.g. eye blinks, head movement, muscle artifacts). All portions of data that were contaminated with artifact were eliminated from the record. The first 60 seconds of artifact-free EEG data were then identified for each of the four time periods (e.g., two SUFFER and two SOCIAL).

Though the design only required one time period for each participant in each condition, two time periods were conducted in each condition in case a participant failed to produce sufficiently clean data during the first iteration of a task. In practice however, all participants produced the requisite 60 seconds of clean EEG data for all time periods. As such, only one time period in each condition per participant was subsequently analyzed. In order to heighten the contrast between conditions, the more behaviorally extreme period in each condition was selected for subsequent analysis. In other words, in the SUFFER condition, the relevant period with the higher behavioral score (Intensity plus Unpleasantness) was selected, while in the SOC condition, the relevant period with the lower score (Intensity plus Unpleasantness) was selected. When there were ties between two periods, the chronologically earlier period was selected for analysis.

The described behavioral ranking strategy was based on the contention that ratings of the sensory and affective dimensions of pain would offer an indirect measure of the extent to which a participant had “suffered” during a particular time period. As outlined in the introduction, this contention is based on

both the interrelatedness of the sensory, affective and suffering aspects of pain (Price, 2002), and also on evidence that increases in the suffering related variable of pain catastrophizing have been found to be associated with increases in both the intensity (Tripp et al., 2006) and unpleasantness (Geisser et al., 1994) of chronic pain.

LORETA analysis. The LORETA-key software was used in order to apply the inverse solution method of Pascual-Marqui (1999). As a first step in the planned LORETA analysis, an average current density (A/mm/3) was calculated for each participant, in each condition, within each of the investigated bandwidths, at each voxel within the LORETA solution space. There are 2394 such 7*7*7 ml voxels within the LORETA solution space, which is restricted to cortical grey matter. The investigated bandwidths were: Theta (4-7.5 Hz), Alpha 2 (11-12 Hz), Beta (13-30 Hz), and Gamma 1 (30-50 Hz).

For each individual, a planned comparison was then conducted in order to identify voxels that were activated to a significantly different extent between the conditions within the broadly defined ROI (medial aspects of BA 24, 32, 8/9,10 and 11). To perform these contrasts the SUFFER and SOCIAL maps for each individual were randomly reshuffled 4,000 times across conditions according to the t-max approach (Congedo, Lubar & Joffe, 2004). Through this process a histogram was created that identified the t-score falling at the 99th percentile across these many permutations. This t-score then served as a critical value that was used to identify any individual voxels in the observed contrast that fall above it. These voxels would then be declared significant at the $p < .01$ level (Nichols &

Holmes, 2001). Finally, group maps (n=7) were created for each of the conditions, and the t-max approach was again used to identify any voxels that were significantly different at the group level. Due to the small n size a p value of < .05 was used for these planned group comparisons.

Post-hoc Analysis

Behavioural Results Validity Check

We conducted a post hoc analysis in order to investigate the validity of our use of behavioural difference scores (based on Intensity and Unpleasantness ratings) as measures of participants' depth of "suffering" during the experimental task. In order to conduct this analysis we calculated Spearman's correlations between participants' PDI scores and their task related behavioural difference scores, with the expectation that a significant, positive association would be found. The rationale for this validity check was that, assuming that this measurement approach was valid, participants' with higher PDI scores should be expected to suffer more deeply when invited to do so during the rumination task because that they would have more pain related obstacles to ruminate *upon.*

Individual Level EEG Analysis

During post hoc analysis, the EEG data was considered at the individual level. For each participant all significant voxels in the ROI and within the four relevant bandwidths were identified. Significant voxels within the ROI were identified regardless of whether they were significant in hypothesized direction, or in the opposite direction (see Table 4). We then considered the relationship between participant's putative levels of task induced suffering and their neural

responses. This analysis involved calculating a correlation between participants' behavioural difference scores (Intensity + Unpleasantness $_{(suffer)}$ − Intensity + Unpleasantness $_{(social)}$) and the number of significant voxels they generated within the ROI (Lee et al., 2005; e.g., significant voxels in predicted direction-significant voxels in the opposite to predicted direction).

Results

Planned Analysis

Behavioural Results

A paired t test found that the Pain Intensity NRS ratings were higher in the SUFFER condition than in the Social Condition t (6) = 4.04, p = .007. A paired t test found that the Pain Unpleasantness NRS ratings were also higher in the SUFFER condition than in the Social Condition t (6) = 4.41, p = .004. (See table 2 for relevant means and standard deviations).

Table 3-2: Behavioural Results

Partic-ipant I.D./ Behavioral Rak	Pain Intensity-SUFFER CONDITION (1-10)	Pain Intensity-SOCIAL CONDITION (1-10)	Pain Intensity Difference (0-9)	Pain Unpleasantness-SUFFER CONDITION (1-10)	Pain Unpleasantness-SOCIAL CONDITION (1-10)	Pain Unpleasantness Difference (0-9)	Combined Intensity/ Unpleasantness Difference (0-18)
C / 1	8	2.5	5.5	9.5	1	8.5	14
A / 2	5	1	4	8	1	7	11
F / 3	6	2	4	6.5	2	4.5	8.5
E / 4	3.5	2.5	1	7	2.5	4.5	5.5
G / 5	8	5	3	8	6	2	5
D/ 6.5	4	3	1	6	4	2	3
B / 6.5	4	3	1	4	2	2	3
Mean/ SD	**5.5/ 1.89**	**2.7/ 1.21**	**2.8/ 1.82**	**7/ 1.75**	**2.6/ 1.79**	**4.4/ 2.6**	**7.1/ 4.19**

Group level EEG Results

A planned, group level LORETA analysis failed to find significant between-condition differences in the ROI within any of the four specified bandwidths (Theta minimum *t* value of -2.15 at BA 8: 4,15,59; Alpha 2 maximum *t* value of 1.36 at BA 11: 9, 36, -6; Beta maximum *t* value of 3.25 at BA 10: 25,65,15; Low Gamma maximum *t* value of 2.86 at BA 10: 25,57,15). However, the reader is cautioned that these maximum t scores do not reflect the consistency of activation across the several hundred voxels in question, and they therefore do not reflect activation within the ROI as a whole. While no voxels within the ROI approached significance at the group level, a pattern of activation across the entire ROI was suggestive of trends that appear to be consistent with the hypotheses. In order to illustrate these apparent trends the group level images are included in Figure 2 for qualitative purposes. The colour on these images scaling has been set to highlight qualitative differences and they should therefore be viewed with caution.

Table 3-3: Individual Results in regards to Significant Voxels

Partici-pant ID	*Behavioural Rank**	*Significant Voxel Rank***	*# of Significant Voxels (Predicted -Opposite to Predicted)*	*Theta (4-7.5)*		*Alpha 2 (11-12 Hz)*	*Beta 1and 2 (13-30 Hz)*	*Gamma 1 (30-50 Hz)*
C	**1**	**1**	**12-0=12**	none		none	1	11
A	**2**	**3**	**4-0=4**	none		none	4	none
F	**3**	**2**	**2-0=2**	none		none	1	1
E	**4**	**7**	**0-(-12) = -12**	3		6	3	none
G	**5**	**4**	**2-0=2**	none		none	1	1
B	**6**	**5**	**0-0=0**	*none*		*none*	*none*	*none*
D	**7**	**6**	**0-(-4) = -4**	*none*		*none*	*none*	*4*

Note: underlined numbers were significant in the opposed to predicted direction

*Behavioural Difference Scores (Intensity + Unpleasantness (suffer)) – (Intensity + Unpleasantness (social))

** (# of Significant Voxels Predicted)-(# of Significant Voxels Opposite to Predicted)

Table 3-4: Location/Strength of Significant Voxels (Relative Difference at .05 level)

Participant	Bandwidth	X,Y,Z	BA	T Max Threshold	T score
C	**Beta**	25, 66, -13	11	4.19	5.77
C	Gamma	18 , 66, -13	11		6.15
C	Gamma	25, 59, -6	10		6.15
C	Gamma	18, 66, 1	10		6.15
C	Gamma	18, 66, -6	10		6.15
C	Gamma	25, 52, -13	11		6.15
C	Gamma	25, 59 , 1	10		6.15
C	Gamma	25, 59, -13	11		6.15
C	Gamma	25, 52, 1	10		6.15
C	Gamma	18, 59, -13	11		6.15
C	Gamma	11, 52, 1	10		5.83
C	Gamma	25, 38, -13	11		5.99
A	**Beta**	25, 31, 43	8	4.39	6.17
A	Beta	-10, 38, 57	8		4.57
A	Beta	4, 38, 50	8		5.17
A	Beta	25, 59, 29	10		5.35
F	**Beta**	-17, 66, 8	10	3.64	4.46
F	Gamma	-17, 66, 15	10		4.38
G	***Theta***	*11, 10, 36*	*32*	*4.21*	*4.83*
G	*Theta*	*25, 24 , 43*	*8*		*4.78*
G	*Theta*	*25, 52, 1*	*10*		*4.73*
G	*High Alpha*	*24, 24, 36*	*9*		*-4.36*
G	*High Alpha*	*-24, 52, 1*	*10*		*-5.1*
G	*High Alpha*	*-24, 45, 15*	*10*		*-5.33*
G	*High Alpha*	*-3, 24, -6*	*32*		*-5.55*
G	*High Alpha*	*-10, 38, -6*	*10*		*-5.95*
G	*High Alpha*	*-10, 31, 22*	*32*		*-6.01*
G	*Beta*	*-24, 38, -13*	*11*		*-5.88*
G	*Beta*	*-24, 45, 15*	*10*		*-6.59*
G	*Beta*	*-3, 31, 22*	*24*		*-7.31*
E	**Beta**	4, 66 , 15	10	4.21	8.59
E	Gamma	17, 66, 8	10		14.0
D	***Gamma***	*-10 17 29*	*32*	*4.14*	*-4.85*
D	*Gamma*	*4, 66, 8*	*10*		*-5.37*
D	*Gamma*	*-24, 45, 15*	*10*		*-5.97*
D	*Gamma*	*-10, 38, 15*	*32*		*-6.58*

Notes:

- Voxels in *italics* are significant in the opposite to predicted directions

Post-hoc Analysis

Behavioural Results Validity Check

A significant, positive correlation was found between participants' baseline PDI scores and their task related Behavioural Difference Scores, D (12) = .771, p = .021 (Spearman's correlation, one tailed).

Individual Level EEG Analysis

A significant, positive correlation was also found between participants' Behavioural Difference Scores and the number of significant voxels they generated within the ROI (significant voxels in predicted direction- significant voxels in the opposite to predicted direction), D (12) = .745, p =. 027 (Spearman's correlation, one tailed).

Discussion

The current experiment used LORETA in order to investigate the spatially localized, electrophysiological correlates of negatively valanced, chronic pain related rumination, or "suffering" (Price, 2002). To this end, we asked a sample of participants living with various chronic pain conditions to intentionally ruminate on the interference that chronic pain causes them in their lives. We predicted that, relative to a cognitive control task, the SUFFER condition would be associated with an increase in frontal DMN activity. We formed this hypothesis in response to previously reported evidence of links between: chronic pain related suffering (Baliki et al., 2006); self-referential processing (Price, 2002); and frontal DMN activity (Baliki et al, 2006; Schweinhardt et al., 2008). As such, we specifically hypothesized that during the SUFFER condition the medial, frontal, self-

referencing related regions that have been shown to be preferentially related to chronic pain related suffering would evidence: significantly lower levels of Theta (4-7.5) (Scheeringa et al., 2008); and/or significantly higher levels of Alpha 2 (11-12 Hz) (Jann et al., 2009), Beta (13-30 Hz) Mantini et al., 2007), and/or Gamma (30-50 Hz) (Mantini et al., 2007).

We found statically significant, between-condition differences in the participants' experimental task behavioral rating scores at the group level. This suggests that the experimental task successfully achieved its aim. In other words, the participants did in fact suffer significantly more in the SUFFER condition than they did in the SOCIAL condition. However, despite this evidence of a successful task manipulation, and against our expectations, no evidence of significant, group level EEG differences were found in the predicted directions within any of the four hypothesized bandwidths (see Figure 2 below). As such, our four hypotheses have not been supported.

However, the role of statistical power must be strongly taken into account when interpreting our null group level results. With an *n* of 7, the current sample size was admittedly very small. In these kinds of LORETA analysis, an n of 6 is the absolute minimum required to achieve group level statistical significance and 15 is generally considered adequate (Nichols & Holmes, 2001). As such, it is plausible that the lack of significance results at the group level occurred in large part because of inadequate power. In this light, we will contend that our findings did produce some results that offer conditional support for our hypotheses. We will now present two sources of evidence to support this contention.

The first source of support involves a qualitative consideration of the group level results. While their lack of statistical significance obviously means these group level results must be viewed with caution, reference to Figure 2 indicates that, on the whole, all four bandwidths did show evidence of moving in the expected directions within the frontal DMN. Crucially from our perspective, this trend appears particularly evident when attention is focused specifically on the anterior, mPFC region that previous MRI work has shown to be the region that is most strongly associated with chronic pain related suffering (Baliki et al., 2006; Schweinhardt at. al., 2008) (see darkest cluster in fig. 2 B and corresponding, circled regions in Figs. 2 C-F). As such, we suggest that the group level results offer meaningful, though clearly qualified, support for the contention that chronic pain related suffering involves increased activation of the self referencing related mPFC region in question, and further, that this neural activation equates with electrophysiological changes in the hypothesized directions.

The second source of support we will entertain here involves consideration of the LORETA results at the individual level. This consideration starts with the observation that, though the behavioral manipulation appeared to have achieved the desired effect at the *group* level, there was also clearly strong *between-participant* variability in this regard. In other words, certain participants were apparently able to generate a much stronger phenomenological contrast between the two conditions than other participants were able to. For example, reference to table three indicates that participant C reported a very large between condition

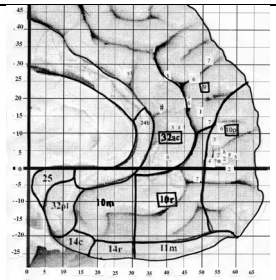
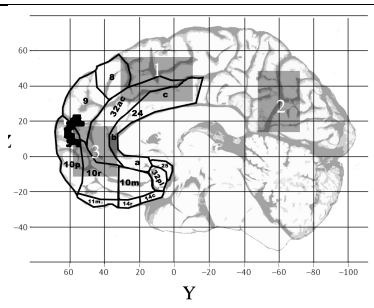
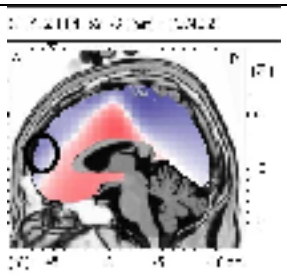
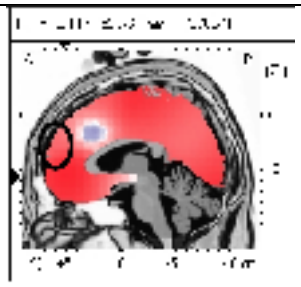
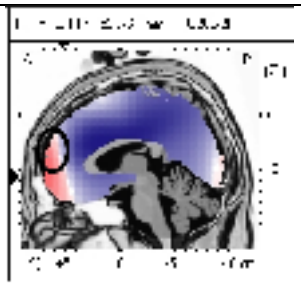
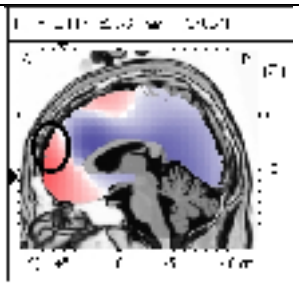
Behavioural Difference Score (e.g., Intensity + Unpleasantness $_{(suffer)}$ – Intensity + Unpleasantness $_{(social)}$) of 14 out of a possible total score of 18. In sharp contrast, both participants B and D only reported behavioral difference scores of three out of a possible total score of 18.

In this light, it becomes noteworthy that there appears to have also been a meaningful relationship between the *degree* to which participants successfully achieved a between-condition "suffering contrast" and the *degree* to which they fulfilled the EEG hypotheses. Reference to the Results section illustrates that there was a significant relationship between participants' Behavioural Difference Scores and the number of ROI voxels that participants activated significantly in the expected directions.

Limitations

The current study has several limitations, three of which will be considered here.

First, there is the study's previously discussed lack of power. This is a key limitation because it makes the group level results difficult to clearly interpret. Replication of the current design with a larger *n* would be necessary in order to resolve the interpretive ambiguity in this regard.

2 A: Brodmann Area Reference (image taken from Öngür, Ferry, & Price, 2003, p. 430).	**2 B: mPFC Region specifically associated with the suffering aspect of arthritic pain** (Schweinhardt et al., 2008) (see darkest cluster)	**2 C: Theta (4-7.5 Hz)**
		
2 D: Alpha 2 (11-12 Hz)	**2 E: Beta (13-30 Hz)**	**2 F: Gamma 1 (30-50 Hz)**
		

Note:

- Results are based on Relative Difference scores between conditions.
- Red indicates that there was more current density within this bandwidth in the Suffer condition relative to the Social condition, Blue indicates that there was less current density within this bandwidth in the Suffer condition relative to the Social condition.

Figure 3-2: Suffer-Social Group Contrast

Finally, the first author conducted all of described data collection procedures while the first and second authors conducted all of the described data analysis procedures. There is therefore the inevitable possibility that experimenter bias distorted the results of the current experiment, despite concerted efforts on the part of all parties involved to prevent this from occurring.

Conclusion

In conclusion, our lack of significant group level results means that our hypotheses cannot be strongly supported. However, on the basis of the arguments presented above, the current study has been interpreted as offering conditional support for the contention that: chronic related suffering involves increased activation in an anterior mPFC cluster (Baliki et al, 2006; Schweinhardt et al., 2008) that is understood to be essential to self referential processing (Northoff et al., 2006); and that this increased frontal, DMN activity corresponds to decreases in frontal Theta and particularly to increases in the faster frequencies (High Alpha -Gamma). A rigorous test of this tentative conclusion would require replication of the current design with a larger sample. However, our tentative interpretation of the current results also indicates that the use of LORETA neurotherapy to help chronic pain patients volitionally down-regulate the neural correlates of their pain related suffering could be made effective by having these patients learn to up-train Theta and/or down-train Alpha2-Gamma within the identified anterior, mPFC region.

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CHAPTER 4

LORETA NEUROTHERAPY FOR CHRONIC PAIN RELATED SUFFERING

Introduction

Chronic pain causes tremendous suffering. Defined as pain that has lasted for more than six months, various studies have found that between 4,000,000 and 7,000,000 Canadians are currently living with this chronic condition (Veillette, Dion, Altier, & Choiniere, 2004). In addition to the personal suffering it causes, the economic impact of chronic pain and chronic pain related disabilities are also immense. In the United States, it has been estimated that $125 billion US is lost every year through direct medical costs and reduced worker productivity (Turk, 2002). The development of efficacious new pain management alternatives is therefore a crucial research priority.

In 2005, DeCharms, Maeda, Glover, Ludlow, Pauly, Soeji, Gabriele, & Mackey used fMRI neurofeedback in an effort to teach a group of eight chronic pain patients to self-regulate their pain. These authors capitalized on the strong spatial resolution of MRI in order to teach their participants how to volitionally down regulate cerebral blood flow (CBF) in a discrete, 1 cm/3, pain related region of the dACC (BA 24; centred at x: 2; y; 16, z: 33). Training was carried out over the course of a single day. Control participants were trained in autonomic biofeedback, a standard chronic pain intervention.

The study produced three key findings. First, the majority of the fMRI neurofeedback participants successfully learned how to volitionally decrease CBF in the targeted region. Second, the neurofeedback group participants reported

average pre-post training drops in pain unpleasantness ratings that were three times larger than the equivalent drops ($p < .02$) reported by control participants. Third, the degrees to which participants showed pre to post training improvement in the ability to volitionally down-regulate dACC activity were significantly correlated with the degrees to which they improved their abilities to down regulate their phasic pain responses ($p < .01$). This third finding was crucial, since it implied a casual relationship between the development of an apparently achievable neural self-regulation skill and the control of chronic pain.

DeCharms et al.'s (2005) results hold striking potential. Unfortunately however, given the prohibitive expense of MRI systems, the widespread clinical use of fMRI neurofeedback will likely remain unrealistic for the foreseeable future. In response to this situation, our team explored the plausibility of adapting DeCharms et al.'s basic approach to use with LORETA neurofeedback, an alternate, modestly priced, clinical modality.

LORETA Neurotherapy

Low Resolution Electromagnetic Brain Tomography (LORETA) (Pascual-Marqui, 1999) is a form of EEG analysis that is being increasingly widely used. LORETA is capable of deducing the activity of discrete cortical regions. While it clearly does not have the same degree of spatial resolution as MRI, LORETA has an established ability to accurately localize neural activity within the cortex (Pascual-Marqui, Esslen, Kochi, & Lehmann, 2002). Therefore, like fMRI neurofeedback, and *un*like traditional EEG neurofeedback, LORETA-based neurofeedback is capable of targeting specific brain regions for training.

To date, four LORETA neurofeedback studies have been identified in the literature. Three of these studies used small, non-clinical samples and trained a single, discrete brain region (Congedo, Lubar & Joffe, 2004; Cannon, Lubar, Congedo & Thorton, 2007; Cannon, Congedo, Lubar, & Hutchens, 2009). The trained regions in these studies ranged in size from 13 cm/3 (Congedo et. al., 2004) to 1 cm/3 (Cannon et. al., 2009). Recently, Cannon, Sokhadze, Lubar, & Baldwin (2008) also reported on a single patient case study in which they used LORETA neurotherapy with a single participant who had a history of heroin and alcohol dependence.

All four of the identified LORETA neurofeedback studies have produced evidence of successful training effects. Further, accessibly priced LORETA neurofeedback systems are now commercially available (Nova Tech EEG; Mesa, Arizona).

Cortical Region Targeted for Training

The dACC region that was targeted for training by DeCharms et al. (2005) is known to play a key role in the experience of "immediate pain unpleasantness", which can be defined as the coarse, aversive feelings that are associated with the affective/motivational aspects of pain (Price, 2002). However, we decided instead to train our participants to regulate "suffering", another aspect of the chronic pain experience. Price (2002) defines chronic pain related suffering as "… reflection related to what one remembers or imagines…" regarding "… perceived interference with one's life, difficulties in enduring pain over time, and implications for the future" (Price, 2002, p. 394).

As this definition makes clear, chronic pain related suffering can be understood as a form of negatively valenced, self-referential processing and it therefore has strong conceptual overlap with the process of *rumination*. In turn, the pervasive, negative impacts of rumination on psychological health in general are becoming increasingly widely recognized (Barnhofer & Chittka, 2010). Regarding chronic pain in particular, the Rumination subscale of the Pain Catastrophizing Scale has been found to be a powerful predictor of disability, while controlling for degree of pain severity (Sullivan, Sullivan, & Adams, 2002). As such, the amount of suffering a patient carries out *in response* to their nocioceptive experience clearly has crucial impacts on how disabling and distressing their chronic pain condition becomes (Sullivan et al., 2001).

As will be discussed below, a particular cluster within the mPFC appears to play a key role in supporting chronic pain related suffering. Crucially, the mPFC cluster in question is significantly larger than the pain unpleasantness related dACC region that was originally targeted for training by DeCharms et al. (2005). Therefore, given the lesser spatial localization abilities of LORETA relative to MRI, and given the clear clinical importance of the suffering aspect of chronic pain, our team concluded that it might be both clinically effective *and* methodologically feasible to target the mPFC for training.

The mPFC and Suffering

Meta-analysis (Northoff et al., 2006) has shown that self referential processing most consistently activates three large clusters along the brain's cortical midline. These are located in the Dorsomedial PFC (DMPFC) (see

Region 1 in Figure 1), the Posterior Cingulate Cortex (PPC) (see Region 2 in Figure 1), and the mPFC (see Region 3 in Figure 1). Of these regions, the mPFC cluster is most robustly associated with self-referential processing. Through his review of relevant literature, Lieberman (2007) concludes that "reflecting on one's current experience leads to remarkably consistent activation of the mPFC (BA 10) across a variety of different tasks" (p. 267).

In addition to compelling evidence that the mPFC is crucial to self-referential processing in general terms, there is also evidence that the mPFC is *specifically* involved with supporting chronic pain related suffering. Baliki et al. (2006) found activity in the mPFC to be specifically associated with the suffering element of chronic back pain. The specific mPFC cluster that Baliki et al. (2006) found to be most strongly associated with pain related suffering fell in medial BA 9/10 (peaks at –12, 58, 20 and 12,60,22). This same mPFC sub-region was also recently found to be specifically associated with the "emotional augmentation" of Rheumatoid Arthritis pain (Schweinhardt et al., 2008) (maxima at BA 10; –4, 66, 8).

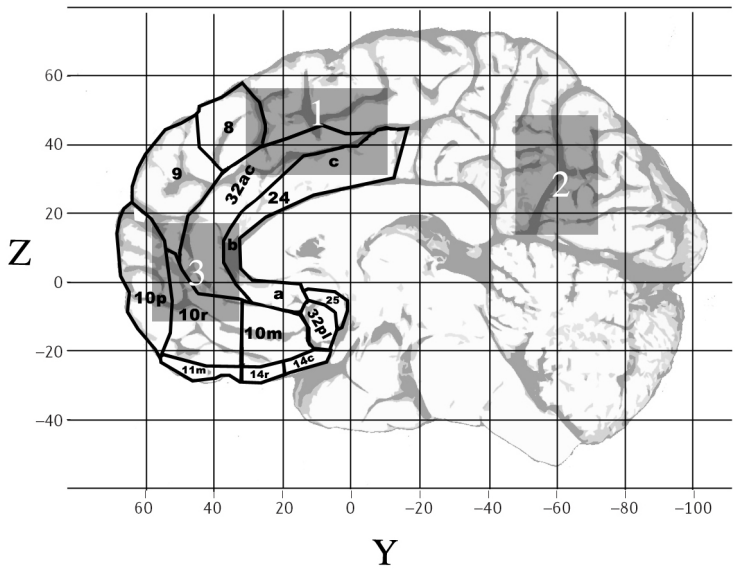


Figure 4-1: Neural Correlates of Self-referential Processing

Summary of regions implicated in self-related tasks. The three rectangular regions are re-drawn from Northoff et. al.'s (2006) meta-analysis of 27 imaging studies of self-referential processing, which found three modality-insensitive activation clusters. The extent in either dimension represent the standard deviation of the cluster. (The Brodmann area background image is adapted from Öngür, Ferry, & Price, 2003, p. 430).

Bandwidths Targeted for Training

LORETA neurofeedback, unlike fMRI neurofeedback, requires that specific electrophysiological bandwidths be selected for training. In our case, these bandwidths were selected with the goal of teaching participants to volitionally down-regulate the selected mPFC region.

In general terms, there appears to be a systematic relation between EEG frequency and neural activation such that increased neural activity correlates with decreases in low frequency power and/or with increases in high frequency power (Scheeringa et al., 2009). This heuristic pointed us toward up-training the slower end of the EEG frequency spectrum. More specifically, we up-trained Theta (4.5-8 Hz) and Low Alpha (8-10Hz).

Frontal Theta

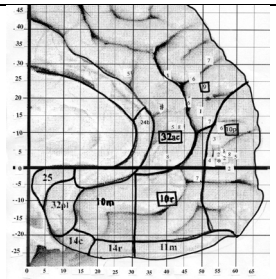
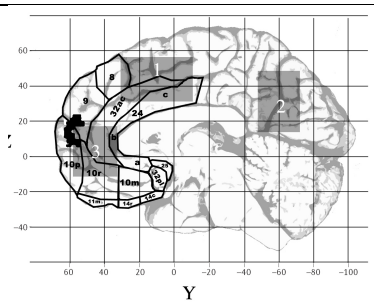
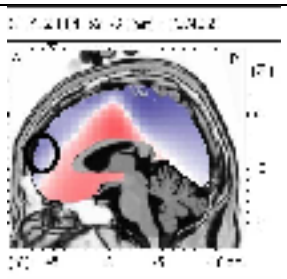
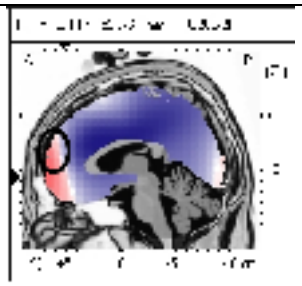
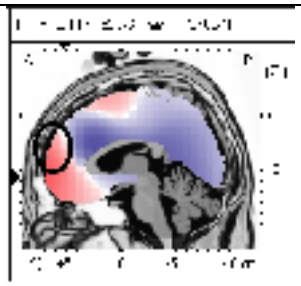
Our decision to up-train Theta was also influenced by the fact that increases in Theta power, most often at frontal sites, are also among the most commonly reported EEG correlates of meditation (Cahn & Polich, 2006), a practice that lessens self-focused rumination.

This decision to up train frontal Theta was further strengthened by the results of a companion study (Ozier, Sherlin, Mueller, Lampman, & Whelton, 2011) that our team conducted, in part, to help us clarify the training bandwidths for the current study. During this earlier study we asked a sample of people living with mixed chronic pain conditions (the same group participants who later served as neurotherapy group members in the current study) to consciously ruminate on the obstacles that their chronic pain created for them while we monitored their

EEG activity. In other words, we asked them to engage in chronic pain related suffering. We then contrasted this "SUFFER" condition with an emotionally neutral, conceptually oriented task. Using LORETA analysis, we found qualitative evidence that the SUFFER condition was associated with *in*creased activity in the excitatory Beta and Gamma bandwidths and with *de*creased Theta activity within the relevant mPFC region (see the darkest region in Figure 2B and the corresponding circled regions in Figure C-E).

Frontal Low Alpha (Alpha 1)

We also selected Alpha for up-training in part because activity in this bandwidth is commonly, though controversially, held to be an inverse correlate of neural activation (e.g., Laufs et al., 2003). Further, increases in frontal Alpha power, like frontal Theta increases, are among the most commonly reported EEG correlates of meditation (Cahn & Polich, 2006). We elected, however, to train Alpha 1 (8-10 Hz) but not Alpha 2 (11-12 Hz). We based this choice on a pair of factors. First, the contention that Low and High Alpha should be considered separately has significant support in the literature (e.g., Jann et al., 2009). Second, numerous meditation studies have found increases in frontal Alpha 1 power but not frontal Alpha 2 power (e.g., Takahashi et al., 2005; Travis et al., 2009).

2 A: Brodmann Area Reference (image taken from Öngür, Ferry, & Price, 2003, p. 430).	**2 B: mPFC Region associated with the suffering aspect of arthritic pain** (Schweinhardt et al., 2008) (see darkest cluster)	**2 C: Theta (4-7.5 Hz) changes associated with chronic pain related suffering**
		
	2 D: Beta (13-30 Hz) changes associated with chronic pain related suffering	**2 E: Gamma 1 (30-50 Hz) changes associated with chronic pain related suffering**
		

Notes:

- LORETA images are taken from Ozier, Sherlin, Mueller, Lampman, & Whelton, 2011
- LORETA results were based on Relative Difference scores between conditions.
- Red indicates that there was more current density within this bandwidth in the Suffer condition relative to the Social condition, Blue indicates that there was less current density within this bandwidth in the Suffer condition relative to the Social condition.
- The LORETA images above did not reach statistical significance, potentially due to a small n (7), and should therefore should be viewed with caution

Fig 4-2: **Electrophysiological correlates of chronic pain related suffering**

Hypotheses

The current study was designed to test three hypotheses. First, that over the course of 10 LORETA neurotherapy training sessions a sample of participants with mixed chronic pain conditions would successfully develop the ability to volitionally up-regulate Theta and Low Alpha (4.5-10 Hz) in the selected anterior, mPFC ROI (medial BA 10; a cluster of five continuous LORETA centered at 5,50,0). Second, that, over the course of training, the participants would show significant improvements in phasic pain regulation ability. Third, that the degree to which participants successfully developed the ability to up-regulate 4.5-10 Hz in the ROI would be significantly positively correlated with improvements in their phasic pain regulation abilities (DeCharms et al, 2005).

In addition, we used quantitative and qualitative methods in a discovery oriented manner in order to investigate the clinical benefits, side effects, and mental strategies associated with the neurotherapy intervention. Exploration of the clinical benefits of the neurotherapy intervention was achieved in part by contrasting these outcome results to analogous improvements demonstrated by members of an active control group. Members of the active control group were trained in Autogenics and standard CBT pain management strategies.

Method

Participants

Participants were recruited through posters at a local pain clinic, through a commercial on local television, and through a newspaper story in the local newspaper. Our inclusion criteria were that potential participants had been living

with any form of chronic pain for a period of at least six months and felt that they would be able to commit to the relatively extended training regime in question. Screening questions were used (see Appendix G) to exclude potential participants who: had suffered a traumatic brain injury; were actively abusing alcohol or drugs; had been diagnosed with a cerebrovascular disease; had been diagnosed with epilepsy or suffered a seizure of any kind; had been formally diagnosed with a sleep disorder; or who were actively suicidal. Fifteen participants (10 females, 5males) took part in the current study. All participants (see Appendices C and E) were Caucasian Canadians and all but one of them was right handed.

Sixteen participants were originally recruited and randomly assigned to two groups. However, this procedure led to clear imbalance in the baseline pain scores between the groups. Four members were therefore asked to switch groups as a means of redressing this imbalance. All four initially agreed. However, immediately before training began one of the participants who had agreed to switch into the Autogenics/CBT group dropped out, citing concerns around possible adverse side effects. This member was not replaced, nor is her data included in Table 1. Participant O, a member of the Autogenics/CBT group, dropped out half way through training. He stated he was dropping out because he did not perceive adequate benefit from the offered skills. Data for this participant are not reported here. Therefore, the study had 14/16 completers (87.5%).

Prior to training all participants completed several, widely used psychometric measures (see below). The participants' pre-training scores on these measures are listed in Table 2. Prior to inclusion in the study all participants were

also given a thorough explanation of the study and written informed consent was obtained from all of them. Participants were offered an hourly wage of $15/hour for their participation. The Research Ethics Office of the University of Alberta approved the study.

Measures

All participants completed several outcome measures at pre and post training. These measures were the Pain Disability Index (PDI) (Pollard, 1981), Short Form- McGill Pain Questionnaire (SF-MPQ; Melzack, 1987), The Center for Epidemiological Studies Depression Scale (CED-S; Radolff, 1977), and Numerical Rating Scale (NRS) asking them to describe their average Pain Unpleasantness and Pain Intensity ratings over the preceding week. All participants also completed an adapted version of the Working Alliance Inventory –Short Form (WAI-SF; Tracey & Kokotovic, 1989) following training. NRS and SF-MPQ ratings were also made during the Pain Control Tests (see Procedures section below). Each of these measures are briefly addressed below.

PDI

The PDI is a seven item self-report measure designed to assess subjective perceptions of how strongly pain impacts levels of daily functioning. Tait and Chibnall (2005) report that the PDI has been used with diverse forms of pain including both chronic and acute and that it has demonstrated strong psychometric properties, including showing good evidence of validity, reliability, and change sensitivity. Tait and Chibnall (2005), for example, assessed four theoretically related variables (i.e., fear-avoidance beliefs) and then attempting to predict

scores related to the PDI two factors (voluntary activity disability and obligatory activity disability). Using this procedure thee authors successfully accounted for 62% of the variance on the voluntary activity sub-scale and 47% of the variance on the obligatory activity sub-scale, thereby providing evidence of the PDI's construct validity.

Short Form- McGill Pain Questionnaire (SF-MPQ)

The SF-MPQ is a 15-item questionnaire that measures the extent to which a variety of sensory (e.g., "shooting") and affective ("sickening") pain descriptors are being experienced. Numerous researchers have found that the SF-MPQ's scores correlate very strongly (Melzack, 2005) with scores on the well validated McGill Pain Questionnaire (Melzack, 1975) even though the SF-MPQ takes much less time to complete. A specific source of factorial validity evidence comes from a study conducted by Wright, Asmundson, & McReary (2001). These authors used confirmatory factor analysis to investigate the SF-MPQ responses of a large group of participants with chronic back pain. Wright et al. found consistency estimates of .78 and .76 for a sensory factor and an affective factor respectively, thereby offering support for the validity of the two-factor structure that had been theoretically proposed by Melzack (1987).

The Center for Epidemiological Studies Depression Scale (CED-S)

The CED-S is a 20-item self report measure that is designed to screen for depressive symptomotology. It has been used widely and in a number of studies has been found to have good internal consistency, acceptable test-retest relaibilty, and a high correlation with the provision of clinical depression diagnoses.

(Wong, 2000). Of particular relevance to the current study, Turk & Okifukji (1994) investigated the CED-S's performance with a sample of 100 chronic pain patients. The participants had a structured clinical interview with a psychologist and also completed the CED-S. Using an adjusted cut score of 19, Turk & Okifukji (1994) found that the CED-S identified 82% of depressed participants as being depressed while correctly classifying 62% of non-depressed participants as being non-depressed.

Numerical Rating Scales (NRS)

The NRS is a commonly used method of measuring pain intensity and unpleasantness. The NRS intensity scales used in the current study were broken into 11 equal units (0-10). NRSs are standardized, easy to administer, and easy to understand measures that have demonstrated strong reliability and validity in chronic pain research (Dworkin et. al., 2005). One example of convergent evidence comes from a study conducted by Bijur, Latimer, & Gallagher (2003). In this study 103 patients reporting to a hospital emergency ward with acute pain rated their pain levels three times over the course of an hour. Across the three time points Bijur et. al. (2003) found that verbally administered NRS ratings correlated very strongly (r=.94) with analogous written pain ratings made on the visual analogue scale (VAS), another very commonly used and well validated self-report pain measure (Dworkin et al., 2005).

Adapted version of the Working Alliance Inventory –Short Form (WAI-SF)

Our design involved unequal therapist contact between groups. We therefore used an edited version of the WAI-SF as a means of helping to ensure

that any between group differences in the outcome measure results were not driven by between group differences in the strength of the working alliance. The WAI-SF is a measure of the therapeutic alliance that is widely used in psychotherapy process research. It includes 12 items that are cumulatively designed to assess the Task, Goal, and Bond aspects of the Alliance construct as it was originally described by Bordin (1979). Busseri & Tyler (2003) investigated the therapies of 54 clients seen at a university counselling centre in order to compare the predictive abilities of the WAI-SF to those of the well researched, 36 item, original Working Alliance Inventory (Horvath & Greenberg, 1989). Busseri & Tyler (2003) found that fourth session Client WAI-SF scores showed an r of .34 with outcome success ($p < .01$), predicting outcome almost as well as the full WAI ($r = .36$). In the current study only the six items of the WAI-SF that measure the strength of the bond were used.

Procedures

Overview

The first author (D.O.), a PhD student in Counselling Psychology, conducted all of the training and data collection sessions under the clinical supervision of the second and third authors (L.S. & H.M), both experienced neurotherapists.

First contact with potential participants was established though telephone screening. These screens were conducted in order to identify potential participants who met the previously described inclusion and exclusion criteria. Following successful telephone screening, all tentative participants met with the first author

so that he could provide a more thorough explanation of the participation requirements and answer any participant questions. Over the next two weeks, members of the neurotherapy group first participated in a companion study that was alluded to earlier (Ozier et al., 2011). Following this, all participants attended the first formal session for the current study and completed the pre-training outcome measures (see Appendices D and F). During these first initial sessions the neurotherapy group members completed the pre-training pain control tasks. Following this, training was carried out on over a six-week period. Training sessions were held on a weekly basis in the Autogenics group, and on bi-weekly basis in the neurotherapy group. Finally, a final meeting was held so that the neurotherapy group members could complete the post training pain control tasks and so all the participants could complete the post training outcome measures. Short, semi structured interviews were also conducted with the neurotherapy group members during these final meetings.

Pain Control Tests

The Pain Control Tests were conducted in a quiet, dimly lit room with each individual sitting upright in a chair. The EEG was sampled with 19 electrodes in the standard 10-20 International placement referenced to linked ears. Data were collected using 19 channel electro-caps (Electro-Cap International, Eaton, OH) and the Mitsar 201 amplifier (Mitsar Co., St. Petersburg Russia). Conductance was measured to ensure that it remained at 5 k Ohms or below.

The OBSERVE task was conducted using standardized instructions (see appendix P for task instructions). The OBSERVE task involved sitting with eyes

closed for a four-minute block during which the participants were instructed to keep their attention focused on their current pain experience without attempting to make it better or worse. Participants were repeatedly encouraged to keep their heads still, to relax their facial/jaw muscles, and to allow their eyes to remain still. Following the OBSERVE task the participants verbally completed the SF-MPQ, an NRS Intensity Scale, and an NRS Unpleasantness Scale in response to their highest pain levels during the block. A three-minute rest was subsequently provided .

The REGULATE condition involved offering participants audio feedback that reflected activity changes in the targeted mPFC cluster. Participants were instructed to try to increase the volume and amount of this feedback as much as possible. Feedback reward thresholds for the REGULATE condition were set to 55% reward based on the relevant EEG ratio during the preceding OBSERVE task. Following completion of the REGULATE task, the previously described rating scales were completed. However, participants were now also asked to make two more ratings strictly in response to their experiences during the REGULATE blocks. These latter ratings were 0-100 for Relaxation (from “not at all relaxed” to “completely relaxed”) and 0-100 for their levels of Self Talk (from “no self talk” to “strong and persistent self talk”).

Only at Time 2, a NO AUDIO condition was also completed following the REGULATE task. The NO AUDIO task involved the same instructions as the REGULATE task except that audio feedback was no longer provided. Our intention for including the NO AUDIO task was both to investigate the degree to

which participants had internalized the neural regulation skills developed during training, and to help clarify the role played by the feedback in allowing the participants to change their brain activity (DeCharms et al, 2005).

The experimental design originally called for neurotherapy participants to engage in "Pain Control Tests" at four points during the process: prior to training, at an earlier stage of the training, at a later stage of training, and after the completion of training. However, due to pain flare ups and other obstacles, the respective participants completed varying numbers of Pain Control Tests (Range: 2-4; Mean =3.25; S.D.: 0.70; Total: 26). As such, only data for each participant's pre and post training Pain Control tests was included in the planned analysis.

Training Protocols

LORETA neurotherapy group. The design called for each neurotherapy group member to receive bi-weekly, one-hour training sessions over the course of six weeks for a total of twelve sessions. However, again due to a range of obstacles including pain flare-ups, the actual number of training sessions was variable (Range: 5-10; Mean=9; S.D.: 1.69). D.O. conducted all training sessions in a quiet, dimly lit room. During training the participants were seated in a recliner and were offered head/neck support if required. Neurofeedback was conducted using 19 channel Electrocap (Electro-Cap International, Eaton, OH), Mitsar 201 amplifier (Mitsar Co., St. Petersburg, Russia), Braintuner LORETA neurofeedback software (Mitsar Co., St. Petersburg, Russia), and a Dell personal laptop computer. Conductance was measured to ensure that it remained at 5 Ohms or below during training. D.O. monitored the participants' 19 channel EEG record

during training and offered verbal prompts whenever artifact began to contaminate the record or the participant appeared to be drowsing.

A four-minute, eyes-closed baseline time period was conducted at the beginning of each training session. Four, five minute, eyes-closed training periods were then conducted (see appendix R for task instructions). Short rest breaks were taken between the training periods. The experimental goal was to teach participants how to increase levels of Theta and Alpha 1 (4.5-10Hz) power within the targeted mPFC cluster, while simultaneously maintaining or decreasing levels of Delta (1-3 Hz) and Gamma 1 (30-40 Hz) power. More specifically, the feedback was based on current density with a five voxel cluster within the mPFC: 5,50,10; 5, 50,0; 10, 55, -5; 15, 60, 5; & 10, 55, 0. The Delta inhibit was adopted as a means of controlling eye movement artifact since most eye movements effect the lower end of the Delta frequency. The Low Gamma inhibit was adopted as a means of controlling EMG artifact (Goncharova, McFarland, Vaughan, & Wolpaw, 2003) Audio feedback was offered in the form of rushing water sounds. The degree of feedback output was based on changes in the ratio between the rewarded bandwidths (4.5-10 Hz) and the inhibited bandwidths (1-3 Hz/ 30-40 Hz). As this ratio increased the audio feedback became louder and as the ratio decreased the feedback became quieter, ceasing all together if the ratio fell below threshold.

Participants were instructed to focus equally on increasing the volume and the consistency of the feedback as much as possible. During the initial training sessions the experimenter suggested the possibility that entering a state of

detached, inner calm, with lowered levels of self-talk may help to produce the feedback (Aftanas & Golocheikine, 2001). Beyond this introductory suggestion however, participants were encouraged to allow the feedback to guide them into their own unique understandings of how to achieve volitional control of the feedback.

Unique reward thresholds were set at the start of each training session. Thresholds for the first training period were set in response to the reward/inhibit ratio that occurred during the baseline period. Within sessions, D.O. dynamically adjusted this threshold from period to period on an as needed basis with the goal of challenging yet not frustrating participant's levels of volitional control. Neurotherapy frequency training protocols are typically designed in order to offer feedback to clients between 60-70% of the time (Heinrich, Gevensleben & Strehl, 2007). We elected to fall on the richer side of this reward spectrum because we wanted to facilitate a state of relaxed detachment. Therefore, during training D.O. dynamically set the thresholds in such a manner that the participant would receive at least some feedback approximately 70% of the time.

Autogenics/CBT group. The design called for each Autogenics/CBT group participant to receive weekly, one-hour training sessions over the course of six weeks, for a total of six training sessions. However, various challenges again meant that the actual number of training sessions was somewhat variable (Range 5-6; Mean = 5.3; SD: 0.53). Sessions were all conducted by D.O. and were held in the same quiet, dimly lit room that was used for the neurotherapy training sessions.

Training sessions involved two key components. The first component (initial 30 minutes of each session) was focused on teaching the participants Autogenics. Autogenics is a relaxation response technique that is akin to a form of self-hypnosis in which patients use mantra and mental imagery in order to enter a state of very deep relaxation. This self-regulation method has shown efficacy as a self-management technique for a wide range of stress related disorders, including chronic headache (Stetter & Kupper, 2002). Participants were introduced to a new set of standardized, recorded Autogenics exercises (adapted from Sadigh, 2001) at the beginning of sessions 1-4. These exercises were additive, and involved teaching the participants to self-induce: a state of muscular relaxation; a sense of imagery-based physical relaxation; a sense of relaxation and somatic heaviness; and finally, a sense of relaxation, heaviness, and warmth. Following the Autogenics recording, time was taken each session to coach the participants around any challenges they were experiencing. Participants were provided with a CD of recorded instructions for each exercise and they agreed to practice for twenty minutes, twice a week. This additional home practice was designed to help balance out the extra training time the neurotherapy participants received by attending training sessions twice a week.

During the second component of each session (latter 30 minutes), the experimenter briefly addressed a key, chronic pain related topic. Members of the autogenics group were not required to practice these supplementary psycho-educational skills between sessions, but were free to do so if they chose. The six topics covered were: the gate control of pain; effective goal setting; pacing

activities of daily living; managing dysfunctional thinking; mindfulness meditation; and sleep hygiene. Material for these CBT based topics was largely adapted from Caudill (1995; contact the first author for a full description of the relevant materials).

Interview

Audio-recorded, semi-structured interviews were conducted with members of the neurotherapy group following completion of the final pain control tests. During these interviews the first author used a series of guiding questions (see Appendix Q) in order to address three a discovery oriented, a priori research questions (see Results).

Analysis

EEG Analysis Strategy

Initial processing of EEG data. To start, the four minute portions of raw EEG data produced by each participant during each task within each pain control test were isolated and then transported into the Eureka! software (Congedo, 2005). The data were then plotted, and carefully inspected and manual artifact-rejection was performed. All episodic artifacts including eye blinks, eye movements, teeth clenching, body movements, or EKG artifact were removed from the stream of the EEG. Average cross-spectral matrices were computed for each of the frequency bands.

LORETA variables. For each individual in each time period, cross-spectral matrices were computed and averaged over 4-second epochs resulting in one cross-spectral matrix for each time period and for each of the discrete

frequencies within each band. Based on previous LORETA analyses (e.g. Sherlin et al., 2007), we used a rectangular window. Sliding overlapping windows (overlap 93.8%) allowed reliable and smooth spectral estimates. The LORETA-Key software package (Pascual-Marqui, Michel, & Lehmann, 1994) was used to compute LORETA current density in the frequency domain directly from the average cross-spectral matrix (Frei et al., 2001). This LORETA implementation incorporates a 3-shell spherical head model registered to a recognized anatomical brain atlas (Talairach & Tournoux, 1988), and makes use of EEG electrode coordinates derived from cross-registration between spherical and realistic head geometry (Towle et al., 1993). The solution space is restricted to cortical gray matter using the digitized probability atlas of the Brain Imaging Center at the Montreal Neurological Institute (Collins, Neelin, Peters, & Evans, 1994), divided in 2394 voxels measuring 7 x 7 x 7 mm.

Learned control of EEG. Investigation of changes in neurotherapy group participants' abilities to volitionally control 4.5-10 Hz, as per our first hypothesis, involved calculating the following formula for each participant during both pain control tests: (average 4.5-10 Hz amplitude within the ROI during the REGULATE block- average 4.5-10 Hz amplitude within the ROI during the OBSERVE block)/ average 4.5-10 Hz amplitude within the ROI during the OBSERVE block; DeCharms et al., 2005). During the analysis of the Time 2 test a third calculation of this kind was performed, but in this case the NO AUDIO block score was used instead of the REGULATE score. A repeated measures

ANOVA was conducted on these three sets of scores in order to look for possible changes across time.

The most recent version of the eLORETA software was used (Pascual Marqui, 2002) to make the computations for the ROI analysis. Though the neurotherapy training was hypothetically based on neural activity within a cluster of only five voxels, we based our analysis plan on the estimation that, in practice, the feedback would arise in response to the current density within a 30 mm sphere around those voxels (J. Kroptov, personal communication, June 1, 2008). Therefore, our goal in defining an ROI was to create a space that would be large enough to capture any training effects, while also being constrained enough to avoid having any training effects be obscured by background activity. To this end, we adopted an ROI that was a 21 mm sphere surrounding the coordinates of 2, 50, 8. In order to help constrain the space we also eliminated any voxels within that sphere that the eLORETA software did not label as belonging to BA 10. This generated a search space that included 94 of the 6238 total eLORETA voxels (1.5 %).

Learned Control of Phasic Pain Responses

In order to test for changes in phasic pain regulation ability, as per our second hypothesis, three percentage change scores were completed for each participant during each Pain Control test. These scores were for Pain Intensity NRS (0-10), Pain Unpleasantness NRS (0-10), and SF-MPQ score. In each case calculating these difference scores involved the following calculation:

(REGULATE block score- OBSERVE block score)/ OBSERVE block score; Farrar et al., 2001). Paired t-tests were used to test for within group differences.

Association Between Learned Control of EEG and Changes in Phasic Pain Regulation

These analyses, related to our third hypothesis, were predicated on calculation of what we will refer to as a "Theta Alpha Learning Index" (THAL LI) score for each participant. The THAL LI was designed to reflect pre to post training changes in participants' degree of volitional control over the targeted bandwidths. The THAL LI was computed using the following formula: ((4.5-10 Hz regulate time 2-4.5-10 Hz observe time 2)/ 4.5-10 Hz observe time 2))- ((4.5-10 Hz regulate time 1-4.5-10 Hz observe time 1)/ 4.5-10 Hz observe time 1)) (DeCharms et al, 2005). Non-parametric Spearman correlations (one tailed) were performed between these THAL LI scores and participants' percentage change scores on the various phasic outcome variables (e.g.., ((Pain UP NRS regulate time 2-Pain UP NRS observe time 2)/ Pain UP NRS observe time 2)) – ((Pain UP NRS regulate time 1-Pain UP NRS observe time 1)/ Pain UP NRS observe time 1)).

Correlation Between THAL LI results and Clinical Changes in the Neurotherapy Group

Two different, discovery oriented analyses were used in order to investigate these relationships.

Outcome measure related procedure. A percentage change score was calculated for each neurotherapy group member for each of the outcome

measures. In each case calculating these difference scores involved the following calculation: (Outcome measure score Time 2- Outcome measure score time 1)/ Outcome measure score Time 1) (Farrar, Young, LaMoreaux, Werth, & Poole, 2001). Spearman correlations (one tailed) were performed between these outcome change scores and participants' THAL LI results.

Interview ranking procedure. During this analysis a naïve rater analyzed the interview transcripts in order to rank the participants according to the amount of benefit they reported experiencing in relation to their pain related experience outside of the sessions. The rater ranked interview transcripts according to the following instructions:

> "According to the contents of this person's interview transcript, please rank them relative to the other participants in terms of how much benefit you believe they gained through participation in the study in regards to a lessening of pain distress, pain intensity, or pain related interference outside of the training sessions."

Spearman correlations (one tailed) were performed between these interview analysis rankings and participants' THAL LI results.

Discovery Oriented Investigation of Clinical Outcome Variable Differences

Paired and unpaired t-tests were used to look for within and between group differences on the relevant outcome measures.

Interview Data

The first author conducted the interview analysis in order to answer three a priori questions (see the results section for a listing of the questions). The

audiotapes were transcribed as a first step of this analysis. The first author then used a basic constant comparative method as described by Leech & Onwuegbuzie (2007) in order to analyze the transcripts. He began this analysis by reading each interview transcript numerous times. He then divided each transcript into meaningful chunks. These chunks were then assigned descriptive codes based on the nature of their content. Next, he compared between the codes that emerged across participants in order to identify pairs of codes that were similar enough that they could be validly merged into a single code. Analysis was considered complete when no new codes emerged from the data and when no further amalgamation between the identified codes could be validly achieved. The remaining grouping of codes were then designated as the "themes" that had emerged in response to the three relevant questions.

Results

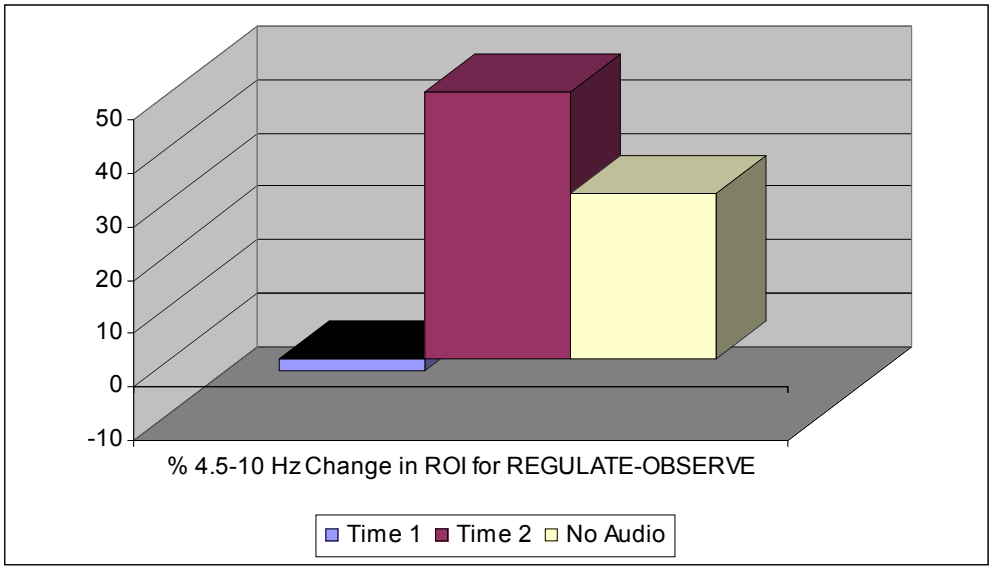
Planned Hypothesis Oriented Results

Hypothesis 1: Improved Volitional Control of 4.5-10 Hz

A repeated measures ANOVA indicated that the three sets of data showed a trend toward having a statistically significant, quadratic relationship, F (1) = 3.90, p = .089 (see fig. 3). Planned, follow up, paired t-tests found that there were no significant differences between: the Time 2 REGULATE-OBSERVE % changes and NO AUDIO-OBSERVE % changes, t (7) = .784 , p =.239, one tailed.; or between the NO AUDIO-OBSERVE % changes and the Time One REGULATE-OBSERVE % changes, t (7) = 1.27, p = .121, one tailed. However, a paired t-test found that the Time 2 REGULATE-OBSERVE % changes were

significantly larger than the Time 1 REGULATE-OBSERVE % changes, t (7) = -2.82, p =.013*, one tailed.

For completeness we also performed separate paired t-tests comparing the Time 1 and 2 results for both of the rewarded bandwidth ranges (Theta and Low Alpha) and for both of the inhibited bandwidth ranges (Delta and Low Gamma). Paired t-tests were used to compare the Time 1 REGULATE-OBSERVE % changes to the Time 2 REGULATE-OBSERVE % changes. No significant differences were found in Delta (1-3 Hz), (Time 1 X=38.62 %; SD: 83.54%), (Time 2: X=129.71; SD: 315.92%), t (7) = -.943, p = .376, two tailed; or in Low Gamma (30-40 Hz), (Time 1 X=28.2%; SD: 66.93 %), (Time 2 X=53.96 %; SD: 131.95%), t (7) = .461, p = .658, two tailed. However, a paired t-test found that the Time 2 REGULATE-OBSERVE % changes in Theta (4-8 Hz) (X=63.33 %; SD: 97.97%) were significantly larger than the Time 1 REGULATE-OBSERVE % changes (X=-6.88 %; SD: 58.93 %), t (7) = -2.65, p = .016*, one tailed. A paired t-test also found that the Time 2 REGULATE-OBSERVE % changes in Low Alpha (8-10 Hz) X=64.75 %; SD: 81.21%) were significantly larger than the Time 1 REGULATE-OBSERVE % changes (X=11.39 %; SD: 67.23), t (7) = 2.11, p = .036*, one tailed.



Time 1 Regulate- Observe % Change	Time 2 Regulate- Observe % Change	Time 2 No Audio- Observe % Change
M = -2.17% (SD = 62.37)	M = 50.1% (SD = 73.40)	M = 31.02% (SD = 35.82)

Figure 4-3: Training related 4.5-10 Hz Changes in the ROI

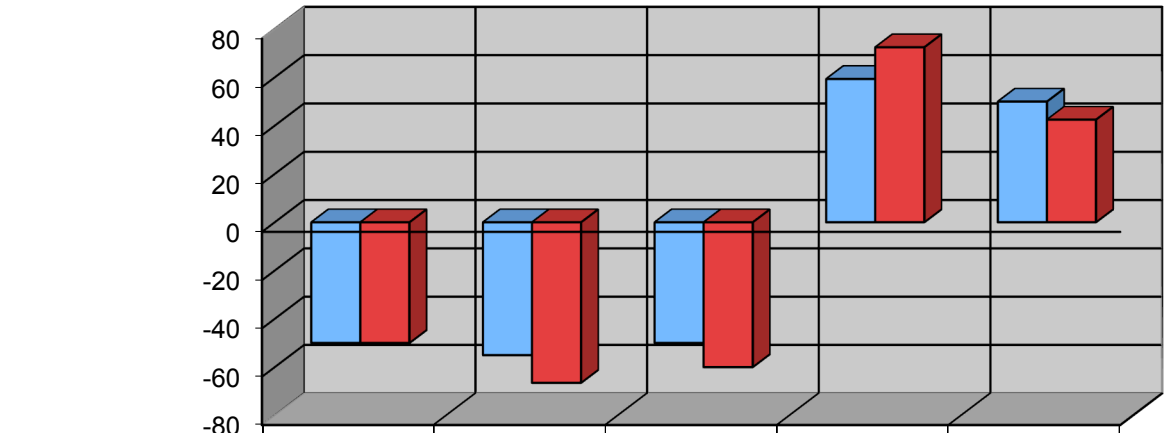
Hypothesis 2: Improved Phasic Pain Regulation

Paired t-tests were used to compare the % changes in the pain control task ratings between the REGULATE and OBSERVE conditions at Time 1 versus at Time 2 (see Figure 4). This analysis found a lack of significant differences in regards to: the NRS pain intensity ratings (Time 1: M = -46.5 %, SD = 46.99), (Time 2: M = -50.1%, SD = 22.24%), t (7) = .237, p = .409, one tailed; NRS pain unpleasantness ratings (Time 1: M = -51 %, SD = 42.19), (Time 2: M = -65.87%, SD = 31.9%), t (7) = .698, p = .254, one tailed; MPQ-SF ratings (Time 1: M =-54.12 %, SD = 37.66 %) (Time 2: M = -57.12 %, SD = 13.6 %), t (7) = .254, p = .403, one tailed; or the Self Talk ratings (Time 1: M =49.37 %, SD = 32.78), (Time 2: X= 50, SD = 25.77), t (7) = -.038, p = .485, one tailed. However, a paired t-test found that the Relaxation ratings at Time 2 (M = 72.5, SD = 12.81) showed a trend toward increased relaxation when compared to the Relaxation ratings at Time 1 (M = 59.37, SD = 24.11) t (7) = -1.43, p = .097, one tailed.

Hypothesis 3: Correlation between THAL LI Results and Changes in Pain Control Task Ratings

Spearman correlations were used to calculate the associations between the THAL LI results and changes in participant's pain control task ratings from Time 1 to Time 2. This analysis found a lack of significant correlations in regards to: the Pain Unpleasantness NRS ratings, D (6) = .395, p = .16, one tailed; the SF-MPQ ratings, D (6) = .096, p =.41, one tailed; the Relaxation ratings, D (6) of .26, p =.26, one tailed; or the Self Talk ratings, D (6) = .125, p =.38, one tailed.

However, a significant positive association was found in regards to the Phasic Pain Intensity NRS ratings, D (6) = .647, p =.04*, one tailed.



	1	2	3	4	5
Pre-Training Scores	-50	-55	-50	59.37	50
Post-Training Scores	-50	-66.5	-60	72.5	42.5

1:Median Pain intensity % drop from OBS to REG block
2: Median Pain unpleasantness % drop from OBS to REG block
3: Median MPQ-SF% drop from OBS to REG block
4: Mean Relaxation rating (Higher number = more relaxation)
5: Median Self talk rating (lower number = less self talk)

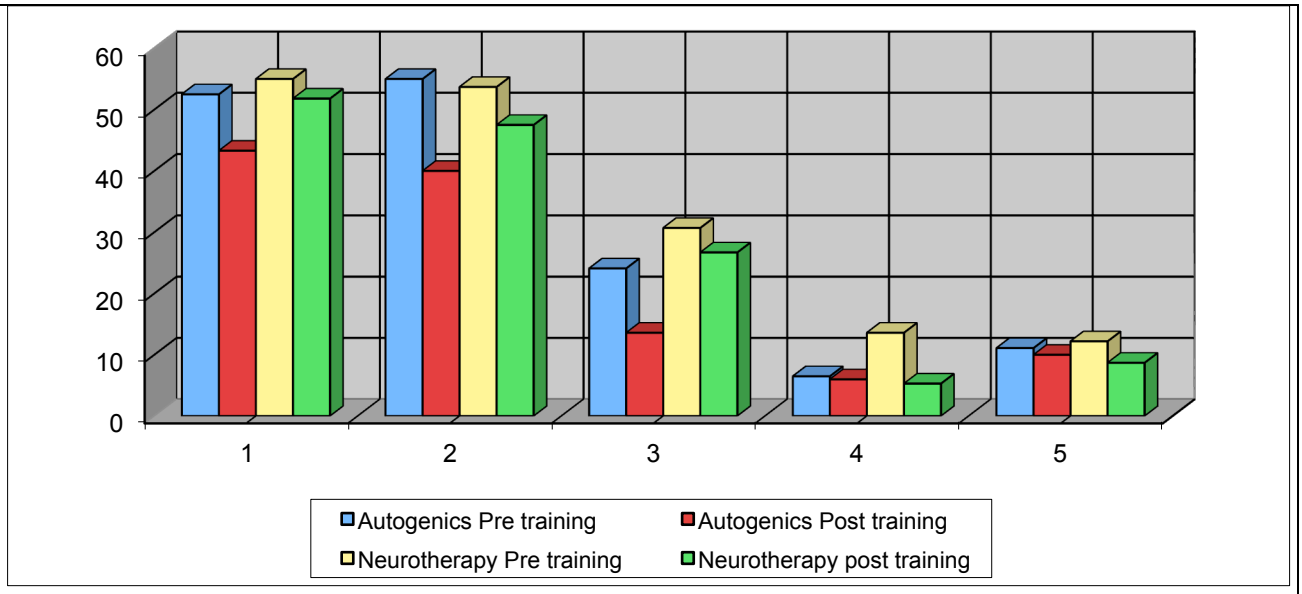
Figure 4-4: Pain Control Task Behavioural Results

Planned Discovery Oriented Analysis

Within Group Clinical Changes

Paired t-tests were conducted to calculate pre to post-training, within group clinical changes within the neurotherapy group (see Figure 5). No significant Time 1 versus Time 2 differences were found in regards to: the Pain Intensity NRS scores, t (7) = .722, p =.246, one-tailed; the Pain Unpleasantness NRS scores; t (7) = .919, p=.194; or the SF-MPQ scores, t (7) = 1.28, p = .239, one-tailed. However, a paired test found that the Time 2 PDI scores were significantly lower than the time 1 PDI scores, t (7) = -2.01, p = .041*. A paired test also found that the time 2 CED-S scores were significantly lower than the time 1 CED-S scores, t (7) = 3.17, p = .008*, one-tailed.

Paired t-tests were conducted to calculate pre to post-training, within group changes clinical changes within the Autogenics/CBT group (see Figure 5). No significant Time 1 versus Time 2 differences were found in regards to: the CED-S scores, t (5) = .257, p = .403, one-tailed; or the SF-MPQ scores, t (5) = .397, p = .39. However, a paired t-test found that the time 2 Pain Intensity NRS scores showed a trend toward being lower than the time 1 scores, t (5) = 1.65, p =.079, one tailed. A paired t-test also found that the time 2 Pain Unpleasantness NRS scores were significantly lower than the time 1 Unpleasantness NRS scores t (5) = 2.66, p = .022*, one tailed. Finally, a paired t-test found that the time 2 PDI scores were significantly lower than the time 1 PDI scores, t (5) = 7.21, p < .001*, one tailed.



	Column 1: Mean Intensity NRS over the last week	Column 2: Mean Unpleasantness NRS over the last week	Column 3: Mean PDI over the last week	Column 4: Mean CED-S over the last week	Column 5: Mean SF-MPQ over the last week
Autogenics Pre	52.5 (25.4)	55 (22.5)	24.1 (10.2)	6.5 (5.3)	11.1 (7.7)
Autogenics Post	43.3 (25.8)	40 (29.6)	13.6 (10.3)	6 (4.2)	10 (8.4)
Neurotherapy Pre	55 (16)	53.7 (20.6)	30.7 (16.4)	13.6 (8.6)	12.2 (8.4)
Neurotherapy Post	51.8 (13.6)	47.5 (15.8)	26.7 (15.9)	5.3 (3.3)	8.7 (4.6)

Figure 4-5: Outcome Measure Data

Between Group Clinical Changes

At Time point 1, permutation t-tests (10,000 iterations) were used to look for between group differences on any of the five outcome measures (see tables A3 and A4 and Figure 5). This analysis showed that there were no significant differences between the two groups at Time 1 in regards to: the Pain Intensity NRS scores t (12) = .227, p = .883, two-tailed; the Pain Unpleasantness NRS scores, t (12) = .10, p = .1, two-tailed; the PDI scores, t (12) = .857, p = .407, two-tailed; or the SF-MPQ scores, t (12) = .245, p = .805, two-tailed. However, a permutation t-test on the CED-S scores showed a trend toward the neurotherapy group having higher depression scores t (12) = 1.76, p = .112, two-tailed.

At Time point 2, permutation t tests were again used to look for between group differences on any of the five outcome measures (see Figure 5). No significant between group differences were found at Time 2 in regards to: the Pain Intensity NRS scores, t (12) = .805, p = .455, two-tailed; the Pain Unpleasantness NRS scores, t (12) = .613, p = .551, two-tailed; the CED-S scores, t (12) = 307, p=.763, two-tailed; or the SF-MPQ scores, t (12) = .318 p = .770, two-tailed. However, a t-test revealed that there was now a trend toward the Autogenics groups' PDI scores being lower, t (12) = 1.74 p = .106, two-tailed.

Finally, in order to control for the possible effects of differing levels of therapeutic alliance the WAI-SF ratings were compared between groups. The WAI-SF rating for one member of the Autogenics group was lost prior to analysis. A permutation t-test showed that the WAI-SF ratings scores in the two groups (neurotherapy group: M = 39.62, SD = 2.06; Autogenics group: M = 39.75,

SD = 1.89) were not significantly different from each other, t (11) = .199, p = .88, two-tailed.

Correlation between THAL LI Results and Clinical Improvement in the Neurotherapy Group

As outlined in the Methods section above, we used two separate, planned, discovery oriented analyses in order to investigate the relationship between degree of learned control of 4.5-10 Hz and degree of clinical improvement in the neurotherapy group.

Correlation with outcome measures procedure. Spearman correlations were used to investigate the relationship between the THAL LI results and changes in the outcome measure scores. This analysis found a lack of significant correlations in regards to all relevant measures, including; the Outcome Pain Intensity NRS ratings with D (6) = .193, p =.32, one tailed; the Outcome Pain Unpleasantness NRS ratings with D (6) = .217, p =.324, one tailed; the Outcome PDI with D (6) = .228, p =.29, one tailed; the Outcome CED-S ratings with D (6) = .048, p=.45, one tailed; or the Outcome SF-MPQ ratings with D (6) = .217, p =.30, one tailed.

Interview ranking procedure. Second, we correlated participants' THAL LI results with their results on the interview ranking procedure. Only seven participants were included in this analysis because participant C's interview recording was indecipherable. A Spearman correlation between THAL LI results and the participants' interview rankings was not significant, D (5) = -.036, p =. 47, one tailed.

Post hoc Analysis

In addition to the planned comparisons described above, we also performed two sets of post hoc analyses.

Correlations between Percentage Change in 4.5-10 Hz and Percentage Change in Phasic Ratings

These analyses were designed to investigate the correlation between percentage changes in the 4.5-10 Hz range and percentage changes in the phasic, pain control test ratings on a trial by trail basis, across participants. The discussion section provides a rationale for the performance of this analysis.

First, we performed this analysis while collapsing across Times 1 and 2 (16 iterations total). Across participants, Spearman's correlation found a lack of significant associations between percentage changes in 4.5-10 Hz and percent changes in any of the relevant variables including: the phasic Pain Intensity NRS ratings, D (14)= .09, p = .71, two tailed; the phasic Pain Unpleasantness NRS ratings, D (14) = .035, p =. 89, two tailed; the phasic SF-MPQ ratings, D (14) = .07, p = .78, two tailed (see Figure 7B); the Relaxation scores, D (14) = -.11, p = .66, two tailed; or the Self Talk ratings, D (14) = -.04, p = .86, two tailed (see Figure 7A).

We then repeated this same analysis but while only considering the Time 1 data. In this case, Spearman's correlation found a lack of significant associations between percentage changes in 4.5-10 Hz and percent changes in the following variables: the phasic Pain Intensity NRS ratings, D (6) = .335, p = .40, two tailed; the phasic Pain Unpleasantness NRS ratings, D (6) = .357, p = .38, two tailed;

the Relaxation ratings, D (14) = -.446, p = .60, two tailed; or the Self Talk ratings, D (6) = .479, p = .23, two tailed (see fig. 8 A). However, a Spearman's correlation between percentage changes in 4.5-10 Hz and percent changes in the phasic SF-MPQ ratings showed a trend being positively correlated, D (6) = .651, p = .08; two tailed (see Figure 8C).

Finally, we repeated the same analysis again but now only considering the Time 2 data. In this case, a Spearman's correlation found a lack of significant associations between percentage changes in 4.5-10 Hz and percent changes in the following variables: the phasic Pain Intensity NRS ratings, D (6) = -.419, p = .30, two tailed; the phasic Pain Unpleasantness NRS ratings, D (6) = .048, p = .91, two tailed; or the Relaxation ratings, D (6) = .184, p = .66, two tailed. However, a Spearman's correlation between percentage changes in 4.5-10 Hz and percent changes in phasic SF-MPQ ratings showed these variables to have a statically significant, negatively correlated relationship with D (6) = -.743, p= .03*, two tailed (see Figure 8D). A Spearman's correlation between percentage changes in 4.5-10 Hz and the Self Talk ratings also showed these variables to have a statically significant, negatively correlated relationship, D (6) = -.735, p = .03* (see Figure 8B).

THALGAM LI Analysis

The second set of post-hoc analysis that we performed involved the use of an alternate, exploratory Learning Index that we constructed in a post hoc fashion (see Discussion section). This new Learning Index, which we will refer to as the "THALGAM LI", was designed to equally reflect changes in 4.5-10 Hz and those

in 51-70 Hz. The following formula was used: ((4.5-10 Hz regulate time 2-4.5-10 Hz observe time 2)/ 4.5-10 Hz observe time 2)- ((4.5-10 Hz regulate time 1-4.5-10 Hz observe time 1)/ 4.5-10 Hz observe time 1)) + ((51-70 Hz regulate time 2-51-70 Hz observe time 2)/ 51-70 Hz observe time 2)- ((51-70 Hz regulate time 1-51-70 Hz observe time 1)/ 51-70 Hz observe time 1)). During post-hoc analysis we reran all of the relevant, planned Learning Index analyses again, but this time while using the THALGAM LI instead of the THAL LI results.

THALGAM LI and phasic pain control improvement. Spearman's correlations failed to find significant associations between the THALGAM LI rankings and pre to post training changes in any of the phasic, pain control task variables, including: the phasic Pain Intensity NRS ratings, D (6) = .33, p = .20, one tailed; the phasic Pain Unpleasantness NRS ratings , D (6) = -.31, p = .22, one tailed; the phasic SF-MPQ ratings, D (6) = -.29, p=.23, one tailed; the Relaxation ratings, D (6) = -.143, p = .36, one tailed; or the Self talk ratings, D (6) = -.238, p = .28, one tailed.

THALGAM LI and clinical improvement. We investigated the relationship between the THALGAM LI results and clinical improvement in two ways.

First, we investigated the relationship between the THALGAM LI results and the outcome measure change scores. Spearman correlations failed to find significant associations between the THALGAM LI results and pre to post-training changes in regards to any of the relevant measures, including: the outcome Pain Intensity NRS results, D (6) = -.08, p = .42, one tailed; the

Outcome Pain Unpleasantness NRS results, D (6) = .18, p = .33, one tailed; the Outcome SF-MPQ results, D (6) = -.37, p =.18, one tailed; the Outcome PDI results, D (6) = -.38, p = .17, one tailed; or the Outcome CED-S results, D (6) = .35, p = .18, one tailed.

Second, the transcript rating ranking procedure was again used, but this time with the THALGAM LI results. A Spearman's correlation found a significant correlation between these variables, D (5) = .821, p = .01***,** one tailed (see Figure 10).

Planned Interview Data Analysis

The interview analysis was designed to answer three a priori research questions. Each of these questions is listed below, followed by the relevant classes of answer that emerged, and also by the number of participants who mentioned each class of answer. Example quotes have been provided in order to help illustrate the relevant themes.

Participant C's entire interview recording was indecipherable. Portions of participant H's audio recording were also indecipherable (the portions related to questions 2 and 3). Therefore, question number one involved an n of 7 and questions 2 & 3 involved an n of 6. Only themes identified by a minimum of at least two participants are listed below.

1) <u>What benefits did participants attribute to their participation?</u>

    - **Improved knowledge of chronic pain, chronic pain management, chronic pain research and/or encouraged to learn more about these topics (7/7 participants reported).**

Participant H said, “I just think it was extremely beneficial, rewarding, because it gives me more knowledge.”

- **Lessening of pain during sessions (6/7).** In describing her experience during particularly effective training sessions participant G said, “I felt like that I had absolutely no pain…which was really bizarre.”
- **Lessening of pain distress, pain intensity, or pain related interference outside of training sessions (ranging from the 1-2 hour period immediately after sessions to extensive periods of time between sessions) (6/7).** In describing her experience in the hours immediately after training sessions, participant H said, “when I left here I was, for all intents and purposes, pain free”. Alternately, in describing her experience between sessions, participant F said, “I did notice a change for sure. I wasn’t having as much pain, and if I was I could recover from it faster…”.
- **Enjoyed having time with the experimenter (3/7).** Participant B said that he, “ really enjoyed working with” the experimenter.
- **Increased sense of mindful awareness in a non-pain related contexts (2/7).** Participant A said, “I think for a lot people, and me included, there is a lot in my life I just do. Every day I get up. Every day I do these things and I don’t think about them and I don’t actually experience them. And what I’m noticing is that

whether it's something that I am doing that I'm enjoying, something that I am doing that am really not enjoying, I am… I am more there. More focused."

- **Increased self-awareness in a non-pain related context, such as increased senses of intuition or insight (2/7).** Participant A, who is a nurse, said, "It's hard to explain but … I'm more aware of me and how I'm feeling. Like I'll be standing near a patient and I will suddenly notice that I am very tense. And I know that it's not me that's very tense, it's actually the patient I'm responding to …I sit near a patient and just kind of quietly monitor how that person is doing by how I'm feeling."
- **Improved sleep (2/7).** Participant A said, "I have always been a light sleeper. And for many years, you know, I would wake up many times during the night. So what I'm finding is that over the course of doing this I'm sleeping longer periods during the night. And I actually sleep, not just drifting in circles."

2) <u>What side effects did participants attribute to participation?</u>

- **Transient headache, usually lasting no more than an hour after training (4/6).** In describing her occasional headaches, participant G said, "It's dull. Not intense at all. You know, I would rate it as maybe a 3 you know it's there, maybe a 4 on a bad day. It goes away on its own. By the time I drive home it's usually gone."

- **Transient dizziness during training (2/6).** In describing a brief episode of dizziness that occurred on one session, participant D said, "at the 7-minute point I kind of had that one freak-out...that was unpleasant. I got really hot and became dizzy..."

3) What strategies did the participants use in order to increase the neurofeedback?

- **Altering of the breath by making it slower, more shallow, suspending it, and/or extending the exhale (4/6)**. Participant E explained that, "there are times when I was breathing deeply and I find that I feel… like, really relaxed and breathing like really shallow and really slow".
- **Focusing and refocusing attention on the breath, the audio feedback, or some other object of awareness (4/6).** Participant said, **"**Usually I concentrate on my breathing…When my mind starts getting busy… 'oh – no, start breathing again' and sort of get those thoughts out of my mind."
- **Use of mantra (2/6)**. Participant D said that he would sometimes repeat, "…words in a mantra style…like 'continuous'…because I wanted the feedback to be continuous."

Discussion

We will begin the discussion by briefly addressing each of our hypotheses. We will then consider several pertinent discovery oriented results. Finally, we will offer an integrative interpretation of our overall results.

Hypothesis 1: Volitional Control of 4.5-10 Hz

It appears that our LORETA neurotherapy protocol achieved successful training effects, thereby supporting for our first hypothesis. Two sources of evidence support this conclusion. The first, and more important, of these sources is the significant difference (p= .013) between the percentage changes in the targeted bandwidths when comparing the time one and time two results (see Columns 1 and 2 in Figure 3). The second source of evidence of successful training effects is offered by the NO AUDIO task results (see column three in Figure 3). The fact that the NO AUDIO results were well over the Time 1 results suggests that by the end of training the participants had successfully internalized a degree of volitional control over their EEG responses. However, the fact that the NO AUDIO results also remained *below* the Time 2 results (which were recorded during the same session) suggests that the neurofeedback played a key role in the observed results, and that the observed 4.5-10 Hz changes were not simply the result of a generic process such as increased relaxation.

Hypothesis 2: Improved Control of phasic pain

As expected, the neurotherapy participants showed improved abilities to regulate their phasic pain responses (see Figure 4). However, these changes did not achieve statistical significance. This lack of statistical significance indicates that we cannot rule out the possibility these improvements were a random event and our results therefore fail to support our second hypothesis. However, it is notable that all three measures of phasic pain regulation ability showed evidence of moving in the same, hypothesized direction. This pattern of results, in

combination with our very small sample size, leads to the strong possibility that a lack of power, rather than a lack of clinical efficacy, led to the lack of statistical significance in this regard. Investigation of the validity of this conclusion will clearly require replication with a larger *n*.

Hypothesis 3: Theta Alpha Learning Index (THAL LI) Results

Our third hypothesis was that there would be a significant, positive correlation between participants' degree of pre-post training improvement in volitionally controlling 4.5-10 Hz (as reflected in their THAL LI results) and their degree of improvement in regulating their phasic pain responses during the pain control task. We had expected this result to constitute a direct analogue of DeCharms et al.s' (2005) finding that the more their participants became able to volitionally down regulate the dACC the more improvement in phasic pain regulation they showed.

This final hypothesis was entirely unsupported. Reference to the relevant Results section indicates that, over all, participants' THAL LI rankings and their phasic pain regulation change scores were very weakly correlated. Of the five variables in question, only the NRS intensity change scores showed a significant association with the THAL LI rankings, and this correlation was in the opposite to expected direction. This unexpected pattern of results was consistent with our discovery oriented, outcome measure results. Namely, according to two separate forms of analysis, the THAL LI rankings were almost completely uncorrelated with participants' degrees of clinical improvement from pre- to post training.

We began our efforts to make sense of these unexpected findings by questioning the validity of the central assumption upon which our design was based. Namely, that up training 4.5-10 Hz in our ROI would be clinically useful because this activity would be associated with reductions in chronic pain related rumination/suffering. We tested this assumption by looking at the correlations that emerged between percentage changes in 4.5-10 Hz (REG-OBS conditions) and the percentage changes in the phasic ratings that emerged across both the pre and post training pain control tasks. DeCharms et al. (2005) conducted an equivalent analysis and found a highly significant relationship between percentage changes in the dACC BOLD and percentage changes in their participants' phasic pain scores. Reference to Figures 6A and 6B illustrates that, in sharp contrast to DeCharms et al. (2005), in the current experiment these two forms of percentage change appear to have been essentially *un*correlated.

In other words; if, against our expectations, there truly is no meaningful relationship between the neural variable we trained and the phenomenological variables we were attempting to influence, this would explain why participants' degrees of success in learning to control that neural variable were not associated with their degrees of improvement in controlling the relevant phenomenological variables.

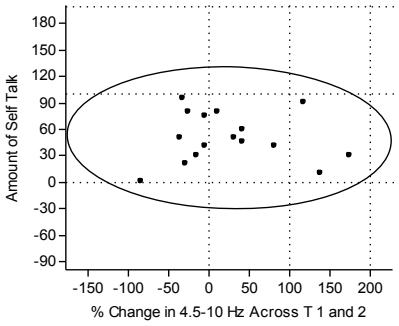
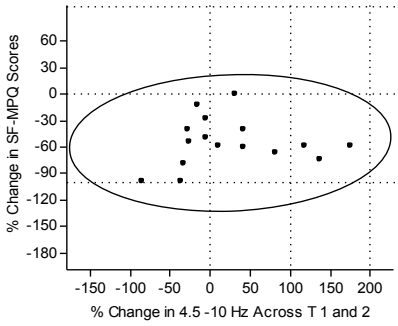
6 A: percentage Change in 4.5 Hz to 10 Hz Correlated with Self Talk ratings ***D* (14) = -.04, *p* = .86 (two tailed)**	**6 B: percentage Change in 4.5 Hz to 10 Hz Correlated with % Change in Phasic SF-MPQ-Scores** ***D* (14) =.07; *p* =.78 (two tailed)**
	

Figure 4-6: Correlates of percentage Change in 4.5 Hz Across Pain Control Tasks 1 and 2

However, we suggest that our results also support an alternate explanation of these findings. We will devote a substantial portion of the remaining discussion to presenting and supporting our alternative explanation for these key, unexpected results.

Detailed Consideration of the Hypothesis 3 Results

Our proposed explanation emerges in large part from post-hoc analysis of the relevant brain and behaviour associations at Time 1 *as compared* to Time 2. Reference to the Results section illustrates that these correlations shifted from an unexpected direction at Time 1 to the expected direction at Time 2. In the case of the SF-MPQ (p = .009) and the Self Talk ratings (p =. 02) the differences between these two sets of correlations were extreme enough to be statistically significantly different (see Figure 7 A-D). This strongly symmetrical pattern of results means that when the relevant associations are collapsed across Times 1 and 2 these opposing patterns cancel each other out, creating the impression that percentage change in 4.5-10 Hz had no meaningful relationships with the phenomenological variables in question. In other words, our results suggest that not only did the amount of 4.5-10 Hz change from Time 1 to Time 2 (see Figure 7), but that that its *meaning* changed as well.

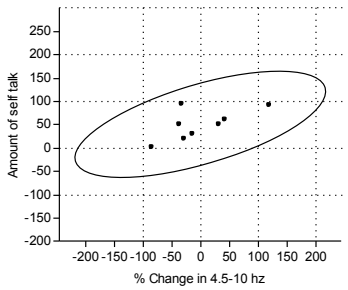
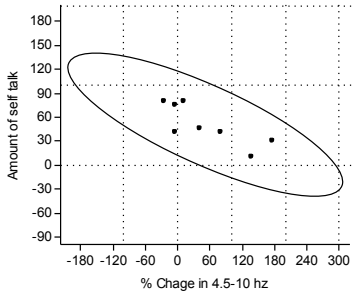
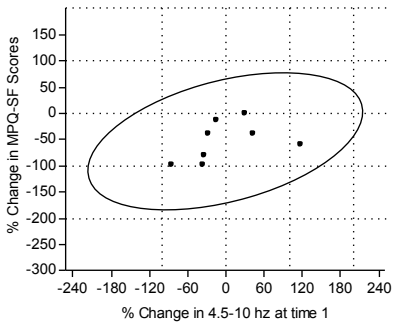
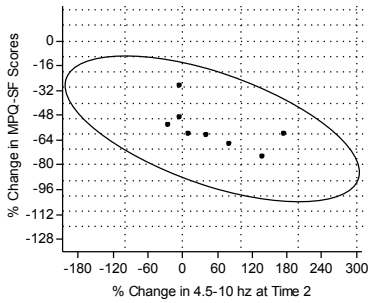
7A: percentage Change in 4.5 Hz to 10 Hz Correlated with Self Talk at Time 1 ***D* (6)= .479; *p* =.23 (two tailed)**	**7 B: percentage Change in 4.5 Hz to 10 Hz Correlated with Self Talk at Time 2** ***D* (6) = - . 735, *p* = .03*** (two tailed)
	
7 C: percentage Change in 4.5 Hz to 10 Hz Correlated with percentage Change in Phasic SF-MPQ-Scores at Time 1 ***D* (6) = .651, *p* = .08 (two tailed)**	**7 D: percentage Change in 4.5 Hz to 10 Hz Correlated with percentage Change in Phasic SF-MPQ-Scores at Time 2** ***D* (6)= -. 743, *p*=.03* (two tailed)**
	

Figure 4-7: Correlates of 4.5-10 Hz % Change at T1 vs. T2

Our interpretation of this seemingly paradoxical finding rests on the fact that there are commonly held to be two different *varieties of* Theta (Mitchell, McNaughton, Flanagan, & Kirk, 2008). The first is putatively generated in the Hippocampus and is therefore typically referred to as "Hippocampal Theta". Currently, the most influential perspective maintains that Hippocampal theta is fundamentally involved with processes related to learning and memory (Kahana, Seelig, & Madsen, 2001). The second form of Theta, "frontal midline Theta" (fm Theta), is putatively generated by the mPFC/rostral ACC (Tsujimoto, Shimazu, & Isomura., 2006), close to the location of our neurotherapy training site. Fm Theta is most commonly associated with the processes of working memory and focused attention (Mitchell et al., 2008). As such, fm Theta has commonly been found to increase with cognitive load during mental tasks and also to increase during meditation (Mitchell et al., 2008).

Most saliently, from our perspective, Hippocampal Theta and fm Theta appear to have opposing associations with anxiety/anxious rumination. We will briefly address the relationship between Hippocampal Theta and anxiety and then the relationship between fm Theta and anxiety.

Reinforcement sensitivity theory (Gray & McNaughton, 2000) is an influential theory of emotion, motivation, and personality. It postulates that the septo-hippocampal system is *the* key structure within the brain for resolving between-goal conflict, and that in human beings this process "is experienced as anxious rumination" (Andersen, Moore, Venables, & Corr., 2009, p. 157). According to reinforcement sensitivity theory, when a between-goal conflict

arises the septo-hippocampal system uses the Theta rhythm to set up recursive loops between itself and the brain regions that are representing the goals that are in conflict. This process allows the "least negative" goal to eventually "win", thereby resolving the conflict. Support has been garnered for reinforcement sensitivity theory and for the links that it proposes between hippocampal activation, hippocampal theta, and anxiety (McNaughton, 1997).

The most salient piece of this support, in regards to the current discussion, comes from a recent study of the electrophysiological correlates of anxious rumination (Andersen et al., 2009). These authors recorded full scalp EEG while a group of participants were instructed to ruminate on a matter of personal significance. Results showed that rumination was associated with diffuse Theta increases across the scalp. Direct measurement of the electrophysiological activity of the Hippocampus is not possible using scalp based EEG. However, region-by-region analysis revealed that the parieto-occipital was the only region of the scalp to demonstrate even stronger 4-8 Hz increases than the other regions. This region of the scalp is consistent with the location of the Posterior Cingulate Cortex (PCC), which Andersen et al. (2009) point out is a "major target of Hippocampal efferents" (p. 167). Andersen et al. (2009) therefore conclude that anxious rumination involves: increases in Hippocampal Theta; which differentially activates the PCC; which in turn sets up diverse, recursive loops within the cortex; which ultimately leads to the diffuse Theta increases that can be measured across the scalp. In other words that, consistent with reinforcement sensitivity theory

(Gray & McNaughton, 2000), anxious rumination is fundamentally driven by increases in Hippocampal Theta.

In contrast, fm Theta has been associated with various factors that are anti-correlated with anxiety and/or anxious rumination. These include improved cognitive performance, lessening of state anxiety, lower levels of Neuroticism (Mitchell et al., 2008), phasic reductions in mental self talk (Aftanas & Golocheikine, 2001), and easier recovery from depression (Pizzagalli, 2010).

The differing relationships between anxiety and the two forms of Theta are most compellingly illustrated by relevant drug research. This research shows that while anxiolytics tend to *de*crease Hippocampal Theta they tend to simultaneously *in*crease fm Theta (Mitchell et al. 2008). In sum, Hippocampal Theta seems to be positively associated with anxiety/rumination while fm Theta seems to be negatively associated with anxiety/rumination.

Before we continue outlining our explanation of the null THAL LI results, we will briefly highlight a strongly relevant methodological aspect of the Andersen et al. (2009) study. These authors had originally hypothesized that personally salient, anxious rumination would be associated with increased activation of the ACC, and would therefore be associated with increased levels of *fm Theta* (as opposed to Hippocampal Theta). In fact, they did find 4-8 Hz power increases at electrode Fz during anxious rumination as predicted. However, analysis revealed that these 4-8 Hz increases were not specific to the mPFC in any way, but were instead associated with increases in diffuse, scalp wide (putatively Hippocampal) Theta. This episode clearly speaks to the methodological

challenges of separating out the influences of Hippocampal Theta from those of fm Theta.

Based on the foregoing ideas, we can now move toward presenting our tentative explanation for the null THAL LI results.

It seems likely that at Time one at least some of our participants found completion of the REGULATE condition to be frustrating and anxiety provoking, given that they were instructed to increase the feedback while presumably having very little idea of how to do so. It also seems likely that, after multiple training sessions, any participants who responded in this way initially would have felt less anxious while completing the REGULATE condition at Time two. Evidence that this kind of shift in background emotional tone occurred is provided by the Relaxation ratings, which showed a strong pre-to post training trend toward increased and more consistent levels of relaxation (see Figure 4). In light of the phenomenological correlates of Hippocampal Theta that were outlined earlier, such a lessening of anxiety should have led our participants to generate relatively less Hippocampal Theta at Time two.

Alternately, it seems likely that, never having practiced the task before, our participants would have been relatively *un*able to volitionally produce fm Theta at Time One. Following training, we contend that at least some participants became better able to do so. This contention is consistent with our training results in Low Alpha. Unlike fm Theta, Low Alpha was not contaminated by a problematic confound. At Time one the participants were relatively unable to volitionally increase their levels of absolute power in the Low Alpha range.

However, following training they demonstrated a statistically significant improvement in their ability to do so (p=.036). This finding supports the credibility of our contention that, through the provided training, our participants should also have been able to learn how to volitionally increase levels of fm Theta.

We therefore propose that, at the group level, levels of Hippocampal Theta levels went down from Time 1 to Time 2 while levels of fm Theta levels went up. This interpretation would account for the fact that at Time one percentage changes in 4.5-10 Hz (putatively being driven by Hippocampal Theta) were associated with hindering phenomenological changes, while at Time 2 percentage changes in 4.5-10 Hz (putatively being driven by fm Theta) were associated with helpful phenomenological changes.

According to our interpretation, percentage changes in 4.5-10 Hz *were* meaningfully associated with percentage changes in the relevant phenomenological variables, but in two overlapping and opposing ways. However, even if our interpretation in this regard is correct, our methodology prevents us from knowing, at the *individual* level, which form of Theta drove each individual participant's THAL LI results. In other words, a participant who inadvertently learned to produce more Hippocampal Theta from Time 1 to Time 2 could have achieved a higher THAL LI ranking than a participant who, as we had implicitly intended, learned to produce more fm Theta. Without the ability to make these distinctions, we contend that the THAL LI became incapable of

validly serving its intended function. We will return to this methodological limitation in the final section of the article.

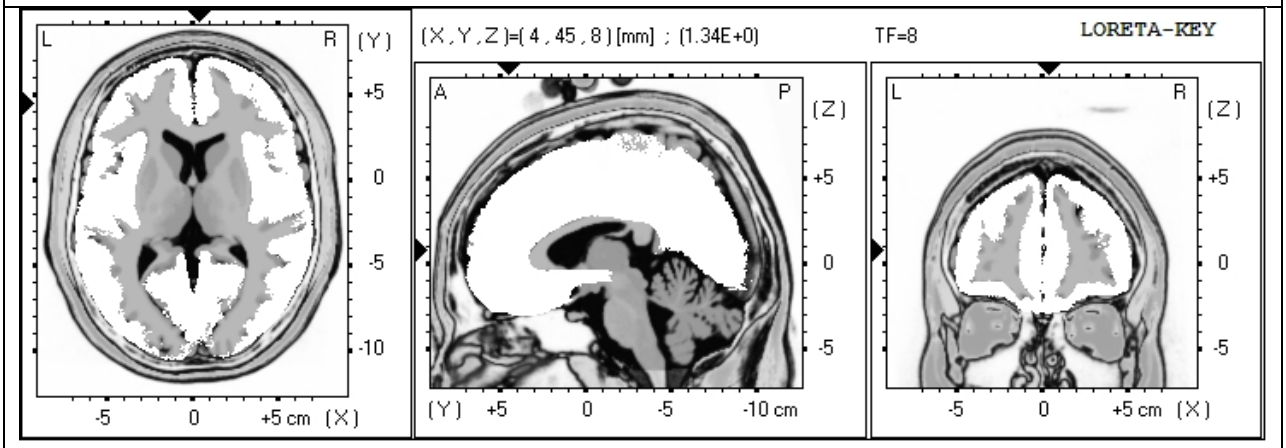
Discovery Oriented Findings around High Gamma (51-70 Hz)

We made several discovery-oriented findings around High Gamma activity (51-70 Hz) that we believe to have important implications for the methodological challenges described above. However, we also believe that these High Gamma related findings may have relevance to the issue of chronic pain related suffering in their own right. Therefore, we will first briefly address these results on their own terms before relating them back to our previous discussion.

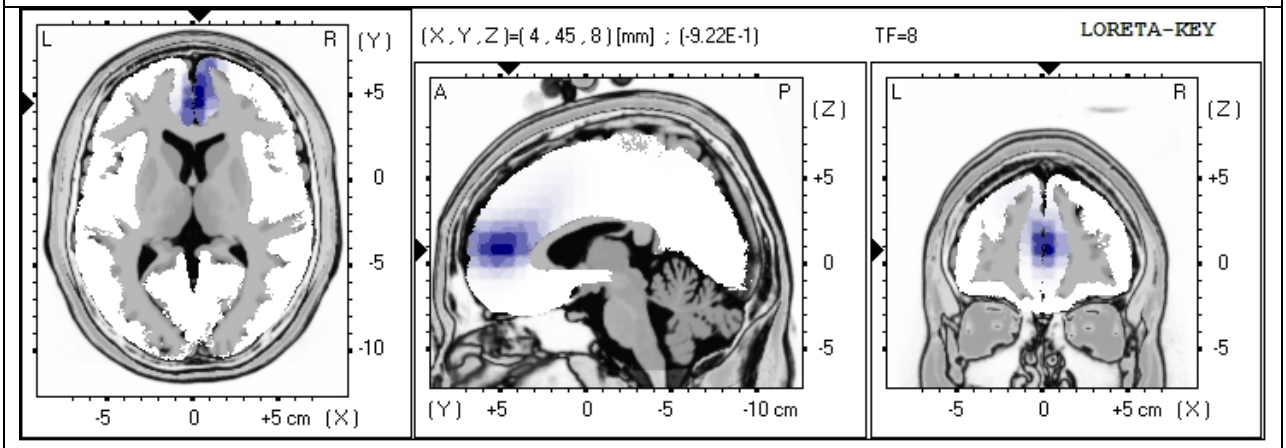
Figure 8 illustrates that, at Time one, no region of contrast was intense enough to be visually evident within the High Gamma range (51-70 Hz). Alternately, at Time two, the REGULATE task was associated with an area of focused High Gamma decrease in the mPFC. This focused cluster of High Gamma band decrease (maxima at 4, 55, 7) is noteworthy for several reasons. First, it fell directly within the region that we trained (centered at 9, 54, 2) (see Figure 9B). Second, it also fell directly within the region of BA 10 that, as discussed at the outset, shows "remarkably consistent activation" (Lieberman, 2007, p. 267) during self-referential processing (see Box 3 in Figure 9C). Finally, it fell very close to the relevant maxima reported in the two identified MRI studies of chronic pain related suffering (Baliki et al. ,2006; Schweinhardt et. al., 2008). In fact, our Gamma decrease maximum fell only several millimeters from the maxima of –4, 66, 8 reported by Schweinhardt et. al. (2008; see darkest region in Figure 9 C).

The potential significance of these finding becomes clearer in light of evidence that neural activation of the mPFC appears to be positively correlated with Gamma activity. Mantini, Perrucci, Del Gratta, Romani, & Corbetta (2007) conducted an experiment using a combined fMRI-LORETA methodology. They found that, in the resting state, MRI BOLD activity within the mPFC was most strongly associated Gamma band activity. Further, Jerbi et al. (2009) recently used intracranial recording to show that an externally oriented cognitive task of the kind that invariably causes mPFC deactivation was strongly associated with High Gamma decreases in this brain region. In this light, the cluster of High Gamma deactivation we identified suggests that, at the group level, our training protocol successfully achieved the intended neural deactivation within our training ROI.

8 A: Time 1



8 B: Time 2



Note: These group level LORETA images did not reach statistical significance, potentially do to the small n (8). These images are therefore included here for qualitative purposes and should be viewed with caution. However, the visual linearity on these images was set at the most stringent setting available in order to highlight those areas of contrast that showed the strongest trends toward significance.

Figure 4-8: High Gamma changes in REGULATE-OBSERVE contrast

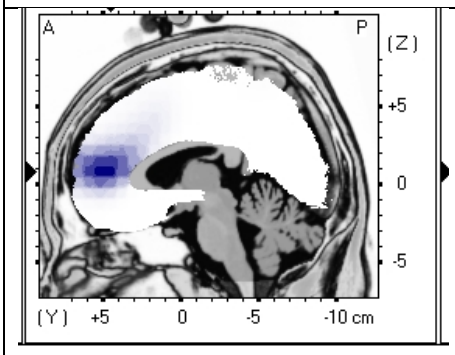
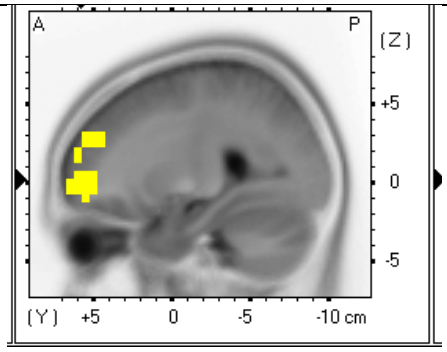
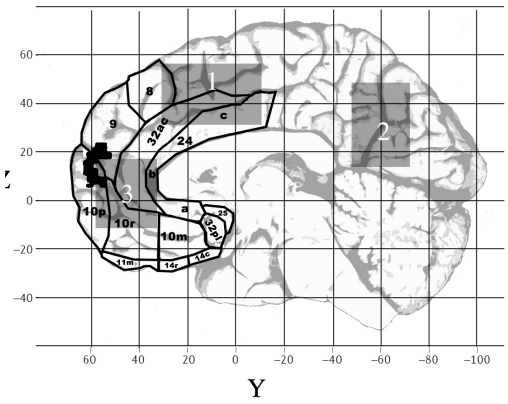
9 A: Focus of the High Gamma Decrease found at Time 2 in the current study	**9 B:** Region around the vowels that were targeted for Training in the current study	**9 C**: Region that Schweinhardt et. al. (2008) found to be specifically associated with the suffering aspect of arthritic pain (see blackened region-background image adapted from Öngür, Ferry, & Price, 2003, p. 430).
Maxima at 4,55,7	**ROI Centered at 9,54,2**	**Maxima of –4, 66, 8**
		

Figure 4-9: Training related Changes in High Gamma

Integrative Interpretation of Results

We will now attempt to integrate our High Gamma related findings back to our 4.5-10 Hz oriented results and, in particular, to consideration of our third hypothesis. The recent findings of Meltzer, Fonzo, & Constable (2009) offer a crucial foundation for the integrative interpretation we will propose below. Using a LORETA-MRI design, these authors engaged a sample of participants in an externally oriented, cognitive task. Meltzer et al. (2009) found that the inevitable region of mPFC BOLD deactivation was found to clearly overlapped with a region of 4-8 Hz *in*crease, as observed with LORETA. Crucially, these frontal theta increases were also accompanied by Hippocampal *de*activation, as measured by fMRI. In other words, by using MRI to rule out the potential confounding influence of Hippocampal Theta, Meltzer et al. (2009) produced direct evidence that *fm* Theta increases, and therefore putatively Gamma Band decreases (Jerbi et al., 2009), are associated with neural deactivation of the mPFC.

We are now in a position to offer an integrative interpretation of our overall results. This interpretation rests on the following, clearly speculative, conceptualization of chronic pain related suffering. Namely, that chronic pain related suffering is a form of maladaptive, self-referential processing (Price, 2002). That at a neural level this suffering correlates with mPFC activation (Lieberman, 2007). That this activation manifests electrophysiologically, most notably, as increases in the Gamma band (Jerbi et al., 2009; Seigle, Condray, Thase, Keshavan, & Steinhauer, 2010). That Hippocampal Theta is *positively* correlated with anxious rumination (Andersen et al., 2009; Gray & McNaughton,

2000) and therefore is also *positively* correlated with anxiety related, mPFC centered, Gamma band activation (Adhikari, Topiwala, & Gordon, 2010). Conversely, that fm Theta is *negatively* correlated with self focused rumination (Aftanas & Golocheikine, 2001) and therefore is also *negatively* correlated with mPFC Gamma activity (Canolty et al., 2006; Meltzer et al., 2009). And ultimately, that this latter pair of negative correlations provides a mechanism through which increases in fm Theta can help to ameliorate chronic pain related suffering.

Adopting this conceptualization of chronic pain related suffering suggests that our neurotherapy participants should have shown improvement in their pain regulation abilities to the extent that they learned how to *de*crease mPFC Gamma, putatively by learning how to *in*crease fm Theta. In turn, this possibility suggested to us an alternate means of analyzing our results in a way that could overcome the methodological limitations of our original design. Namely, we developed a new Theta Alpha Gamma Learning Index (THALGAM LI) that was designed to separate out the influences of fm Theta from those of Hippocampal Theta. It achieved this by equally rewarding participants for learning to *in*crease ROI 4.5-10 Hz and learning to *de*crease 51-70 Hz.

In opposition to the THAL LI results, the results for this new THALGAM LI showed promise. Evidence was produced that higher rankings on the THALGAM LI were meaningfully associated with participants' degrees of pre to post training clinical improvement. Across the seven members of the neurotherapy group that were included in the interview ranking analysis, the

THALGAM LI rankings were significantly correlated with the rated degree of clinical improvement (see Figure 10). The results of this analysis therefore suggest that, while not all of our neurotherapy participants successfully developed the ability to deactivate the mPFC, the extent to which our participants learnt to master this skill was associated with how much benefit they derived from participation.

The clinical potential of our THALGAM LI results is most clearly illustrated by the results of participant G. Figure 10 demonstrates that she was a strong outlier in terms of how much clinical benefit she derived from participation. She reported striking improvements in both physiological and life functioning. These improvements were much stronger than those reported by the second ranked participant, F. At the same time, participant G's raw THAGAM LI score (198) was more than *twice* as large as participant F's second ranked score (82). In other words, the one participant who seems to have derived exceptional clinical benefits during this study was also the participant who appears to have achieved by far the highest degree of mastery over the skill in question.

Participant G reported the lowest self-talk scores at time 2 and also stressed more than any other participant how quiet her mind became in her training "zone". A final note-worthy aspect of participant G's results involves the breath control strategy that she reportedly noticed herself using in order to enter her zone. Again, as described in the Results section, several other participants also altered their breathing patterns in order to increase the neurofeedback. However, participant G was the only participant who stressed both how *shallow* her

breathing naturally became and also how she would naturally start suspending her breath for an extended time following each inhale (with an approximate rhythm of five seconds in, five seconds hold, five seconds out).

In sum then, participant G's demonstrated a combination of the following factors: a strategy of very slow, relaxed, shallow breath with extended periods of breath holding; the strongest experience of mental quiescence; the strongest putative deactivation of the mPFC region that is clearly crucial to self referential processing; and the strongest derived clinical benefit.

This overall pattern of results is especially interesting in light of relevant research that has been conducted into the practice of Transcendental Mediation (TM). TM is a widely studied meditative technique that is designed to help practitioners enter a state of "Transcendental Consciousness", which is defined as involving " a complete mental quiescence in which thoughts are absent yet consciousness if maintained" (Travis & Wallace, 1997, p. 39). Regular entry into a state of Transcendental Consciousness has been found to be associated with a broad range of positive health benefits (Orme-Johnson, 1987). Not surprisingly, with increasing years of TM practice a state of Transcendental Consciousness becomes easier for practitioners to access and this state also becomes more deeply integrated into the practitioner's experience (Mason et al., 1997; Travis, Arenander, & DuBois, 2004).

Participant ID	THALGAM LI Rank/ THALGAM LI Raw Score	Interview Rank of Perceived Benefits	Relevant Benefits	Example quote
G	**1** **/198**	**1**	**-markedly less pain intensity throughout week** **-markedly less pain related distress throughout week** **-able to return to work with confidence after having been unable to do so** **-markedly improved sleep** **-lowered blood pressure (160/90 to 120/60)** **- lowered resting pulse from 84 to 60**	**"The reality was that it was a success… I don't have the pain and the pain was the defining part of my whole life…It's remarkable for me…"**
F	**2** **/82**	**2**	**-less pain intensity throughout week** **-less pain related distress throughout week** **-improved resiliency after exercise** **-more energy** **-less PRN use**	**"I did notice a change for sure. I wasn't having as much pain, and if I was I could recover from it faster…"**
A	**3** **/74**	**5**	**-less pain intensity throughout week** **-less pain related distress throughout week** **-improved sleep**	**"even when it really hurts… it doesn't matter as much, it doesn't consume as much"**
D	**4** **/53**	**4**	**-less pain intensity for several hours after sessions**	**"it seems to have reduced my pain immediately after I've done training"**
H	**5** **/23**	**3**	**-less pain intensity for several hours after sessions**	**"when I left here I was, for all intents and purposes, pain free"**
B	**6** **/-20**	**7**	**-none**	**"I really enjoyed working with you… What else?…nothing in particular"**
E	**7** **/-74**	**6**	**-less pain related distress throughout week**	**"The most valuable for me has been that reflection from coming here and talking with you has brought things up"**

Fig. 4-10: Associations between THALGAM LI rankings and Interview

Analysis Ranking of Perceived Benefits : *D* (5) =.821; p=.012* (Spearman's one tailed)

At the same time, relevant EEG related research suggests that the state of Transcendental Consciousness is specifically associated with increases in 6-10 Hz activity (Mason, et al., 1997). Very recent work with LORETA also showed the practice of TM to be associated with reductions in frontal Gamma power (Travis et al., 2010). Finally, and most strikingly, episodes of transcendental consciousness have been found to be preceded by periods of spontaneous breath suspension lasting 10 seconds or longer (Farrow & Herbert, 1982; Travis &Wallace, 1997).

Taken together, these TM related findings suggest the intriguing possibility that the LORETA neurofeedback may have helped participant G learn in a very accelerated fashion how to deeply enter a state equivalent to "transcendental consciousness", and that repeatedly doing so prompted a clinically useful shift in the way that she processed her pain experience.

Limitations

Our study has several limitations, four of the most salient of which we will address here.

First, the meaning of our results is obscured by our small n. Our lack of power meant that several of our key results, including the group level LORETA images, involved suggestive trends rather than statistically significant findings. As such, we cannot rule of the possibility that these non-significant results in question were random in nature.

Second, we can not rule out the possibility that our apparent Gamma related findings were driven by changes in EMG artifact, since muscular activity tends to

manifest in this range (Goncharov, 2003). This possibility is mitigated against by the fact that the raw EEG data was carefully artifacted in order to avoid this kind of contamination. However, our lack of an external EMG sensor means that we cannot entirely rule out this possibility.

Third, our proffered explanation as to why our THAL LI failed to perform as anticipated necessarily calls into question our apparent successes in up-training 4.5-8 Hz. In other words, we cannot ensure that this apparent training success wasn't inadvertently caused by teaching our participants to generate higher levels of Hippocampal theta. However, two previously discussed factors argue against this conclusion. First, the participants increased their levels of relaxation from Time 1 to Time 2, which is consistent with increases in fm Theta but not Hippocampal Theta. Second, our observed High Gamma decreases are also consistent with an increase of fm Theta but not of Hippocampal Theta (Meltzer et al., 2009; Adhikari et al, 2010).

Finally, the first author conducted all of described training and data collection procedures while the first and second authors conducted all of the decribed data analysis procdures. There is therefore the inevitable possibility that experimenter bias distorted the results of the current experiment, despite concerted efforts on the part of all parties involved to prevent this from occurring.

Conclusion

In conclusion, we appear to have successfully trained a cohort of people with mixed chronic pain conditions to up-train 4.5-10 Hz in the mPFC using LORETA neurofeedback. The neurotherapy intervention seems to have promoted

consistent clinical changes at the group level, including statistically significant reductions in the PDI and the CED-S. However, on the whole these clinical changes were modest when compared to the results of our active control condition, which outperformed the neurotherapy intervention on several outcome measures, including the crucial PDI (see Figure 5). These between group results should perhaps not be surprising given that CBT with a strong relaxation component is a comprehensive and widely practiced pain management modality with very strong evidence of efficacy (Vlaeyen & Morley, 2007). These between group results may therefore be an early indication that LORETA neurotherapy's meaningful potential with this population is to become another addition to the existent repertoire of useful, adjunctive modalities for chronic pain management.

The statistically significant improvements in depressive symptoms that we observed in the neurotherapy group also bear brief mention here, particularly given our small sample size (see Figure 5). Our depression related findings appear to be consistent with the recent results of Paquette, Beauregard & Beaulieu-Prévos (2009). These authors reported success in alleviating depression through the use of a neurotherapy protocol that down-trained Beta in the frontal midline region. Our results therefore suggest that a variant of the current LORETA neurotherapy protocol could prove to be an effective intervention for depression.

Returning to our primary focus, our individual level results also appear to offer some hope that LORETA neurotherapy may have the potential to evolve into a more primary chronic pain management modality. This hope is most strongly demonstrated by the results of participant G. If future research

participants are able to develop the same kind of mastery that she apparently achieved over her mPFC activity; and if these patients then also derive the same degree of clinical benefits that she did, this would suggest that LORETA neurotherapy has the potential to become a truly powerful new modality in the management of chronic pain.

Regardless, establishing the potential value of this modality for chronic pain management will require much more work, potentially starting with a replication of the current design with a larger sample. In the case of a replication, several methodological refinements would seem to be indicated. First, use of external EMG sensors to better rule out the possible influence of EMG artifact would seem essential. Second, adoption of a training protocol involving simultaneous up training of 4-10 Hz and inhibition of 51-70 Hz should be considered. (The potential contributions of Low Alpha, which were not a focus of our current interpretation, could also be valuable to clarify in future research). Third, experimenting with the distinct breathing pattern reported by participant G could prove useful. Finally, use of a technique such as Independent Components Analysis would be invaluable, as it would help to separate out the influences of Hippocampal versus fm Theta.

Should follow-up studies strengthen the general conclusion that LORETA neurotherapy has potential as a chronic pain management modality; important follow-up questions would then be raised around what *kinds* of clients are most likely to benefit from this approach. Questions of this kind become important in light of compelling evidence indicating that specific therapeutic interventions are

most useful when they are applied with specific kinds of clients (Beutler, Harwood, Kimpara, Verdirame, & Blau, 2011**).** Treatment-to-client matching variables may have accounted, at least in part, for the variability of clinical response that was found found in the current study (see Figure 10). Therefore, if warranted, clarifying the kinds of clients who will be most likely to benefit from receiving this training could be invaluable in allowing LORETA neurotherapy to fulfil its clinical potential.

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Chapter 5

CONCLUSION

This dissertation is comprised of three articles. The first article, contained in chapter two, is a theoretical work. The latter two articles, contained in chapters three and four respectively, each describe an experimental study. This conclusion will briefly summarize the content of each of these articles. Following summarization of the two experimental studies, additional remarks will also be made around key implications that the findings would have for replications of the current study designs. In the case of the chapter four study, brief consideration will then also be given to the future potential of LORETA neurotherapy as an intervention for chronic pain. Finally, short concluding remarks will be made.

Chapter Two Article

Article two describes a theoretical model that is grounded in complexity theory (Siegel, 2009). The model argues that the human mind emerges through the dynamic functioning of three, large-scale, interacting neural systems. Two are dedicated to hot and cold cognition, while the third system mediates between these forms of cognition. The article outlines how differences in the interactions between these systems relate to changes in level of experiencing, a psychotherapy process variable that has been found to correlate with outcome (Whelton, 2004). The article then uses this neural model to conceptualize two different forms of psychopathology. Finally, we consider the implications of the neurological model for the treatment of psychopathology.

The theoretical model contained in chapter two attempts to integrate material from typically disparate domains. Most fundamentally, the model attempts to work *across* two of Wilber's (2000) four truth claim quadrants: an "inside" quadrant that considers the client's inner experience at the level of the mind; and an "outside" quadrant that considers the client's neural behavior at the level of the brain. The model's broad scope also means that it is clearly speculative in nature. However, in part through its use of complexity theory as a bridge between mind and brain, the model attempts to consider the experiencing process from a neurological perspective in a way that is both generative and as respectful as possible to the two truth claim quadrants involved.

Chapter Three Study

The chapter three study sought to clarify the electrophysiological correlates of the suffering aspect of chronic pain (Price, 2002). This study's hypotheses were predicated on the idea that chronic pain related suffering can be usefully understood as a maladaptive form of autobiographical self-related processing (Baliki et al, 2006). It was therefore predicted that chronic pain related suffering would be associated with increased activation of the Default Mode Network (DMN), given the well established association between self referential processing and DMN activity (Buckner et al, 2008). It was further expected that this electrophysiological activation would be most strongly centered in the mPFC/DMPFC, given the especially strong association between this region and self referential processing (Lieberman, 2007), and given the results of previous

fMRI investigations into the suffering aspect of chronic pain (Baliki et al, 2006; Schweinhardt et al., 2008).

The group level, LORETA contrast comparing the SUFFER and SOCIAL conditions in the chapter three study did not produce the expected pattern of statistically significant differences. Therefore, this study's hypotheses were not supported. However, the observed results were still interpreted as offering some conditional support for the study's hypotheses. This interpretation was based on three factors. The first was that the study's very small n made a lack of power a credible explanation for the lack of significant, group level results. The second was the presence of visual trends in the group level LORETA images that seemed generally consistent with the hypotheses, particularly within the most strongly relevant mPFC/DMPFC ROI. The third factor was based on the fact that there was strong variability in the strength of the "suffering contrast" the individual participants were able to achieve. Notably, a pattern emerged in which the more strongly a participant achieved a "suffering contrast", the more strongly he or she demonstrated the expected pattern of electrophysiological responses.

Clearly, the lack of statistical significance at the group level means that replication would be required to test the validity of the proffered interpretation. A pair of adaptations to the current design would seem advisable during such a replication. The first would be to substantially increase the sample size. At least a two-fold increase in the n would seem ideal, given the current n of 7 and the fact that an n of 15 is generally considered adequate for LORETA analysis of this kind (Nichols & Holmes, 2001). The second adaptation would be to select a more

homogenous sample of chronic pain patients who were all experiencing at least moderate levels of functional impairment. The participants in the current study also served as members of the LORETA neurotherapy group during the chapter four study. Participation in the chapter four study's neurotherapy group was quite demanding for someone living with chronic pain, requiring travel and attendance at bi-weekly sessions over a period of six weeks. Therefore, partly to help avoid excessive levels of participant drop out from the neurotherapy group during the chapter four study, participants with relatively low levels of functional impairment levels were not excluded from participation. As such, members of the chapter three study had strong variability in their baseline PDI scores (range: 6-54/70). However, the chapter three study also found that the extent to which participants were able to achieve the desired behavioral contrast between the SUFFER and SOCIAL conditions was significantly correlated with their baseline PDI scores. Therefore, it may be both experimentally advantageous and more feasible for a stand-alone replication of the chapter three study to select a sample of participants with consistently higher PDI scores.

Chapter Four Study

The chapter four study was designed to test the feasibility and effectiveness of using LORETA neurofeedback to help people with chronic pain to lessen their suffering. The neurotherapy protocol was designed to help members of the neurofeedback group to volitionally down-regulate mPFC activity, based on the contention that suffering is a maladaptive form of overly rigid self-referencing, Members of an active control group were trained in Autogenics and CBT.

The chapter four study produced a mixed pattern of results. First, members of the neurotherapy group demonstrated evidence of having successfully developed self-control of their neural activity in the intended manner. Members of the neurotherapy group also evidenced statistically significant pre-post training clinical improvements in mood and degree of functional impairment, two key chronic pain related domains. On the other hand, the expected improvements in phasic pain regulation did not achieve statistical significance, the observed improvements in pain regulation did not correlate with brain changes in the originally anticipated manner, and the active control group outperformed the neurotherapy group in several outcome domains.

The overall impression left by this pattern of results is that LORETA neurotherapy may hold substantial potential as a chronic pain management modality, but that substantial work would need to be done in order to verify and then, if indicated, fulfill this potential.

One aspect of the required work would involve the continued application of LORETA neurotherapy to chronic pain. Most essentially, this would require subsequent experimental trials, potentially beginning with an adapted replication of the current study design. As mentioned in the chapter four, several adaptations can be recommended for a replication of the chapter four study design. Namely: the inclusion of external sensors for better artifact control; the use of a training protocol that involved the simultaneous up-regulation of 4-10 Hz and down-regulation of the 51-70 Hz within the mPFC; and incorporation of the control

strategies reported by participant G, the study participant who appeared to have derived the most substantial benefit from participation.

On another front, improvements to the modality itself will be very helpful, and perhaps even necessary, if LORETA neurofeedback is to be successfully developed into a front line, chronic pain management intervention. Three of the most important potential improvements will be briefly outlined here.

The first improvement, the integration of analytic techniques as such as Independent Components Analysis (ICS) into LORETA neurotherapy, was briefly alluded to in chapter four. ICA is a data analysis technique that decomposes the raw EEG results into clusters based on the primary generators of the activity in question (Congedo & Joffe, 2006). This extra level of analysis would theoretically allow only activity that was associated with a selected cluster to be targeted for training. So, for example, the use of ICA informed LORETA neurofeedback in the chapter four study would have allowed the training of theta activity that was associated with a mPFC centered cluster, while avoiding the training of theta that was associated with a Hippocampal cluster. If LORETA is to fully capitalize on its potential, it seems essential that ICA or analogous techniques be successfully integrated into the modality (Congedo & Joffe, 2006). For only once this has been achieved will LORETA neurotherapists be able to practice with adequate confidence that they know both *where* and *what* they are training. The chapter four study challenges involving fm versus Hippocampal Theta stand as a testament to the importance of this issue.

The second area in need of improvement involves the software in question. The Braintuner LORETA neurofeedback software (Mitsar Co., St. Petersburg, Russia) that was used in the chapter four study lacked several key features that hampered the training process. Most saliently, during training the software did not visually reflect ongoing changes in each of the four relevant bandwidths. Instead, it only provided a single bar graph that reflected the changing *ratio* of the rewarded and inhibited bandwidths (e.g., 4.5-10 Hz as the denominator and 1-3.4 and 30-40 Hz as the numerator). This meant that it was difficult for D.O. to know during training whether changes in the feedback were originating from training related changes (in the denominator) and/or artifact related changes (in the denominator). Granted, external artifact sensors would have helped in the regard. However, this remains a prime example of the kind of software feature that developers will need to provide in order to make LORETA neurofeedback systems both user friendly and transparent enough to thrive (Congedo & Joffe, 2006), if future experimental findings indicate that this is warranted.

A final area of needed improvement is in the relevant hardware. Appropriate application of full cap EEG is a labor intensive, time-consuming process. Numerous chronic pain management techniques, such as Autogenics, exist that that do have any requirements of this kind. Therefore, simplification of the headgear needed to do LORETA neurofeedback would be very helpful and would increase the relative attractiveness of this modality. Low cost, EEG headsets have recently emerged on the market (($300 for a 14 channel version; see emotiv.com). These new headsets reportedly use saline sensors and do not require any special

preparation of the scalp. If headsets of this kind can be further developed, commercialized, and validated with LORETA analysis this would present a significant step forward for the potential utility of LORETA neurofeedback.

General Conclusion

Until fairly recently, issues of consciousness and the self were considered outside the domain of cognitive neuroscience (Damasio, 1999). Yet in recent years there has been an explosion of interest in these topics. This surge of research activity has created a tremendous opportunity for the occurrence of cross-discipline interactions between cognitive neuroscientists and people, such as psychotherapists, who have long made consideration of these core human issues a central part of their work. Ultimately, these interactions have the potential to lead to the emergence of more effective ways of understanding and ameliorating human suffering, including the terrible suffering of chronic pain. This dissertation has been an effort to contribute, in some small way, toward fulfilling this potential.

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APPENDICES

Appendix A

Table A 1: Demographic Data for Chapter Three Study Participants

Participant ID	AAge	Gender	Handedness	Occupation	Pain Condition/ Primary Location	Duration (years)	Other Major Health Conditions	Meds-Daily Dosage in Mg (Not Including PRN)
A	52	F	R	Nurse	Arthritis in L.Back	3.5	No	Omeprzole 20
B	55	M	R	Manager/ Biologist	Chronic Knee Pain	20	No	None
C	59	F	R	Teacher	Degenerative spondy-lolitheis in lower back	2.5 years	-Sleep apnea -High blood pressure	Diovan 160 mg
D	32	M	R	Teacher	Chronic Pelvic Pain	1.5	Sinus Problems	none
E	51	F	R	Teacher	Arthritis and Degenerative Disk Disease	15	Thyroid problems/ Obesity	Piroxicon 20 mg
F	57	F	R	Retired	Chronic neck and Back Pain	3.5	none	none
G	24	F	R	Nurse	Chronic Headaches and Chronic Back Pain	5.5	none	none
X=	**47.1**							

Appendix B

Table A 2: Baseline Data for Chapter Three Study Participants

ParticIpant ID	PDI	Av. Pain INT VAS (0-10) over last 7 days	Av. Pain UNPL VAS (0-10) over last 7 days	CEDS	Av.SF-MPQ over last 7 days
A	33	5	6	22	7
B	6	5	4	3	6
C	54	7	6	11	22
D	6	4	3	13	11
E	38	5.5	5	7	8
F	22	8	8	2	15
G	33	6	4	13	12
X=	27.4	5.8	5.1	10.1	11.6

Appendix C

Table A 3: Demographic Data for Chapter Four Study/ Neurotherapy Group Participants

Partic-Ipant ID	Age	Gen-der	Hand	Occupation	Pain Condition/ Primary Location	Dura-tion	Other Major Health Cond-itions	Meds-Daily Dosage in Mg (Not Including PRN)
A	52	F	R	Nurse	Arthritis in L.Back	3.5 years	No	Omeprzole 20 mg
B	55	M	R	Manager/ Biologist	Chronic Knee Pain	20 years	No	None
C	59	F	R	Teacher	Degene-rative spondy-lolitheis in lower back	2.5 years	-Sleep apnea -High blood pressure	Diovan 160 mg
D	32	M	R	Teacher	Chronic Pelvic Pain	1.5 years	Chronic Sinus Problems	none
E	24	F	R	Nurse	Chronic Headaches and Chronic Back Pain	5.5 years	None	none
F	57	F	R	Retired	Chronic neck and Back Pain	3.5 years	none	none
G	51	F	R	Teacher	Arthritis and Degener-ative Disk Disease	15 years	Thyroid Problems/ Obesity	Piroxicon 20 mg
H	65	F	R	Retired	CRSD	6 years	none	None
X=	**49.3**							

Appendix D

Table A 4: Chapter Four Study Neurotherapy Group Pre-Training Scores

Partic-Ipant ID	**PDI**	**Av. Pain INT VAS (0-100) over last 7 days**	**Av. Pain UNPL VAS (0-100) over last 7 days**	**CEDS Over last 7 days**	**Av.SF-MPQ over last 7 days**
A	31	50	60	22	7
B	10	60	60	3	2
C	50	70	60	19	28
D	14	50	40	12	10
E	53	80	90	27	16
F	31	60	60	3	20
G	41	40	40	14	8
H	16	30	20	9	7
X=	**30.7**	**55**	**53.7**	**13.6**	**12.2**

Appendix E

Table A 5: Demographic Data for Chapter Four Study/ Autogenics Group Participants

Partic-Ipant ID	Age	en--der	Hand	Occupation	Pain Condition/ Primary Location	Dura-Tion (years)	Other Major Health Cond-itions	Meds-Daily Dosage in Mg (Not Including PRN)
I	32	M	R	Tech-nician	Lower back Shoulder Knee	3	None	Naproxen
J	83	F	R	Retired	Osteo-arthritis Osteoporo sis Back pain	30	Drop foot Spinal Stenosis	Flavoxate 200 Hydro ? 25 Zoniclone 7.5 Lyrica 75
K	61	F	L	Admin-istrator	Knee pain	9	None	Cozaar 50
L	65	F	R	Retired	Arthritis in hip	5	None	Glucose-Mine Sulfate
M	60	M	R	Manage r	Nerve pain	2.5	None	Apo-Hydro 25 Norvasc 10
N	39	F	R	Researc h Tech	Chronic Eye Irritation	1.5 years	Infertility Related concerns	None
O	42	M	R	Enginee r	Shoulder Pain Knee Pain	5	None	None
X=	**54.5**							

Appendix F

Table A 6: Chapter Four Study Autogenics Group Pre-Training Scores

Partic-Ipant ID	PDI	Av. Pain INT VAS (0-100) over last 7 days	Av. Pain UNPL VAS (0-100) over last 7 days	CEDS	Av.SF-MPQ over last 7 days
I	34	30	30	16	22
J	22	60	70	3	6
K	24	50	40	9	9
L	39	90	90	1	9
M	16	65	60	4	21
N	12	20	40	6	2
O	29	50	40	9	5
X=	**25**	**52.1**	**52.8**	**6.8**	**13.1**

Appendix G

Participant Screening Questions for Chapter Three and Four Studies

(Adapted form from Congedo, 2003, p. 78).

1) Have you ever had an injury to your head?
2) Have you ever been unconscious?
3) Have you ever been diagnosed with any form of mental disorder?
4) Do you currently take or have you ever taken any psychotropic medications?
5) If you are currently taking medications what are the purposes, dosages etc.?
6) In the last month have you taken any non-prescription drugs (marijuana etc)?
7) Do you have a history of alcoholism? How much do you drink now?
8) Have you ever been diagnosed with cerbrovascular disease?
9) Do you have a history of migraines?
10) Have you ever been diagnosed with epilepsy? Have you ever had a seizure of any kind?
11) Have you ever been diagnosed with ADHD?
12) Have you ever been diagnosed with any kind of sleeping disorder?
13) What times during the week would you be consistently available to come to the Education clinic for one hour meetings once or twice a week?
14) What would your goals be in participating in this study?

Appendix H

Informed Consent for Study Three/Neurotherapy Participants for Study Four

Informed Consent

The purposes of this study are to compare the effectiveness of two different approaches to pain management and to also to discover how chronic pain effects the brain. It is hoped that this study will both increase our understanding of chronic pain and improve our abilities to manage it.

This study will be conducted by the principal researcher, Douglas Ozier, and may be included with the complete study in his doctoral dissertation, in partial fulfillment for a Ph.D. in Educational Psychology. Dr. William Whelton in the Department of Educational Psychology at the University of Alberta will supervise this study. Dr. Horst Mueller, a Registered Psychologist in private practice in Edmonton, will provide additional clinical supervision.

Project summary: If you decide to participate you will be asked to attend 18 meetings over a 11-week period (18 hours total). Your involvement will move through a number of stages. Each of these stages will involve a number of training and/or data collection sessions. Mr. Ozier will conduct all of these sessions. These sessions will be held at the Education Clinic located in the Education building of the University of Alberta. Each of these stages will now be explained so that you will know what you will be asked to do if you decide to participate.

Stage One-Pre-training stage.
You will be asked to attend four 60-minute sessions in this stage. During each session you will be attached to the EEG system.

- In the first session you will be shown the EEG system. This system allows us to monitor the electrical activity of your brain. This system only monitors and provides feedback as to the brain's activity. In other words, while naturally occurring electricity goes from your brain into the machine, no electricity goes from the machine into your brain. You will then be attached to the EEG system. In order to connect you to the EEG system we will put a cap with 19 small sensors on your head. Electrode gel will then be applied to each of these sensors. An earclip electrode will then be attached to each ear after the earlobe has been cleaned with a special solution. All gels and solutions used will be hypoallergenic. This total process will be designed to cause as little discomfort as possible. You will then be taught several techniques for increasing and decreasing your pain levels.
- In the second session you will be asked to alter your pain levels during four short blocks. During two of these two-minute blocks you will be asked to relax as much as possible and to decrease your pain as much as possible. During the other two-minute blocks you will be asked to tighten your body in such a way as to increase your pain. Increasing your pain for these short periods will cause a certain degree of discomfort but you will not be asked to increase your pain beyond levels that you feel comfortable tolerating. We will ask you to do this to help us understand

how your brain processes pain when it is getting worse. In this session you will also be asked to think about a variety of other topics.

- In the third session you will be asked to perform two tasks. These tasks will involve: sitting quietly and thinking about various topics.
- In the fourth session you will again be asked to increase and decrease your pain during four, two-minute blocks.

Stage 2- Training Stage

You will be asked to attend 12, 1-hour, individual training sessions with Mr. Ozier over six weeks. During these sessions you will be attached to the EEG system while it monitors your brain and provides you with audio feedback as to your brain's activity. You will then be taught to use this feedback in order to consciously activate or deactivate parts of your brain in particular ways that may help you to control your pain.

Stage 3- Post-training Stage

This stage will involve two 60-minute sessions.

- In the first session you will be asked to use the provided feedback to control your brain activity and pain in the manner taught during the training stage. You will then be asked to fill out the same questionnaires that you will out at the start of the study.
- In the last session you will be asked to repeat the same activity but with no feedback. You will also be asked to have a short audiotaped conversation with Mr. Ozier about your experiences in the study.

Potential Risks.

- Attaching the EEG electrodes to the scalp involves using special gels. These gels are designed to be hypoallergenic but a small chance remains that they could cause a mild skin reaction.
- Applying the EEG electrodes also involves rubbing the small areas of scalp beneath each of the 19 electrodes. This process will be done as gently and carefully as possible but a small degree of discomfort during this process could still happen. However, this might be of more of a problem for you if your pain condition causes you to have a really strong pain reactions in the skin of your for head and scalp.
- During several points in the study you will be asked to make your pain worse for several 2-minute periods to help us understand what happens in your brain when pain is getting worse. However, you will never be asked to increase your pain beyond a level that is too high for you and you will always be given a chance to lower your pain again afterwards.
- It is not expected that participating in the neurotherapy training portion of this study should cause any adverse side effects. However, it is possible that you may experience any one of the following side effects that people occasionally report when undergoing traditional EEG neurofeedback training:
    - Sleep problems
    - headaches

- Feelings of dizziness
- Decreased motivation or energy
- Irritability
- Tiredness
- Sadness or other emotional responses
- Occurrence of strongly emotional memories

When the listed side effects do occur they usually go away quickly. However, if you decide to participate it will be important for you to tell Mr. Ozier if you are experiencing any of the listed problems or any other negative side effects. This will allow him to make appropriate changes to your protocol under the supervision of Drs. Whelton and Mueller.

A new version of neurofeedback called LORETA will be used in this study. This approach is similar to traditional EEG neurofeedback except that it allows for training of n a more specific area within the brain. Three studies have thus far been conducted using LORETA neurofeedback, none of them involving participants with chronic pain. None of these studies reported any adverse effects. However, the newness of this approach makes it possible that there could be unanticipated side effects that cannot currently be predicted from existing research.

- During several points in the study you will be asked to make your pain worse for several 2-minute periods. You will never be asked to increase your pain beyond a tolerable level and you will always be given a chance to down regulate your pain after increasing it. Despite these caveats however, the act of raising your pain will likely be an unpleasant task for you.

Potential Benefits. If you participate in this group it is reasonable to expect that you will learn some new skills that will help you to manage your pain better. If you participated in all 6 data collection sessions and a minimum of 60% of your training sessions you would receive an honorarium equivalent to $10 for each hour attended (between $120-$180 depending on number of sessions attended). Your parking or transit costs would also be reimbursed at each session up to $5.

Research Assistants. Volunteer research assistants may play a variety if supportive roles during this project such as helping to attach the EEG headgear during data collection. All research assistants will comply with the University of Alberta Standards for the Protection of Human research Participants. All such assistants will also be required to sign a confidentiality agreement stating that they will respect the confidentiality of participants in the study.

Confidentiality. Only Mr. Ozier and Dr. Whelton will have access to any study materials that identify you personally as a participant in this study. The data gained during this study will be disseminated for professional reasons but you will be assigned a code so that you will not be able to be identified. All relevant records will be locked in a file cabinet in Mr. Ozier's office or residence for a period of no less than 5 years.

Rights. You will be free to withdraw from the study at any time. Should you decide to withdraw before fulfilling the described conditions you will not receive the honorarium. If you withdraw from the study the data collected during your participation will be erased and not be included in the study should you make such a request. If you choose to participate in this study, all identifying information that is provided in the data will be kept confidential and your anonymity will be maintained. You will be assigned a code number that will be used in all documentation and record keeping. After five years, all paper data will be shredded. Should you desire a copy of the final copy of the research report you will simply need to indicate this before the end of your last session. A copy of the report will then be sent to you at no charge.

Uses of Data. Data will be used within Mr. Ozier doctoral dissertation. Data may also be used in other scholarly work such as in journal articles, conferences, or presentations. Further, the EEG data along with minimal descriptive information (e.g., age, gender, nature of pain condition) may also be included in an EEG database that is currently being constructed to help propagate the use of LORETA EEG. The data for all of these uses will be handled in compliance with the University of Alberta Standards for the Protection of Human Research Participants.

If you have any concerns or questions about this research study, please contact:

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or
Dr. Robin Everall
Associate Professor and Chair
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University of Alberta
Edmonton, Alberta, Canada T6G 2G5

Consent to participate:

I have read and understood the nature of this study and the contents of the consent form. I have a copy of the information and consent form for my own records. By signing below, I agree to participate in this study.

Signature of Participant Date

Signature of Researcher as Witness Date

Appendix I

Informed Consent for Study Four Autogenics Group

Informed Consent

The purposes of this study are to compare the effectiveness of two different approaches to pain management and to also to discover how chronic pain effects the brain. It is hoped that this study will both increase our understanding of chronic pain and improve our abilities to manage it.

This study will be conducted by the principal researcher, Douglas Ozier, and may be included with the complete study in his doctoral dissertation, in partial fulfillment for a Ph.D. in Educational Psychology. Dr. William Whelton in the Department of Educational Psychology at the University of Alberta will supervise this study. Dr. Horst Mueller, a Registered Psychologist in private practice in Edmonton, will provide additional clinical supervision.

Project summary: If you decide to participate you will be asked to attend 7, 70 minute meetings over a 7 week period (8 hours total). Your involvement will move through a number of stages. Each of these stages will involve a number of training and/or data collection sessions. Mr. Ozier will conduct all of these sessions. These sessions will be held at the Education Clinic located in the Education building of the University of Alberta. Each of these stages will now be explained so that you will know what you will be asked to do if you decide to participate.

- In this treatment group you would be asked to attend seven seventy minute long sessions with Mr. Ozier over seven weeks. The focus during these sessions will be on learning autogenic relaxation techniques and thermal biofeedback. This is a kind of relaxation strategy in which people learn to raise their hand temperature to help them relax and lessen their pain. During the training stage you will also be asked to practice warming your hand at least two times a week for 15 minutes each in between classes. During sessions you will also be taught several other pain control/relaxation techniques and will be offered information on a number of pain management topics such as goal setting. You will also be provided with a thermal biofeedback device and asked to practice autogenics/thermal biofeedback at home once a week. During training you will also be asked to rate your pain at various points and to fill out pre and post training rating scales.

Potential Risks. It is not expected that participating in this study will have any negative effects.

Potential Benefits. If you participate in this group it is reasonable to expect that you will learn some new skills that will help you to manage your pain better. You will also

Rights. You will be free to withdraw from the study at any time. Should you decide to withdraw before fulfilling the described conditions you will not receive the honorarium. If you withdraw from the study the data collected during your participation will be erased and not be included in the study should you make such a request. If you choose to participate in this study, all identifying information that is provided in the data will be kept confidential and your anonymity will be maintained. You will be assigned a code number that will be used in all documentation and record keeping. After five years, all paper data will be shredded. Should you desire a copy of the final copy of the research report you will simply need to indicate this before the end of your last session. A copy of the report will then be sent to you at no charge.

Uses of Data. Data will be used within Mr. Ozier doctoral dissertation. Data may also be used in other scholarly work such as in journal articles, conferences, or presentations. Further, the EEG data along with minimal descriptive information (e.g., age, gender, nature of pain condition) may also be included in an EEG database that is currently being constructed to help propagate the use of LORETA EEG. The data for all of these uses will be handled in compliance with the University of Alberta Standards for the Protection of Human Research Participants.

If you have any concerns or questions about this research study, please contact:

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Consent to participate:

I have read and understood the nature of this study and the contents of the consent form. I have a copy of the information and consent form for my own records. By signing below, I agree to participate in this study.

Signature of Participant Date

Signature of Researcher as Witness Date

Appendix J

Pain Disability Index (Pollard, 1981) (Selected Items)

Instructions: The rating scales below are designed to measure the degree to which aspects of your life are disrupted by chronic pain. In other words, we would like to know how much pain is preventing you from doing what you would normally do or from doing it as well as you normally would. Respond to each category indicating the overall impact of pain in your life, not just when pain is at its worst.

For each of the 7 categories of life activity listed, please circle the number on the scale that describes the level of disability you typically experience. A score of 0 means no disability at all, and a score of 10 signifies that all of the activities in which you would normally be involved have been totally disrupted or prevented by your pain.

Family/Home Responsibilities: This category refers to activities of the home or family. It includes chores or duties performed around the house (e.g. yard work) and errands or favors for other family members (e.g. driving the children to school).
No Disability 0__. 1__. 2__. 3__. 4__. 5__. 6__. 7 __. 8__. 9__. 10__. Worst Disability

Recreation: This disability includes hobbies, sports, and other similar leisure time activities.
No Disability 0__. 1__. 2__. 3__. 4__. 5__. 6__. 7 __. 8__. 9__. 10__. Worst Disability

Social Activity: This category refers to activities, which involve participation with friends and acquaintances other than family members. It includes parties, theater, concerts, dining out, and other social functions.
No Disability 0__. 1__. 2__. 3__. 4__. 5__. 6__. 7 __. 8__. 9__. 10__. Worst Disability

Occupation: This category refers to activities that are part of or directly related to one's job. This includes non-paying jobs as well, such as that of a housewife or volunteer.
No Disability 0__. 1__. 2__. 3__. 4__. 5__. 6__. 7 __. 8__. 9__. 10__. Worst Disability

Appendix K

Short Form McGill Pain Questionnaire (Melzack, 1987) (Selected Items)

Instructions: Check the column to indicate the level of your pain for each word, or leave it blank if it does not apply to you.

Pain Quality	Mild	Moderate	Severe
Throbbing			
Shooting			
Stabbing			
Sharp			
Cramping			

Appendix L

Center for Epidemiologic Studies in Depression Scale (CED-S),

(Radloff, 1977), (Selected Items)

Instructions: Below is a list of the ways you might have felt of behaved.

Please tell me how often you have felt this way during the past week.

	Rarely or none of the time (less than one day)	**Some or a little of the time (1-2 days)**	**Occasionally or a moderate amount of the time (3-4 days)**	**Most or all of the time (5-7 days)**
I was bothered by things that usually don't bother me				
I did not feel like eating; my appetite was poor				
I felt that I could not shake off the blues, even with help from my family and friends				
I felt that I was just as good as other people				

Appendix M

Abbreviated Version of the Working Alliance Inventory

Instructions: The sentences below describe some of the different ways a person might think or feel about his or her therapist. As you read the sentences mentally insert the name of your therapist in place of _____in the text. Below each statement inside there is a seven point scale: If the statement describes the way you always feel (or think) circle the number 7; if it never applies to you circle the number 1. Use the numbers in between to describe the variations between these extremes.

		Never	**Rarely**	**Occasionally**	**Sometimes**	**Often**	**Very Often**	**Always**
1.	What I am doing gives me new ways of looking at my problem.	1	2	3	4	5	6	7
2.	I believe likes me.	1	2	3	4	5	6	7
3.	_____does not understand what I am trying to accomplish in therapy.	1	2	3	4	5	6	7
4.	I am confident in ’s ability to help me.	1	2	3	4	5	6	7
5.	_____and I trust one another.	1	2	3	4	5	6	7
6.	I feel that ------ appreciates me.	1	2	3	4	5	6	7

Appendix N

Numerical Rating Scales

NRS Pain Intensity Rating Scale

0----------100

"no pain" **"pain as bad as it could be"**

NRS Pain Unpleasantness Rating Scale

0----------100

"not bad at all" **"the most unpleasant feeling possible for me"**

Relaxation Rating Scale

0----------100

"Not at all relaxed" **"As deeply relaxed as possible"**

Mental Self Talk Rating Scale

0----------100

"No mental self talk" **"Very strong and persistent mental self talk"**

Appendix O

Chapter Three Study Task Instructions

Social Condition Task Instructions:

"I will now ask you to spend the next 2 minutes thinking about _____(insert the participant's pre selected choice from among the following topics: Globalization of world trade; the right to vote; role of government social programs in Canadian society; the commercialization of outer space; NAFTA). During this task reflect on_____, thinking about this topic in a dispassionate way, simply considering the various issues that the topic raises".

Suffer Condition Task Instructions:

"I will now ask you to begin thinking about yourself for the next 2 minutes. More specifically I would like you to ruminate about the role of chronic pain in your life. During this time please ruminate on the way that pain interferes with your life, the suffering it causes, and the obstacles that it presents for you."

Appendix P

Chapter Four Study Pain Control Task Instructions

"During the next 4 minute block I will ask you to sit with your eyes closed. I would like you to attend to your current pain. Try to keep your awareness n your pain experience. Don't try to make your pain either better or worse, just allow yourself to be aware of your pain as it is. If you find your mind wandering just note that and come back to awareness of your pain. During this time period I will also ask you to keep your jaw, forehead, facial muscles relatively relaxed and your eyes relatively still. Please begin" (Begin OBSERVE condition).

(At 1 minute) 'Allowing your awareness to remain on your pain experience, as it currently is, not trying to make it better or worse. Allowing the jaw, forehead, and facial muscles to remain relaxed, and your eyes to remain still as you do this. "

(At 2 minutes) 'If your mind wanders just bring awareness back to your pain as it currently is."

(At 3 minutes) "For just one more minute allow yourself to be aware of your current pain experience as it is, not making it better or worse. Allowing the jaw, forehead, and facial muscles to remain relatively relaxed and the eyes to be still."

(At 4 minutes) "Thank you. I will now ask you to provide several ratings in response to your experience over the last 4 minutes"(Conduct ratings).

"Now please take a 3 minute break, sitting quietly with eyes open"

(After 2 minutes of the break) "During the next 4 minutes you will receive audio feedback in the sound of waves. Changes in the amount and volume of the

feedback will reflect changes in the region of your brain called the mPFC. During this 4-minute block please attempt to increase both the amount and volume of the audio feedback. As you do this, it is important to remember to keep your eyes, forehead, jaw and facial muscles relaxed as tension in these areas will interfere with the feedback. I will ask you to begin in 20 seconds." (Conduct REGULATE Block).

(After 4 minutes). "Thank you. I will now ask you to provide several ratings in response to your experience over the last 4 minutes"(Conduct ratings).

Appendix Q

Post-Training Interview Questions with Neurotherapy Group Participants in the Chapter Four Study

1) What benefits, if any, did you derive from participating in this study?
2) What negative side effects, if any, did you experience as a result of participating in this study? (After they answer, list any of the following possibilities that they may not have already mentioned). Before we move on to the next question I would like to tell you a list of side effects that other people have occasionally reported experiencing during neurotherapy. Please look back over the course of your involvement in the study to see if you may have experienced any of the following: sleep problems, headaches, dizziness, decreased motivation of energy, irritability, tiredness, sadness of other emotional responses, or the occurrence of strongly emotional memories.
3) Please describe any strategies that you used in order to try and control the feedback.

Appendix R

Neurotherapy Training Session Instructions

Following the impedance check and prior to the baseline block:

"During the next 4 minutes I would like you to just relax and allow yourself to let your mind go wherever it naturally goes, remaining open to any thoughts or images that enter your mind" (Conduct the 4 minute baseline block, then verbally administer rating scales). Prior to each training block:

"During the next block you will receive audio feedback in the sound of waves. Changes in the amount and volume of the feedback will reflect changes in the region of your brain called the mPFC. During this 4-minute block please attempt to increase both the amount and volume of the audio feedback. As you do this, it is important to remember to keep your eyes, forehead, jaw and facial muscles relaxed as tension in these areas will interfere with the feedback. I will ask you to begin in 20 seconds." (Conduct the training block, then verbally administer rating scales).