Influence of acute exercise on association memory for emotional and neutral pictures

by

Danielle Olafson

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Department of Psychology
University of Alberta

Abstract

Introduction: The beneficial effects of chronic exercise on hippocampal volume and associated memory functions are well studied, especially in the context of aging and dementia. These effects are thought to be mediated by multiple exercise-induced physiological and molecular factors (e.g., cortisol, BDNF, neurotransmitters), which directly or indirectly influence hippocampal structure and function. However, whether an acute bout of exercise can influence memory functions is less clear. In humans, association memory, i.e., relational memory for two or more items has been associated with hippocampal function, and some studies have examined how acute exercise may affect associative memory performance. Acute exercise also influences mood, but effects on emotional types of memory are sparse and equivocal. In the current study, we used an association memory task with emotional and neutral picture pairs, previously shown to engage the hippocampus, and to produce an emotional memory bias favoring neutral pairs of images over emotional (negative, high-arousing) pairs. The purpose of the current study was to test whether differing intensities of exercise change emotional association memory performance in this task.

Hypotheses: We tested two alternative hypotheses. Compared to low-intensity exercise and no-activity controls: 1) High intensity exercise will nullify arousal effects of the emotional materials on memory and decrease the typical memory bias for neutral picture pairs. 2) High intensity exercise will intensify the typical memory bias, creating an even larger memory advantage for neutral pairs. In addition, based on previous non-emotional association memory studies, we predicted: 3) High intensity exercise will increase overall association memory regardless of emotional valence of the pictures.

Methods: In a pseudorandomized blinded experiment, 95 undergraduate students were assigned to one of three experimental groups: A high intensity group in which participants cycled to 90%

of their maximum heart rate (n=31), a low intensity group which leisurely cycled to no more than 50% of their maximum heart rate (n=33), and a no-activity control group watching a nature video (n=31). Heart rate was continuously monitored to measure physiological reactivity. The memory task (from Madan et al., 2017) contained negative and neutral picture pairs, tested association memory through associative recognition, and was conducted before and after the intervention.
Results: Results indicated that the exercise intervention was successful. Both the low and high intensity groups had the same resting heart rate, but the high-intensity group demonstrated more pronounced heart rate changes compared to the low intensity group throughout the intervention. Average association memory performance, differential memory for neutral versus emotional pairs, and subjective memory performance were indistinguishable between groups, with clear evidence for null findings based on Bayesian statistics, although the high intensity group showed atypical memory performance already prior to the intervention. Within the high intensity group, participants who had a greater physiological response to the intervention demonstrated better memory both before and after the intervention than individuals with a weaker response. **Discussion and conclusion:** Based on these outcomes, acute exercise seems ineffective to change performance in emotional association memory, with Bayes factors conclusively suggesting null-findings. Nevertheless, outcomes could also be linked to a variety of experimental factors including high variability of the memory bias across participants, recruitment/sampling, test duration, and other uncontrolled factors (dispositional fitness levels, recent real-life exercise, time of day). The relationship between the responsiveness to high intensity exercise and memory mirrors similar findings in previous literature, indicating that responsiveness to higher intensities of exercise is related to better memory. This suggests that participants who are physiologically more responsive (higher heart rate) to high intensity exercise may have better memory

performance regardless of acute exercise. In conclusion, future studies with healthy, young participants may focus on non-emotional association memory tasks with a shorter duration and may benefit from more intensive investigation of participant fitness levels as well as additional heart rate measures (e.g., variability, fluctuations) in order to ascertain whether exercise-based association memory changes are restricted to individuals with a stronger response to exercise.

Preface

This thesis is an original work by Danielle Olafson. The research project, of which this thesis is a part, received research ethics approval from the University of Alberta Research Ethics Board, Project Name "Neuro-metabolic effects of acute exercise on association memory", No. Pro00077772, 1/21/2020.

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List of Abbreviations

5-AFC: 5-alternative forced choice

A-A: alpha-amylase

ACSM: American College of Sport's Medicine

ANOVA: analysis of variance

BDNF: brain derived neurotrophic factor

BF_{10}: Bayes factor for support for H1 over H0

BPM: beats per minute

CO_2: carbon dioxide

DASS-21: Depression, Anxiety, Stress Scales

EEM: emotional enhancement of memory

fMRI: functional magnetic resonance imaging

G1-G3: Experimental groups

GNET: George non-exercise test

GXT: graded exercise test

HPA: hypothalamic-pituitary-adrenal axis

HR: heart rate

IAPS: International affective picture system

IGF-1: insulin-like growth factor

JoM: judgement of memory

LTEQ: Leisure time exercise questionnaire

MET: metabolic equivalent score

MRI: magnetic resonance imaging

MTL: medial temporal lobe

MVPA: Moderate to Vigorous Physical Activity

NN: pair of negative images

nn: pair of neutral images

O_2: oxygen

PANAS: Positive and Negative Affect Scale

PAVS: Physical Activity Vital Sign

rCBF: regional cerebral blood flow

RPE: rate of perceived exertion

RPM: revolutions per minute

V1-V3: Visits (within subs designs)

VO_{2max}: maximum (max) volume (V) of oxygen (O_2)

1. Introduction

Cardiorespiratory fitness and physical exercise have long been recognized as one such stimulation with positive effects on physical, mental, and cognitive health (Basso & Suzuki, 2017; Chang, Labban, Gapin, & Etnier, 2012; Hillman, Erickson, & Kramer, 2008; Kramer, Erickson, & McAuley, 2008). Many studies have investigated possible brain changes after physical exercise that may underlie cognitive changes (Erickson, Hillman, & Kramer, 2015; Hillman et al., 2008). The cognitive domains mostly affected include memory, attention, executive function, and information processing speed (Chang et al., 2012; Ludyga, Gerber, Brand, Holsboer-Trachsler, & Puhse, 2016; Verburgh, Konigs, Scherder, & Oosterlaan, 2014). Several recent reviews have summarized exercise-cognition links and while the overall effects are small, they are mostly positive. However, due to variability in protocols, cognitive outcomes remain a challenge to examine as a whole (Chang et al., 2012; Ludyga et al., 2016). Exercise cannot be considered a cure-all or '"magic pill" for improved cognition in general, but close attention has to be paid to details of the cognitive task at hand, the type and intensity of exercise as well as the cohorts (Chang et al., 2012; Labban & Etnier, 2018; Ludyga et al., 2016). The following background section will first introduce known relationships between exercise and cognition, with a focus on acute exercise interventions and two commonly examined types of episodic memory: Association memory and emotional memory. I will conclude this section by discussing previous findings regarding the combination of emotional and association memory outside the exercise literature, leading to my hypotheses on how exercise might influence emotional association memory.

1.1 Exercise and cognition

The biological basis for exercise effects on cognition has been studied extensively in animal models, and some of these findings have been replicated in humans. Typically, non-human animal studies tested neurochemical, anatomical, and neurophysiological effects of chronic exercise (often weeks to months) (Korol, Gold, & Scavuzzo, 2013; Pagliari & Peyrin, 1995; Radák et al., 2001). Most of these studies have focused on chronic exercise-induced changes of the hippocampus and the associated effects on hippocampal-dependent cognitive-behavioural measures (Basso & Suzuki, 2017; Berchicci, Lucci, & Di Russo, 2013; Erickson et al., 2011; Korol et al., 2013; Newman, Scavuzzo, Gold, & Korol, 2017).

Human studies on relationships between exercise and cognition research can be divided into observational and interventional research. Earlier studies were largely observational, focusing on populations which were objectively 'fit', typically measured by assessing VO_{2max}, i.e., maximal oxygen uptake which measures lung function and increases with habitual exercise, or self-reported engagement in physical activity, and comparing their cognitive functions to those of 'less fit' individuals (Erickson et al., 2009; Kramer et al., 2008; Themanson & Hillman, 2006). This approach is common, especially in aging (Berchicci et al., 2013; Kramer, Erickson, & Colcombe, 2006; Nakata, Yoshie, Miura, & Kudo, 2010) or other populations where interventions may logistically be more difficult to implement than in healthy young individuals university student cohorts (Hakansson et al., 2017; Hegberg, Hayes, & Hayes, 2019; Piao et al., 2013). Such observational research (comparing fit vs not fit populations) has generally found that adults who are more fit tend to outperform their less physically fit counterparts across cognitive domains (Alfini et al., 2016; Erickson et al., 2009; Maass et al., 2016).

While observational designs have high face-validity, the immediate physiological and behavioural effects of exercise are difficult to study in such designs. In addition, even if fit and unfit populations are matched in core demographic variables like age, sex, and education levels, they may differ in other, uncontrolled variables. In contrast, interventional designs allow to explore how an experimental physical exercise intervention will affect some measurable outcome, e.g., cognitive functions. Interventional exercise studies assess effects of chronic (regular bouts of) exercise or acute (single bout of) exercise. Chronic exercise is typically defined as a long-term intervention in which participants engage in routine prescribed exercise over a designated period of time (typically 3-10 weeks) (Li, O'Connor, O'Dwyer, & Orr, 2017). Oftentimes researchers will use longitudinal measurements of changes in cardiovascular fitness, such as VO_2 max, to assess success of the chronic exercise intervention (Alfini et al., 2016). Research in this domain often focuses on how exercise could be used as a long-term treatment, e.g., to protect against neurodegenerative diseases (Kramer et al., 2006). Overall, results of such interventions point to small but positive effects on cognition (Basso & Suzuki, 2017; Chang et al., 2012; Etnier & Chang, 2009; Ludyga et al., 2016). In some studies, cognitive changes were accompanied by brain changes, typically in the hippocampus (Erickson et al., 2011; Holmes, Galea, Mistlberger, & Kempermann, 2004; Redila & Christie, 2006). For example, Erickson et al. (2011) had 120 healthy older adults begin a chronic exercise program which led to improvements in memory and a 2% increase in hippocampal volume after 6 months and 1 year (est. reversal of 1 to 2 years of age-related volume loss). Additionally, they found that this increase in hippocampal volume was related to significantly greater serum levels of BDNF (brain-derived neurotrophic factor) which is a neurotrophin, a protein which promotes neural proliferation and supports neural functioning. Chronic and acute exercise has been shown to enhance DNA demethylation on the BDNF gene which causes an increase in the expression of BDNF in the brain and body (Egan et al., 2003; Etnier et al., 2016; Hakansson et al., 2017; Korol et al., 2013). BDNF is one of the main proposed mechanisms for cognitive improvement in response to exercise (Griffin et al., 2011; Keyan & Bryant, 2017; Leckie et al., 2014; Maass et al., 2016; Marosi & Mattson, 2014). Similarly, (A. Thomas et al., 2016) had 62 sedentary, healthy adults participate in a 6-week cycling program and found that by the end of the six weeks there was a significant increase in hippocampal volume accompanied by an increase in myelination. This program included monitored training sessions five times per week at an intensity ranging from 55%-88% of their maximum heart rate (considered "light" to "hard" exercise intensity, further outlined in section 1.2.1), and were encouraged to reach the 'hard' intensity in the later sessions. Interestingly, six weeks after the last exercise session when participants reported returning to their sedentary lifestyle, their hippocampal volume had returned to baseline, implying that chronic exercise interventions may only transiently increase hippocampal volume. In an interesting 'anti-intervention' neuroimaging study, the authors collected baseline perfusion-weighted MRI imaging data from elite athletes to measure resting cerebral blood flow (rCBF) in gray matter and the hippocampus (Alfini et al., 2016). The athletes then refrained from strenuous exercise for 10 days. Imaging data collected intermittently during this extended period of cessation from exercise showed a significant decrease in overall rCBF in gray matter, with the deterioration being most pronounced in hippocampal tissue and starting around 10 days post-cessation. This outcome suggests that the cerebrovascular system can be quite sensitive to even short-term increases/decreases in exercise, and that the brain adapts rapidly to changes in exercise (Alfini et al., 2016).

While the majority of the intervention-based literature uses chronic exercise interventions, there is a rapidly growing body of work which examines the effect that acute exercise can have on cognition and the brain (Chang et al., 2012). Acute exercise can be defined as a singular bout of physical exercise, resulting in a deviation from resting state (often quantified by change from resting heart rate) (Chang et al., 2012). In a meta-analysis, Chang et al. (2012) found that an acute bout of exercise can lead to cognitive improvements although overall effect sizes were small across studies available at the time, and domains of cognitive improvement were rather variable. While chronic exercise interventions may best model real-life exercise regimens, they are laborious to implement, time-consuming for the participants, and the outcomes are susceptible to the influence of factors that can change over time (motivation, age, injury, life stress…etc). Even in studies with shorter interventions (3-5 weeks), issues of protocol adherence/monitoring can arise and unless researchers are directly supervising and monitoring each training session, it is difficult to ensure that participants are compliant (Chang et al., 2012; Frith, Sng, & Loprinzi, 2017; Labban & Etnier, 2018; Tomporowski & Ellis, 1986). Thus, due to the ease of adherence, time restraints, and other factors, acute exercise interventions are becoming more popular (Chang et al., 2012; Frith et al., 2017; Labban & Etnier, 2018).

Given the evidence from chronic exercise studies, there is generally a consensus that physical fitness has effects on the brain, especially the hippocampus and related behaviours. However, as can be gathered from the brief discussion of the evidence above, there are inconsistencies in how exercise type and intensities as well as control groups are defined, as well as differences in outcomes. This will be further elaborated on in the next section 1.2.

1.2 Acute exercise and cognition

This section will outline the prior research on acute exercise and cognition, and discuss improvements to hypothesis testing and exercise studies. Acute exercise can improve general cognitive functioning (Chang et al., 2012; Etnier et al., 2016; Lambourne & Tomporowski, 2010; Pesce, 2012; Sibley & Etnier, 2003) and can be defined as a singular bout of exercise which is not repeated over a long time course (Chang et al., 2012). Research in the field of acute exercise and cognition is variable and many factors such as exercise intensity, duration, participant fitness levels, timeline to cognitive task, and cognitive task must be considered when establishing a protocol, or evaluating results from prior studies. Given this there is large variability across existing studies with regard to the level or intensity of acute exercise interventions, and the cognitive tasks. In acute exercise intervention studies, the intensity or impact of the intervention should ideally be demonstrated by an objective measure such as a change in heart rate, blood pressure, CO_2 to O_2 output in breath, or blood lactate, and//or participants should be queried about their rate of perceived exertion (Chang et al., 2012; Etnier et al., 1997; Kelly et al., 2014; McMorris & Hale, 2015). Given the consistent relationship observed between physiological factors like this (heart rate, blood pressure, blood lactate…etc) and exercise, these all are appropriate objective measurements of an individual's responsiveness to an exercise intervention (Basso & Suzuki, 2017; Budde et al., 2010; Carro, Trejo, Núñez, & Torres-Aleman, 2003; Chang et al., 2012; Coutts, Rampinini, Marcora, Castagna, & Impellizzeri, 2009; Egan et al., 2003; Erickson, Gildengers, & Butters, 2013; Goekint et al., 2008; Griffin et al., 2011; Hakansson et al., 2017; Hegberg et al., 2019; Jeanneteau et al., 2012). However, many studies in this area have not physiological measurements like this, which complicates interpretation and comparisons of their outcomes (Chang et al., 2012; Frith et al., 2017; Labban & Etnier, 2018; Tomporowski &

Ellis, 1986). Chang et al., (2012) found that while positive effects were found in various timings of exercise paradigms relative to cognitive testing, results varied depending on factors like the duration of exercise, intensity, and the type of cognitive task. For example, reviews of the literature find that measures of memory do not always yield reliable effects in response to acute exercise; short-term and working memory do not seem to benefit, while long-term memory does (Chang et al., 2012; Tomporowski, 2003). Chang et al., (2012) also found that if cognitive performance is assessed during exercise, that positive effects on cognition are only evident if the participant is physically fit, less fit participants tend to experience negative effects of acute exercise on cognitive performance. Furthermore, current prevailing public perceptions of the beneficial effects of exercise could cause expectancy-driven placebo effects if not controlled by the experimental design (Lindheimer, O'Connor, McCully, & Dishman, 2017). Placebo effects are rarely controlled in exercise intervention studies, and when directly studied, it is difficult to draw a conclusion as some find evidence of a placebo effect while others reported no placebo effects (Desharnais, Jobin, Côté, Lévesque, & Godin, 1993; Lindheimer et al., 2017; Szabo, 2013). In a review, Szabo (2013) concluded that both physical exercise and placebo effects likely contribute to the cognitive benefits of acute exercise, but that it is dependent on the individual's strength of expectancy: If the participant expects that exercise has strong effects on cognition, they were more likely to show cognitive benefits compared to participants who did not expect exercise to have a strong effect. Furthermore, the current literature remains uncertain about the situations and extent in/to which the placebo effect is responsible for cognitive improvements after exercise, and advise that research in this field must do its best to control for expectation biases (Szabo, 2013).

Among the most critical factors to influence cognitive outcomes is the intensity of the acute exercise intervention. However, predictions about effects of acute exercise on cognition differ depending on theoretical views: Drive theories, the inverted U hypothesis, or the transient-hypofrontality hypothesis (Huttermann & Memmert, 2014; Loprinzi, Day, & Deming, 2019; Tomporowski & Ellis, 1986). The drive theory predict that the greatest benefits will be observed at the greatest exercise intensity (Zaichkowsky & Naylor, 2004). Drive theories assume that as exercise increases, so does the activation of the hypothalamic-pituitary-adrenal axis (HPA) (Mastorakos & Pavlatou, 2005) which produces endogenous factors that target the hippocampus and the amygdala. Thus, exercise that is more intense should theoretically lead to greater improvements in cognition and memory (Mastorakos & Pavlatou, 2005). The inverted U hypothesis states that an acute bout of exercise of light-to-moderate intensity is optimal for exercise-induced cognitive improvements (Arent & Landers, 2003). If the exercise intensity is too light or too hard, cognition will not improve, or may even be impaired (Chang et al., 2012; Tomporowski, 2003). Lastly, the transient hypofrontality hypothesis suggests that cognitive (in particular prefrontal) functions will be impaired at higher exercise intensities due to the need to reallocate metabolic and cognitive resources away from the cognitive task and towards producing and sustaining the motor demands created by the exercise (Dietrich, 2006). The hypofrontality hypothesis and inverted U hypothesis suggest that when exercise intensity is too high, metabolic resources will be limited, and/or the production of exercise-induced hormones like cortisol may disrupt cognitive processes such as memory consolidation (Loprinzi, Day, et al., 2019).

As already alluded to, the hippocampus is one of the most critical brain region involved in memory consolidation that has been found to be sensitive to exercise interventions, chronically and acutely. Not surprisingly, many cognitive studies have therefore focused on episodic memory which critically relies on functions of the medial temporal lobe, and the hippocampus in particular Episodic memory refers to long-term memory for specific events and their temporal/spatial context. Retrieval of episodic memories involves explicit and conscious recollection (Tulving, 2002). While emotional memory, especially in the animal literature often refers to implicit forms of memory (e.g., fear-conditioning), in which memory is acquired and retrieved without conscious recollection or awareness of memory. Implicit emotional memory tasks such as conditioning or priming are rarely studied in the context of exercise interventions in humans and not covered in the current thesis.

The following sections give an overview on previous studies examining the impact of acute exercise on two specific types of episodic memory: Association memory relying primarily on hippocampal functions and emotional episodic memory, which additionally requires amygdala functions.

1.1.1. Acute exercise and association memory

Association memory is memory for two or more stimuli which must be retrieved together, for example, remembering that a picture of a plane was paired with a picture of a fish. Association memory tasks include a variety of materials and modalities, such as word pairs, face-name pairs, picture pairs, item-location pairs, or word-colour pairs, and so on. Linking the two elements together typically requires intentional encoding instructions in human research, i.e., instructing participants to memorise the information as a pair. The hippocampus is critical for successful association memory (Caplan, Sommer, Madan, & Fujiwara, 2019; Cohen et al., 1999; Hrybouski et al., 2019; Lisman et al., 2017) and regarded as a ‘hub’ which supports the binding of discrete information into associated pairs (Wang et al., 2014). Given the hippocampi's direct involvement with association memory combined with its sensitivity to exercise, researchers have begun to explore the effect exercise may have on association memory. In order to find relevant human studies that examined the effects of acute exercise on association memory, I conducted a systematic literature search that is outlined briefly here.

I searched five databases (Cochrane Library, SPORTDiscus, CINAHL, MEDLINE, and Scopus) in December 2019 using the following search terms: "exercise" (and several synonyms including acute, single bout, gym*, walk*, treadmill, run*, danc*, yoga, aerobic, anaerobic) combined with the logical operator, 'AND" with "cognition", "mem*", "long term*", "episodic", "association". Throughout every screening stage, studies were assessed by two coders and disputes were settled by a third coder. From a total of 3075 studies, duplicates were excluded, leaving 1852 to be screened. Based on abstracts, studies were excluded if they did not include exercise or cognition or were done on animals. A total of 1551 irrelevant studies were excluded and 301 studies went to full-text assessment which proceeded in two steps. First, studies were excluded if the sample was a non-healthy population or contained individuals younger than 18 years of age, or if the exercise intervention was chronic rather than acute. The first stage of full-text evaluation, excluded 163 studies, leaving 138 studies. Final inclusion criteria demanded that the memory task be an associative episodic memory task. A total of twelve studies were identified (total N= 857) based on these criteria. These studies are summarized in Table 1.1. on the next pages.

Table 1.1: Summary of prior acute exercise/association memory studies

Authors	Partici-pants	Interventions	Intensity*	Association-memory task	Study Procedure	Other Measures	Hypotheses	Main Outcomes
Wingate, Crawford, Frith & Loprinzi, (2018)	n = 120 75% female Age (y): 18-35	- **G1, G4**: "Brisk walking" for 15 mins at ~57% max HR - **G2, G5:** Pro-/ retroactive interference, no-activity control - **G3, G6:** No interference, no-activity control	Light	Word pairs, AB/AC paradigm *Encoding:* Intentional *Retrieval:* cued recall **G1-G3**: Proactive interference, recall AB pairs **G4-G6**: Retroactive interference, recall AC pairs	Exerc. (con) → Encoding → Retrieval after 0 min	*Fitness:* MVPA	Exercise reduces proactive and retroactive interference. Exercise enhances associative memory.	No effect of exercise on associative memory (**G2** = **G5**), and retroactive interference (**G4** = **G5**). Detrimental effect of exercise on proactive interference (**G1** > **G2**)
Hotting, Schickert, Kaiser, Roder, & Schmidt-Kassow, (2016)	n = 81 50% female Age (y): M = 22	- **G1:** cycling exercise for 30 mins at 80% max HR - **G2:** cycling exercise at <57% max HR - **G3:** No-activity control	Hard, light	Word-novel word pairs *Encoding:* Intentional *Retrieval:* cued recall	Encoding → Exerc. (con) → Retrieval after 20 mins & 1 day	*Saliva:* Cortisol *Blood:* BDNF *Fitness:* FQPA, physical test: est. VO2 max	Exercise (high intensity > low intensity) during consolidation improves associative memory. BDNF, cortisol, and retention are positively correlated	High-intensity exercise increased association memory after 1 day, compared to no-activity (**G1**>**G3**). Positive correlation between exercise-induced increases in BDNF and retention
Griffin et al, (2011)	n = 47 0% female Age (y): M= 22	- **G1:** Graded cycling exercise to max HR, maintained for 9-30 mins - **G2:** No-activity control	Maximum	Face-name pairs *Encoding:* Intentional *Retrieval:* cued recall	Encoding → Retrieval → Exerc. (con) → Encoding → Retrieval, imm.	*Blood:* BDNF and IGF-1	Exercise improves associative memory and this increase is reflected in exercise-induced	Exercise increased association memory in parallel to increases in BDNF.

Authors	Partici-pants	Interventions	Intensity*	Association-memory task	Study Procedure	Other Measures	Hypotheses	Main Outcomes
							increases in BDNF	
Schmidt-Kassow et al, (2014)	n = 49 51% female Age (y): M= 22.1	- **G1:** Treadmill for 30 mins at <50% of max HR - **G2:** No-activity control	Very light	Word – novel word pairs *Encoding:* Intentional *Retrieval:* cued recall	Encoding during exerc. (con) → Retrieval after 1 day	*Salivary:* cortisol (exp.1) *Blood:* BDNF (exp.2)	Exercise during encoding improves associative memory. BDNF, cortisol, and memory are positively correlated	Exercise during encoding increased associative memory after 1 day. Positive correlation between exercise-induced increases in cortisol (but not BDNF) and memory
Schmidt-Kassow et al, (2013)	n =105, 100% female Age (y): M= 22.7	- **G1-G2:** Cycling for 30 mins to ~68% max HR - **G3:** No-activity control	Moderate	Word – novel word pairs *Encoding:* Intentional *Retrieval:* cued recall	**G1/G3**: Encoding/rest during exerc. (con) → Retrieval after 30 mins & 2 days **G2**: Exerc. (con) → Encoding → Retrieval after 2 days	*Blood:* BDNF *Fitness:* FQPA	Exercise during and before encoding improves associative memory via increases in BDNF better than no exercise. BDNF and memory are positively correlated.	Exercise during encoding increased memory at either delay, especially after 2 days No effect of BDNF.
McNerney & Radvansky, (2015)	n = 136 Age (y): M = 19.22	- **G1:** 2 mins intervals of sprints for 10 mins to ~71% max HR - **G2:** 30 mins of Sudoku	Moderate	Word pairs *Encoding:* Intentional *Retrieval:* cued recall	**Visit 1:** Exerc. (con) → Encoding → Retrieval, imm. & 7 days	--	Exercise improves associative, procedural and text memory	Regardless of exercise timing (before/after memory tasks), exercise improved procedural and text memory but

Authors	Partici-pants	Interventions	Intensity*	Association-memory task	Study Procedure	Other Measures	Hypotheses	Main Outcomes
				And other non-associative memory tasks	**Visit 2:** Encoding → Exerc. (con) → Retrieval, imm. & 7 days			had no influence on verbal paired-associates learning.
Loprinzi, Koehler, et al, (2019)	n = 120 76% female Age (y): M= 21.2	- **G1/G3:** Treadmill walking for 15 minutes at 50% of HR - **G2/G4:** no-activity control	Very light	Object-location-timing *Encoding:* Incidental *Retrieval:* cued recall **G1, G2:** Instructed episodic memory specificity in retrieval	Exerc. (con) → Encoding → Retrieval, imm.	--	Episodic-specificity induction (**G1**, **G2**) and exercise (**G1**, **G3**) improve associative memory **(G1>G2 =G3>G4)**	No main effect of exercise on association memory. Trend for additive effects of exercise and episodic-specificity induction.
Johsnon, Yao, Zou, Xiao, & Loprinzi, (2019)	n = 24 54.2% female Age (y): M= 21.5	- **Visit 1:** sprints to ~76% max HR - **Visit 2:** Mental imagery of the same exercise	Moderate	Word pairs *Encoding:* Intentional *Retrieval:* cued recall Object-location-timing *Encoding:* Incidental *Retrieval:* cued recall	Exerc. (con) → Encoding → Retrieval, imm.	*Fitness:* MVPA	Exercise and imagined exercise will have similar effects on memory.	No significant difference in memory after real or imagined exercise.
Coleman, Offen, &	n = 52 52% female Age (y):	- **G1, G3:** Alternating 1 min intervals of walking and jump	N/A	Object-location pairs	**G1, G2:** Exerc. (con)→	*Cognition:* Selective	Exercise group should have better recognition	Exercise improved associative

Authors	Partici-pants	Interventions	Intensity*	Association-memory task	Study Procedure	Other Measures	Hypotheses	Main Outcomes
Markant, (2018)	M= 19.7	rope for 10 min, to 6/10 a perceived exertion scale - **G2, G4:** Active control: alternating 1 min intervals of walking and watching a video for 10 minutes		*Encoding:* Intentional *Retrieval:* cued recall	Encoding→ Retrieval, imm. → Exerc. (con) → Attention task **G3, G4:** Exerc. (con) → Attention task → Exerc. (con) → Encoding → Retrieval, imm.	attention task, other tasks	and object location memory. Gender-specific effects: Women have better associative memory overall, men benefit most from exercise-effects on memory	object-location memory in men only, and restricted to men whose memory was tested after two exercise sessions
Van Dongen, Kersten, Wagner, Morris & Fernandez, (2011) Exp. 1 only	n = 72 66.6% female Age (y): M= 21.9	- **G1, G2:** Ergometer for 35 mins at 80% max HR - **G3:** No-activity control	Hard	Object-location pairs *Encoding:* Intentional *Retrieval:* cued recall of location by object cue, confidence ratings	**G1:** Encoding → Retrieval, imm. → Exerc. → Retrieval after 3 hrs and after 2 days **G2, G3:** Encoding → Retrieval, imm. → 3 hr delay → Exerc. (con) → Retrieval after 2 days	*Imaging:* *f*MRI	Research goals: To test whether post-learning exercise affects memory retention in a time-dependent manner. To test the neural substrate of memory retrieval after exercise.	Delayed exercise (**G2**) after encoding improved association memory at 48h compared to immediate (**G1**) or no exercise (**G3**). Delayed exercise **(G2)** increased hippocampal pattern similarity for correct responses during retrieval at 48h

Authors	Partici-pants	Interventions	Intensity*	Association-memory task	Study Procedure	Other Measures	Hypotheses	Main Outcomes
Loprinzi, Day, et al, (2019)	n = 24 70.8% female Age (y): M= 21.9	- **G1:** Treadmill running for 20 mins to 70% max HR - **G2:** No-activity control	Moderate	Word pairs *Encoding:* Intentional *Retrieval:* cued recall	Encoding during exerc. (con) → Retrieval during exerc. (con)	*Fitness:* MVPA	High-intensity exercise leads to lack of metabolic resources (~hypofrontality) and leads to impaired memory for information encoded or retrieved during exercise	Association memory was impaired in the exercise group compared to the no-activity control.
Winter et al, (2007)	n = 27 0% female Age (y): M= 22.2	- **Visit 1:** No-activity control - **Visit 2:** intense: 2 sets of sprints for 3 mins with 2 min breaks at ~94% max HR - **Visit 3:** moderate: running for 40 mins at ~70% max HR	Maximum, moderate	Picture-non-word pairs *Encoding:* Intentional *Retrieval:* cued recall	Exerc. (con) → Encoding → Retrieval, imm.,mins, 7 days, 8 months	*Blood:* BDNF, monoamines, lactate levels *Fitness:* FFKA, physical test to determine lactate threshold	Both maximum and moderate intensity exercise improve learning and memory. Monoamine levels may have relationship to memory performance.	Maximum intensity exercise improves recall after 15 minutes (not later). No memory improvement for moderate. Absolute dopamine and epinephrine levels after maximum intensity exercise were related to better memory (immediate and long term).

* Intensity of the exercise intervention, staging based on standards set by the American College of Sport's Medicine (American College of Sports Medicine, 2010, p.2); Abbreviations: AA: Alpha amylase; BDNF: Brain derived neurotrophic factor; DASS-21: Depression, Anxiety, Stress Scales – 21 items; FFkA: Freiburger Fragebogen zur koerperlichen Aktivitaet; G1-G3: Experimental groups; GNET: George Non-Exercise Test, HR: Heart rate; IAPS: International Affective Picture System; LTEQ: Leisure time exercise questionnaire, PANAS: Positive and Negative Affect Scale, PAVS: Physical Activity Vital Sign; V1-V3: Visits (within subs designs).

The results from these studies will be discussed and interpreted based on moderators used in previous reviews on similar topics (Chang et al., 2012; Etnier et al., 1997; Lambourne & Tomporowski, 2010; Tomporowski & Ellis, 1986): Sample characteristics, study design, exercise intensity, and memory task (type and timing).

Sample Characteristics and Study Design

While overall sample sizes ranged from 24 to 136 participants, these were typically split into several experimental conditions arriving at around 20-30 participants per condition. All twelve studies were conducted on young adults (18-35 years of age). Two studies included only men (Griffin et al., 2011; Winter et al., 2007), one study included only women (Schmidt-Kassow et al., 2013), and the remaining nine studies included both men and women.

With regard to study design, most of the studies were between-subjects, but few used within-subject designs (Johnson, Yao, Zou, Xiao, & Loprinzi, 2019; Winter et al., 2007). The effect of exercise was typically compared to either no-activity control (Griffin et al., 2011; Loprinzi, Day, et al., 2019; Loprinzi, Koehler, et al., 2019; Schmidt-Kassow et al., 2013; Schmidt-Kassow et al., 2014; Wingate, Crawford, Frith, & Loprinzi, 2018) or an alternative activity (Coleman, Offen, & Markant, 2018; McNerney & Radvansky, 2015). Furthermore, there were studies using two exercise groups with different intensity (Hotting, Schickert, Kaiser, Roder, & Schmidt-Kassow, 2016; Winter et al., 2007). Finally, Johnson et al. (2019) had no control group and instead used two intervention groups: exercise and visualized/imaginary exercise. The number and type of control group(s) showed no conceivable pattern in findings across studies as outlined in Table 1.2 and Figure 1.1.

Table 1.2: Findings in twelve association memory studies by control group

	No-activity control	Alternative activity control	Intense & light exercise vs. no-activity
Better association memory	Griffin et al, (2011) Schmidt-Kassow et al, (2014) Schmidt-Kassow et al, (2013) Van Dongen et al, (2016)	Coleman et al, (2018) (in men only)	Hotting et al, (2016) (intense vs. control) Winter et al, (2007)
Worse association memory	Loprinzi, Koehler, et al, (2019)		
No effect	Loprinzi, Day et al, (2019) Wingate et al, (2018)	McNerney & Radvansky, (2015) (within subject) Johnson et al, (2019)	

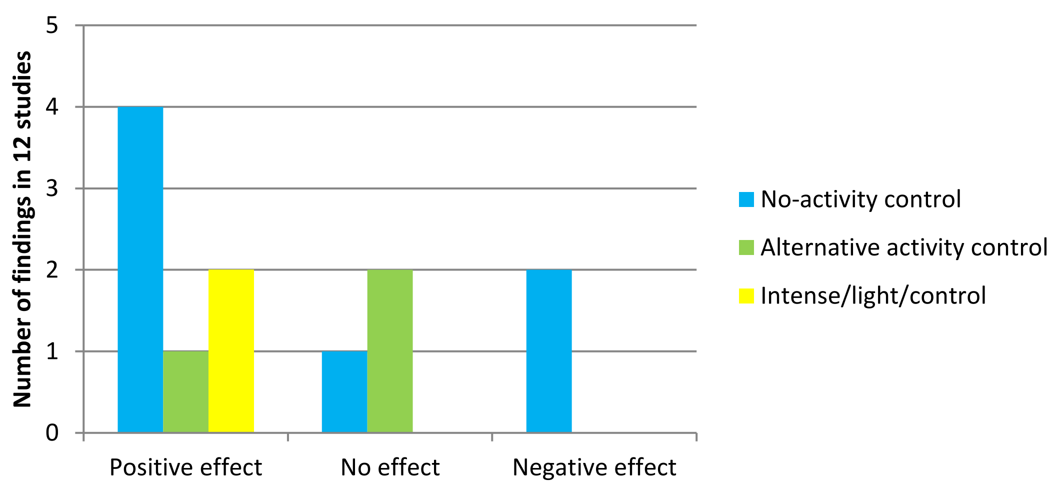

Figure 1.1: Findings in twelve association memory studies by study design. "Positive effect" refers to better associative memory with exercise intervention relative to control(s)

Exercise Intensity

Exercise intensity is one of the most important and most frequently considered moderators of effects on cognition (Chang et al., 2012). Consequently, several of the twelve association memory studies explicitly hypothesized that exercise intensity would be a critical factor for the magnitude or presence of association memory effects (Hotting et al., 2016; Loprinzi, Day, et al., 2019; Winter et al., 2007) based on drive theories, the inverted U hypothesis, or the transient-hypofrontality hypothesis (see section 1.2). Since no standard classification of exercise intensity was used that was comparable across studies, I re-classified all exercise interventions according to guidelines by the American College of Sport's Medicine (ACSM). The ACSM defines five different intensities of exercise by providing percentage-based ranges of heart rate (Table 3). This scale was chosen due to its unambiguous ranges, as well as its use in previous reviews of exercise-cognition interactions (Chang et al., 2012).

Table 1.3: Exercise intensities and respective heart rate percentage ranges (percentage of max. HR) based on the American College of Sport's Medicine (2010, p.2).

Exercise intensity	Exercise intensity range (% of max HR)
Very light	<50%
Light	50% – 63%
Moderate	64% – 76%
Hard	77% – 93%
Maximal	94% and up

Only one study was not possible to classify in this way as it provided insufficient information on heart rate (Coleman et al., 2018). Instead, I used the authors' description to classify this study's exercise intensity on a scale of Rate of Perceived Exertion (RPE).

Of the twelve studies examining influences of acute exercise on memory, two used very light intensity exercise (Loprinzi, Day, et al., 2019; Schmidt-Kassow et al., 2014), two used light intensity exercise (Hotting et al., 2016; Wingate et al., 2018), five had moderate intensity exercise (Loprinzi, Koehler, et al., 2019; McNerney & Radvansky, 2015; Schmidt-Kassow et al., 2013; Winter et al., 2007), two used hard intensity (Hotting et al., 2016; Van Dongen, Kersten, Wagner, Morris, & Fernandez, 2016), and two used maximal intensity (Griffin et al., 2011; Winter et al., 2007). Two studies used more than one exercise intervention of differing intensities (Hotting et al., 2016; Winter et al., 2007) and were counted twice. Table 1.4 and Figure 1.2 summarise the direction of the study findings by exercise intensity.

Table 1.4: Findings in twelve association memory studies by exercise intensity.

	Very light	Light	Moderate	Hard	Maximal
Better association memory	Schmidt-Kassow et al, (2014)	-	Schmidt-Kassow et al, (2013)	Hotting et al, (2016) Van Dongen et al, (2016)	Winter et al, (2007) Griffin et al, (2011)
Worse association memory	-	-	Loprinzi, Koehler, et al, (2019)	-	-
No effect	Loprinzi, Day, et al, (2019)	Hotting et al, (2016) Wingate et al, (2018)	Winter et al, (2007) McNerney & Radvansky, 2015) Johnson et al, (2019)	-	-

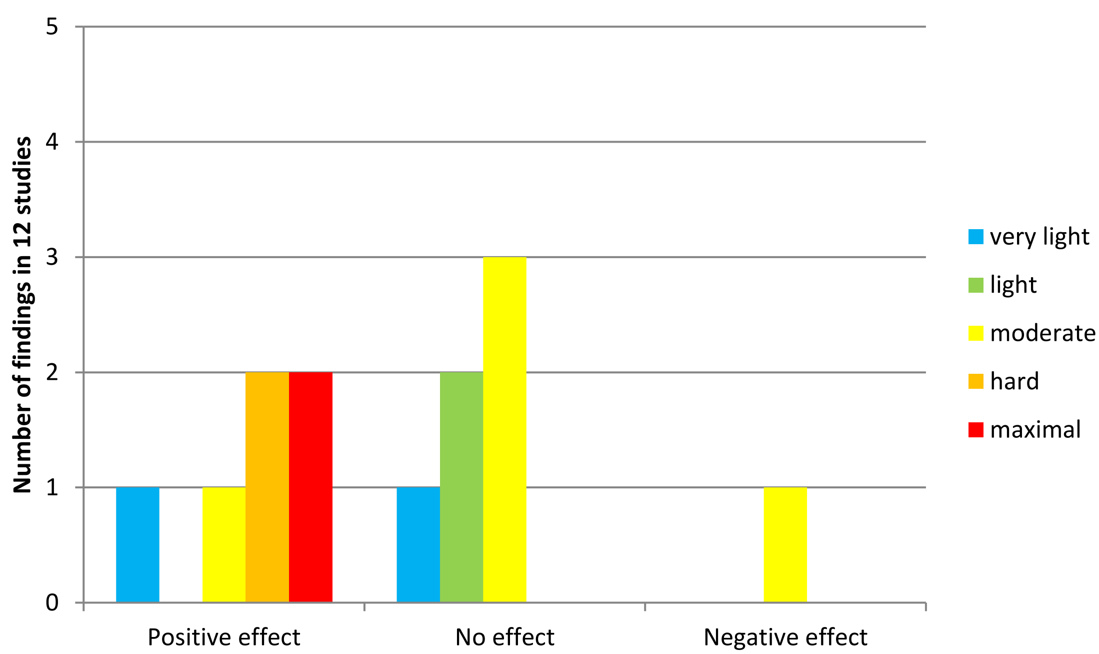

Figure 1.2: Number of findings in twelve association memory studies by exercise intensity.

As apparent in Figure 1.2, exercise intensity seemed to have an influence on associative memory effects. In the two studies in which maximal intensity exercise was used, positive effects on association memory performance were observed (Griffin et al., 2011; Winter et al., 2007). Griffin et al. (2011) found that a graded exercise test (GXT), which pushed participants to their absolute maximum, led to improved performance on a face-name matching task, compared to a sedentary control group. Similar positive results were obtained by Winter et al. (2007), when participants exercised at maximum intensity and demonstrated quicker recall for picture-non-word associations compared to when they engaged in moderate-intensity exercise. The two studies which had participants exercise to a hard intensity level also reported significantly improved association memory (Hotting et al., 2016; Van Dongen et al., 2016). In Hotting et al. (2016), hard-intensity (but not light-intensity) exercise led to better retrieval of word-novel-word pairs after one day. In experiment 1 of Van Dongen et al. (2016), object-location learning was improved by exercising to hard intensity levels at three hours following encoding, with retrieval occurring after two days. In contrast, the two studies using light intensity exercise found no significant effects on association memory and four out of five studies with moderate levels of exercise either observed no effect, or a negative effect on memory (Johnson et al., 2019; McNerney & Radvansky, 2015; Winter et al., 2007). Hotting et al. (2016) directly compared effects of light intensity to hard intensity exercise, with positive findings only for hard intensity and no effect for light intensity.

Timing of intervention relative to and type of memory task

Owing to the described differences in exercise intensity, classification of the findings by the type of material/task as well as delay between encoding and retrieval is complicated. However, Table

1.5, Figure 1.3, and Figure 1.4 provide an overview based on findings from the twelve studies. The majority of the studies used cued recall procedures, typical for association memory tasks. While there was no obvious pattern across findings by type of material (verbal, visual, or mixed), it seems that delayed retrieval was more likely affected by acute exercise than immediate retrieval. When interpreting the outcomes as a function of differences in timing between the exercise relative to the memory task (before/after/during encoding or retrieval) the majority of studies performed the exercise either prior to (n=6/12) or after encoding (n=3/12), but always before retrieval. The remaining studies (n=3) had participants exercise during encoding. However, two of these studies used stationary cycling (Schmidt-Kassow et al., 2013; Schmidt-Kassow et al., 2014), while only one of the twelve studies deviated from these standard protocols and had participants exercise on a treadmill while simultaneously encoding and retrieving word pairs (Loprinzi, Day, et al., 2019). Using this design, Loprinzi, Day, et al. (2019) observed a negative influence of exercise on association memory. I suggest that when interpreting this result the increased cognitive demand that treadmill exercises require for balance and coordination should be taken into account (i.e., transient hypofrontality). This interpretation should not be extended as boldly to Schmidt-Kassow et al. (2013) or Schmidt-Kassow et al. (2014) as stationary cycling is far less mentally demanding (requires far less coordination than a treadmill workout).

Table 1.5: Number of findings in twelve association memory studies by task modality, and delay time.

	Verbal	**Visual**	**Mixed**	**Immediate retrieval**	**Delayed retrieval**
Better association memory	Winter et al, (2007) Griffin et al, (2011) Schmidt-Kassow et al, (2013) Schmidt-Kassow et al, (2014) Hotting et al, (2016)	Coleman et al, (2018)	Van Dongen et al, (2016)	Winter et al, (2007) Griffin et al, (2011) Van Dongen et al, (2016) Coleman et al, (2018)	Winter et al, (2007) Schmidt-Kassow et al, (2013) Schmidt-Kassow et al, (2014) Van Dongen et al, (2016) Hotting et al, (2016)
Worse association memory	Loprinzi, Koehler, et al, (2019)			Loprinzi, Koehler, et al, (2019)	Loprinzi, Koehler, et al, (2019)
No effect	McNerney & Radvansky, (2015) Wingate et al, (2018)		Van Dongen et al, (2016) Loprinzi, Day, et al, (2019)	McNerney & Radvansky, (2015) Wingate et al, (2018) Loprinzi, Day, et al, (2019) Johnson et al, (2019)	McNerney & Radvansky, (2015)

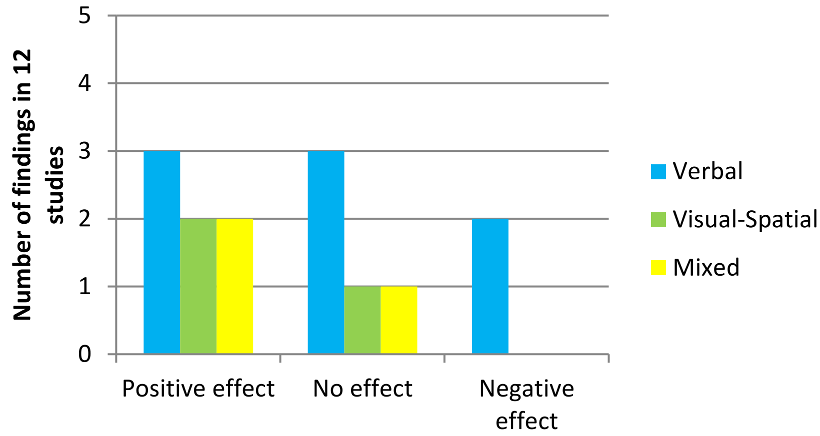

Figure 1.3: Number of findings in twelve association memory studies by task modality.

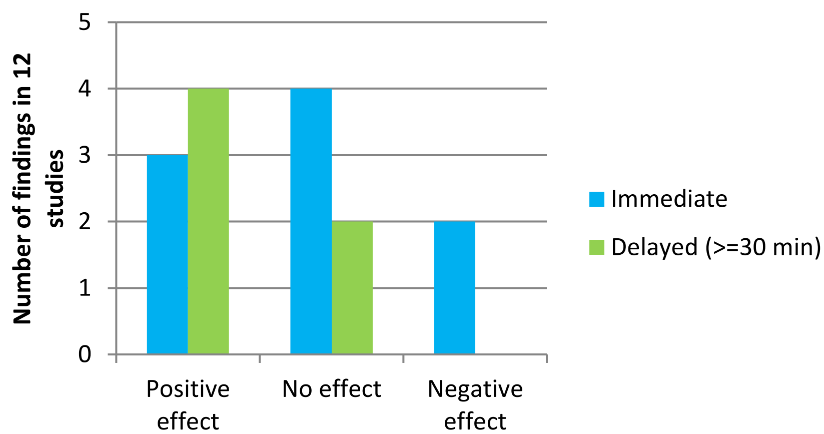

Figure 1.4: Number of findings in twelve association memory studies by retrieval delay time.

In conclusion, findings from these twelve studies on association memory point to more likely benefits of high or maximum intensity exercise intensity on association memory, especially if tested after some delay. However, whether exercise needs to take place immediately prior or after learning remains unclear, as does the question whether some materials or tasks are more sensitive than others.

Although not discussed here in detail, when physiological measurements were taken in some of these studies (e.g., VO2max, cortisol, alpha-amylase…etc), these measurements were typically related to exercise intensity and sometimes also to memory performance (Griffin et al., 2011; Hotting et al., 2016; Schmidt-Kassow et al., 2013; Schmidt-Kassow et al., 2014; Van Dongen et al., 2016; Winter et al., 2007). Thus, physiological measures might be a useful metric to ensure exercise intensity is being reached and may relate to the strength of the exercise effects on association memory.

1.1.2. Acute exercise and emotional memory

Emotionally potent materials are often remembered more vividly and recalled with greater ease, compared to non-emotional materials (Cahill et al., 1996; LeDoux, 1992; McGaugh, 2004; McGaugh, McIntyre, & Power, 2002; Talmi, 2013; Talmi et al., 2013) an effect called the emotional enhancement of memory (EEM). Evolutionarily, EEM is adaptive as learning potentially dangerous or helpful environmental cues is important for survival (LeDoux, 1992; Schumann, Bayer, Talmi, & Sommer, 2018). Mechanistically, EEM is thought to be facilitated by the activation of hypothalamic pituitary adrenal (HPA) axis, which stimulates both the hippocampus and amygdala, and this amygdala activation may cause additional stimulation of the hippocampus, thus improving memory formation (Bass, Nizam, Partain, Wang, & Manns, 2014; McIntyre, McGaugh, & Williams, 2012; Schumann et al., 2018). Physiological arousal in response to emotional stimuli has been shown to underlie memory modifications for emotional relative to neutral items in healthy people (Cahill et al., 1996; McGaugh, 2004; McGaugh et al., 2002; Talmi, 2013; Talmi et al., 2013; Wunsch, Meier, Ueberholz, Strahler, & Kasten, 2019) as well as intrusive memories of emotionally arousing events in clinical populations (e.g., post-traumatic stress disorder) (Hegberg et al., 2019). Thus, increasing physiological levels of arousal via an acute bout of physical exercise may not just increase episodic memory in general, but influence episodic memory for emotional information specifically.

In order to evaluate previous studies using episodic memory tasks with emotional material, I used the outcomes of my systematic literature search that had identified 138 studies which focused on effects of acute exercise interventions on episodic memory in healthy adult populations. Materials in the full-texts of these studies were screened to be emotional in nature and tasks were inspected to be episodic memory tasks. Studies using non-episodic memory tasks, such as conditioning, working memory, or priming were excluded. A total of 4 studies were identified (total N=213) and these studies are summarized in Table 1.6 below. In the context of emotional memory paradigms, the four studies assumed that an acute bout of exercise would increase physiological arousal to some degree, and that this arousal should specifically enhance memory for emotional stimuli (McGaugh, 2004; McGaugh et al., 2002). While some of these studies may use incidental encoding, the retrieval portion of all four requires participants to explicitly recall information they have previously been presented. This allows these memory tasks to be categorized as episodic.

Table 1.6: Summary of prior acute exercise/emotional memory studies

Authors	Participants	Intervention groups	Intensity*	Emotional Memory task	Study Procedure	Other measures	Hypotheses	Outcome
Wade & Loprinzi (2018b)	n = 34 100 % female Age (y): M= 20.7	- **G1**: Treadmill walking at a "brisk pace" for 15 mins - Max. HR (baseline): 130 (79) bpm - **G2**: No-activity control	Moderate	IAPS pictures *Encoding*: Incidental *Retrieval*: Remember/ know recognition	Exercise (con)→ Encoding→ Retrieval after 1, 7, 14 days	*Fitness*: PAVS	Exercise enhances/ slows the decay of emotional memory	Exercise had no influence on recognition memory accuracy at any of the delays.
Keyan & Bryant (2017)	n = 62 68 % female Age (y): 18-36	- **G1**: Stepping exercise with weights for 10 mins, 5 mins at 60-85% of max. HR - **G2**: Easy walking-control	Light to Hard	IAPS pictures *Encoding*: Incidental *Retrieval*: Free recall	Exercise (con)→ Encoding→ Retrieval after 2 days	*Saliva*: Cortisol, BDNF genotype *Fitness*: LTEQ *Mood*: DASS-21	Exercise enhances emotional memory, especially in val66met carriers.	Exercise improved recall of all images. In BDNF val66met carriers only, exercise-induced cortisol enhanced emotional memory
Weinberg, Hasni, Shinohara, & Duarte (2014)	n = 46 63 % female Age (y.): M= 20.41	- **G1**: Resistance leg flexion exercise for 20-30 mins, HR (~80 bpm) unchanged, AA increased - **G2**: Passive leg-movement control	Very light	IAPS pictures *Encoding*: Incidental *Retrieval*: Remember/ know recognition	Encoding→ Exercise(con)→ Retrieval after 2 days	*Saliva*: Alpha amylase *Mood*: PANAS	Exercise-induced arousal improves memory, esp. recollection for negative images	Exercise improved recognition memory for all images, but specifically positive images. Higher responders to exercise-induced arousal had worse recollection for neutral items.

Bruhl, Heinrichs, Bernstein, & McNally (2019)	n =71 42 % female Age (y.): M= 31.41	- **G1**: Cycling for 25 mins at 60 -70% of HR max. - **G2**: Tetris video game play for 25 minutes - **G3**: No-activity control	Moderate	Emotionally traumatizing movie *Encoding*: Incidental *Retrieval*: Recognition memory (true/false)	Encoding→ Exercise(con)→ Retrieval after 7 days	*Fitness*: GNET *Mood*: DASS-21	Tetris and exercise reduce trauma-memory intrusions Exercise, but not Tetris, improves explicit trauma memories	Tetris but not exercise reduced trauma memory intrusions. Neither intervention affected explicit memory for the movie.

* Intensity of the exercise intervention, staging based on standards set by the American College of Sport's Medicine (American College of Sports Medicine, 2010, p.2);

Abbreviations: AA: Alpha amylase; BDNF: Brain derived neurotrophic factor; DASS-21: Depression, Anxiety, Stress Scales – 21 items; FFkA: Freiburger Fragebogen zur koerperlichen Aktivitaet; G1-G3: Experimental groups; GNET: George Non-Exercise Test, HR: Heart rate; IAPS: International Affective Picture System; LTEQ: Leisure time exercise questionnaire, PANAS: Positive and Negative Affect Scale, PAVS: Physical Activity Vital Sign; V1-V3: Visits (within subs designs).

Similar to section 1.2.1, the results from these four studies will be discussed and interpreted based on sample characteristics, study design, exercise intensity, and the type, materials, and timing of the memory tasks. In addition, interactions with mood and mood changes will be addressed.

Sample Characteristics and Study Design

Sample sizes ranged from 34 to 71 participants, split into two experimental groups consisting of 15-30 participants (Keyan & Bryant, 2017; Wade & Loprinzi, 2018b; Weinberg et al., 2014) in three of the studies. One study had three experimental groups of ~23 participants (Bruhl et al., 2019). All four studies were conducted on young adults (18-32 years of age). One study included only women (Wade & Loprinzi, 2018a), the other three studies included both men and women.

All four studies had a between-subjects design, two compared an exercise intervention group to a no-activity control (Keyan & Bryant, 2017; Wade & Loprinzi, 2018b) and two used a passive movement control (Keyan & Bryant, 2017; Weinberg et al., 2014). Both studies which used a no-activity control found no effect of exercise on emotional memory (Keyan & Bryant, 2017; Wade & Loprinzi, 2018b) whereas those with a passive movement control found that while exercise did not affect emotional memory, overall memory, regardless of the emotional valence of the materials, was improved (Keyan & Bryant, 2017; Weinberg et al., 2014).

Exercise Intensity

The exercise interventions included treadmill walking (Wade & Loprinzi, 2018a), weighted stepping exercise (Keyan & Bryant, 2019), resistance training (Weinberg et al., 2014), and cycling (Bruhl et la., 2019). As explained above, in order to standardize the exercise intensities, I re-classified all interventions according to the ACSM guidelines. According to ACSM reclassification, one study used very light intensity exercise (Weinberg et al., 2014), two used moderate intensity exercise (Bruhl et al., 2019; Wade & Loprinzi, 2018b), and one used up to hard intensity exercise (although minimum effort required ranged from light intensity to hard intensity) (Keyan & Bryant, 2019). While (Keyan & Bryant, 2019) had a wide range of intensity they accepted, none of the studies used more than one intensity of exercise. This lack of more than one exercise intensity group within these study designs makes interpretation of these results more difficult, and increases the chances of placebo effects influencing results.

Acute exercise had no effect on memory for emotional materials specifically in all but one study (Keyan & Bryant, 2019). Keyan and Bryant (2019) had participants exercise for 10 minutes total, with five being at a light to hard intensity (60-88% of max heart rate). They found that this acute bout of exercise led to better recall on all visual stimuli overall but of positive stimuli in particular (pictures like a happy child, or ice-cream truck, or puppy). The remaining three studies observed no effect of acute exercise on emotional memory specifically (Bruhl et al., 2019; Wade & Loprinzi, 2018b; Weinberg et al., 2014). The two studies using moderate intensity exercise observed no effects on memory at all (Bruhl et al., 2019; Wade & Loprinzi, 2018b), Weinberg et al. (2014) used very light intensity exercise observed an improvement in memory overall, but not for emotional materials, and, as previously discussed, light to hard intensity exercise in Keyan and Bryant (2019) led to not only an increase in overall memory, but memory for positive pictures specifically. Thus, based on these findings, exercise intensity was unlikely a critical moderating factor of effects across these four emotional memory studies. The lack of research in this specific field, coupled with the lack of proper control groups, and lack of more than one exercise intensity group demands more rigorous research on this topic.

Mood

Trait- and state-levels of (low) mood have been linked extensively to cognition, in particular episodic memory (De Raedt & Koster, 2010; Stawski, Sliwinski, & Smyth, 2009). Therefore, it is important to identify if and how studies of exercise and emotional memory assessed participants' mood prior and after exercising (Basso & Suzuki, 2017). Three of the four studies measured mood to either assess pre-intervention mood differences within subjects to ensure that trait differences were not causing underlying effects, and/or to assess a change in mood following intervention (Bruhl et al., 2019; Keyan & Bryant, 2017; Weinberg et al., 2014). (Weinberg et al., 2014) tested mood using the Positive and Negative Affect Scale (PANAS; (Watson, Clark, & Tellegen, 1988) at the beginning and at the end of their two test sessions. At the beginning of the experiments, Bruhl et al. (2019) and Keyan and Bryant (2019)*,* assessed mood using the short form of the Depression, Anxiety, and Stress-Scales (DASS-21;(Henry & Crawford, 2005); (Lovibond & Lovibond, 1995), a self-report measure of depression, anxiety, and stress within the past 7 days. (Weinberg et al., 2014) did not report outcomes of the PANAS. The studies using the DASS-21 (Bruhl et al., 2019; Keyan & Bryant, 2017) reported no differences in mood between exercise and control group(s), and between BDNF genotypes (Keyan & Bryant, 2017). Potential influences of mood on the link between exercise and memory performance were therefore not further reported or analysed in these studies. Measurements like the DASS-21 allow for a non-clinical assessment of depression, anxiety, and stress; all three of these factors are associated with decreased hippocampal volume, and a decrease in long term memory capability (Marchetti et al., 2018; Owens, Stevenson, Hadwin, & Norgate, 2012). This information coupled with the common usage of an undergraduate population for these research samples, a population known for experiencing high levels of stress, depression, and anxiety, furthers the importance of mood assessment (Owens et al., 2012). Given the ease in which measurements of mood can be assessed this would be an important addition to any study on emotional memory.

Memory Task

Measuring emotional memory in a laboratory setting requires at least some level of response to the emotional nature of the materials (or "emotion-induction"). Visual stimuli are more potent in that regard than verbal materials, and all four exercise studies used visual materials, including static images from the International Affective Picture System (Lang, Bradley, & Cuthbert, 2008) in three of the four studies (Keyan & Bryant, 2017; Wade & Loprinzi, 2018b; Weinberg et al., 2014), whereas Bruhl et al. (2019) used an 'emotionally traumatizing' movie.

While the memory tasks and materials used by Weinberg et al. (2014), Keyan and Bryant (2017), and Wade and Loprinzi (2018a) are typical laboratory assessments of emotional memory in humans, the task used by Bruhl et al. (2019) was unique. Bruhl et al. (2019) sought to induce trauma-like memories via an 'emotionally traumatizing movie', which consisted of scenes of car accidents and surgeries. After viewing the film participants did aerobic exercise to interrupt memory consolidation/processing and decrease later intrusive memories. Similar to the other studies, they predicted better explicit memory for the traumatizing information and at the same time, dissimilarly, they predicted reduced involuntary memories for the trauma information.

Encoding in all four studies was incidental, unlike the intentional learning instructions typically used in association memory studies. That is, rather than telling participants to study and memorize the materials, they were asked to do something else, including passive viewing (Bruhl et al., 2019; Keyan & Bryant, 2017), performing valence-/arousal ratings of each picture (Wade & Loprinzi, 2018a) or performing indoor/outdoor judgements for each picture (Weinberg et al., 2014). Incidental encoding is typical in emotional memory studies, permitting the emotional connotations of the material to exert their influences on memory relatively unaltered, i.e., not 'overtaken' by an explicit encoding instruction that may distract participants from the emotional content.

Retrieval was probed with recognition memory tasks in all but Keyan and Bryant (2017), who used free recall, i.e., having participants describe the previously seen pictures from memory While free recall is an episodic (i.e., hippocampal) memory task, recognition memory can be either episodic or non-episodic. Recognition memory tasks included remember/know judgements in two studies (Wade & Loprinzi, 2018b; Weinberg et al., 2014). Briefly, remember/know recognition memory tasks aim to differentiate episodic from non-episodic recognition memory performance (Yonelinas, Hopfinger, Buonocore, Kroll, & Baynes, 2001). In such tasks, participants are typically instructed that there are two types of memories: 1) Episodic recollection of specific details and contexts of some previous event or stimulus. Such subjective experiences should receive a 'remember' judgement in the recognition memory test. 2) Non-episodic familiarity-based memory without recalling specific details surrounding the previous event or stimulus. Such memories are thought to simply evoke a sense of subjective familiarity with some event or stimulus, but they could only be rated with 'know' judgement. Within this framework, 'remember' judgements would qualify as episodic memory, whereas 'know' judgements would not. Memory performance in the two studies using the remember/know recognition memory distinction was analysed in several ways, adding remember and know judgements into an overall index of memory accuracy, as well as separately for remember- and for know judgements. Both studies also provided data on adjusted recognition memory performance ('discrimination') by subtracting false recognition answers. Weinberg et al. (2014) found that memory recognition improved in response to exercise, while Wade and Loprinzi (2018a) found no impact on recognition memory.

Arousal effects on memory are typically stronger at a delay than immediately (Park, 2005; Sharot & Phelps, 2004) and all four studies implemented a delay before memory retrieval, with none assessing immediate memory. The shortest delay was 24 hours (Wade & Loprinzi, 2018a) and the longest delay was 14 days (Wade & Loprinzi, 2018a); the two studies finding that exercise increased general memory performance used a 2-day delay (Keyan & Bryant, 2017; Wade & Loprinzi, 2018b). The lack of any immediate measure of memory following exercise is understandable based on the emotional memory literature, but adding an immediate retrieval task would be particularly informative for an acute exercise intervention.

Finally, with regard to the order of exercise to memory task, two of the four studies performed exercise first, followed by encoding and delayed retrieval (Keyan & Bryant, 2017; Wade & Loprinzi, 2018b), whereas the other two studies first performed encoding, followed by exercise, and then followed by delayed retrieval (Bruhl et al., 2019; Weinberg et al., 2014), with no conceivable patterns in the outcomes along the order of these tasks.

An overall conclusion is hard to draw, as there are only four studies and mostly non-significant outcomes. It is further unclear from these findings whether exercise might have effects on encoding or consolidation of emotional memory. However, it seems that the outcomes of studies which used harder exercise intensities had more robust outcomes than those that did not. Lack of control groups, lack of additional exercise groups, lack of placebo-effect control, and no immediate memory assessments indicate that the relationship between acute exercise and emotional memory requires more research with better study designs.

1.1.3. Emotional Association Memory

As alluded to already, many studies have reported better memory for emotionally valenced information, relative to neutral information (Cahill et al., 1996; Cahill et al., 2001; Lupien & McEwen, 1997; Wunsch et al., 2019), mediated mainly by increases in arousal associated with emotional, especially negative information (Kensinger & Corkin, 2003a, 2003b; Kensinger, Garoff-Eaton, & Schacter, 2006). As discussed above, elevated arousal activates the HPA axis which produces factors such as cortisol, epinephrine, and norepinephrine that can enhance memories. Cognitively, arousing information may bias attention towards the arousing information and away from non-arousing information (Mather & Sutherland, 2011), leading to better memory for emotional relative to neutral information. Presumably, arousal-based superior memory for individual emotional stimuli should also be observed with pairs of stimuli; however, arousal-induced increases in association memory have been observed only in some cases: Better associative memory for arousal-containing information was observed when the to-be-linked information coincided in time and space, for example, remembering the screen location of a gruesome picture (Kensinger & Corkin, 2003a, 2003b; Mickley Steinmetz, Knight, & Kensinger, 2016). In this case, emotional arousal may enhance memory as this format allows participants to merge or ‘unitize’ the associated information, which then functions as one item with superior memorability (Mather, 2007). However, when explicitly having to study and recall that two *separate* stimuli are paired together, several studies have demonstrated that explicit memory for emotional pairs can be impaired relative to memory for neutral pairs (Caplan et al., 2019; Madan, Caplan, Lau, & Fujiwara, 2012; Madan, Fujiwara, Caplan, & Sommer, 2017).

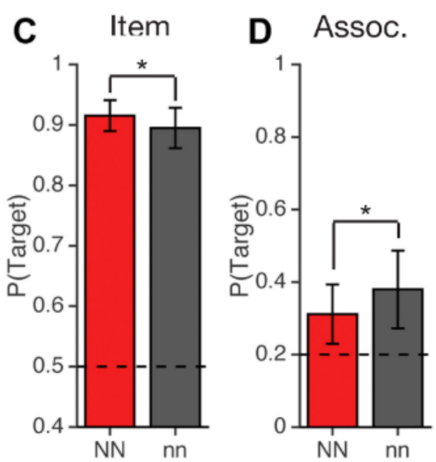

Figure 1.5. Behavioural results from Madan et al. (2017) Experiment 2: Item recognition accuracy (C) compared to associative recognition accuracy (D). NN = Negative picture pairs, nn = neutral picture pairs. P(Target) = probability of retrieval.

For example, Madan et al. (2012) conducted a series of experiments in which verbal-paired associates either contained pairs of negative, arousing or neutral non-arousing words (mixed or pure-valence pairs) and observed a small but consistent associative memory advantage (probed via cued recall) for neutral words, and a robust item-memory advantage for individual negative words. The item-memory advantage for negative words was even more pronounced with higher-arousing taboo words, and model-based outcomes pointed to a direct impact of negative words on encoding of their relationships, whereas item-memory features were boosted.

Further experiments in this series were conducted by Madan et al. (2017). For example, in Experiment 2 of Madan et al. (2017) participants studied pairs of pictures (rather than words) that were either both neutral/low arousing or both negative/high arousing and later performed two types of memory retrieval, an item-recognition task and an associative recognition task using a five alternative forced-choice task. Again, Madan et al. (2017) observed a small but significant advantage of item-memory for negative pictures, compared to memory for single neutral pictures. However, this effect was the opposite for associative memory: associative recognition performance for neutral pairs was superior compared to negative pairs. Thus, in these tasks, arousal was found to impair association memory. Based on additional eye-tracking measures, the authors observed that participants made more eye movements between two neutral than two negative pictures, and conversely, they fixated longer on each individual negative than picture compared to neutral pictures (Madan et al., 2017, Exp. 3). These findings suggested that it might be more difficult to form negative association memory because negative pictures drew attention to themselves rather than their pairing with the other picture. This would result in better item-memory for the individual negative pictures but worse association memory, which is in line with an interpretation of more difficult unitization of negative pairs (Caplan et al., 2019; Madan et al., 2017; Mather, 2007).

There are two hypotheses on the neural mechanisms underlying better associative memory for neutral pairs than negative pairs: The disruption hypothesis (Bisby, Horner, Horlyck, & Burgess, 2016) and the bypassing hypothesis (Madan et al., 2017). As previously discussed, the amygdala is crucial for emotional *item* memory as it processes emotional arousal and mediates the level of activity in other brain regions, whereas the hippocampus is critical for formation of *association* memory. Both the disruption hypothesis as well as the bypassing hypothesis agree that association memory for emotional material should involve these two structures. The disruption hypothesis proposes that the hippocampus is critical for encoding association memory, regardless of the emotional valence of the stimuli. However, it predicts that an increase in amygdala activity in response to emotional content would occur concurrently with a decrease in hippocampal activity: Encoding of negative arousing materials increases amygdala activity and biases attention with subsequently increased memory for the individual item, but amygdala activity disrupts hippocampal activity, which then would hinder the encoding of associations (Bisby et al., 2016; Joels, Fernandez, & Roozendaal, 2011). It is proposed that this disruption is mediated by slow increases in cortisol coupled with rapid arousal-induced noradrenergic activation causing disruptions in hippocampal functioning, while promoting amygdala-based memory consolidation (Joels et al., 2011; Overman & Becker, 2009). Bisby et al. (2016) supports the disruption hypothesis based on their fMRI study using incidental pair learning with pictures that either had the same or different emotional valence (neutral, negative). They probed both item-memory and associative recognition for these pairs and observed association memory reductions accompanied by reduced anterior hippocampal activity during encoding of negative pairs. Instead, amygdala activity promoted subsequent item-memory for negative pictures. Together, their results suggested amygdala-based disruption to hippocampal associative encoding, with simultaneous increases in emotional item-memory.

Conversely, Madan et al. (2017) proposed the bypassing hypothesis, assuming that the nature of the association will dictate the level of hippocampal involvement: When two items can be unitized, association memory for their combination may no longer be reliant on the hippocampus and instead be accomplished by extra-hippocampal medial temporal lobe regions (Quamme, Yonelinas, & Norman, 2007). Conversely, difficult-to-unitize associations require continuous hippocampal involvement in order to be encoded successfully. As mentioned above, since emotional items attract more attention to themselves they may be harder to unitize. Thus, assuming that unitization of negative pairs is more difficult than unitization of neutral pairs, the bypassing hypothesis posits that negative pairs will be encoded less accurately due to the decreased employment of *extra*-hippocampal medial temporal lobe regions, compared to neutral pairs. It also predicts that hippocampal activity will not be disrupted but continue to play a role in association memory formation even when the materials are emotional.

Madan et al. (2017), Exp. 3, observed the expected behavioral effect: Association memory for negative picture pairs was impaired compared to association memory for neutral pairs. Further, they found that only neutral pair encoding improved with extra-hippocampal activation (~ easier unitization). Interestingly, hippocampal activity was not disrupted during learning of negative pairs: Mean levels of hippocampal activity were the same during encoding of negative pairs and neutral pairs, accompanied by a robust increase in amygdala activity during encoding of negative pairs. Amygdala activity (and increased functional coupling within the amygdala) was related to the decrease in association memory for negative pairs. However, *increased* hippocampal activity was observed during encoding of negative pairs that were later successfully remembered, compared to neutral pairs as well as compared to negative that were later forgotten. Thus, when negative pair-encoding succeeded, there was no evidence of amygdala-based disruption of hippocampal-dependent association memory. Instead, to offset a lack of extra-hippocampal activity the hippocampus seemed to act in a compensatory manner during successful encoding of negative pairs. Madan et al. (2017) suggested that higher recruitment of the hippocampus during successful negative pairs learning may compensate for the increased amygdala activity during encoding of negative pairs.

These results pose an interesting question of how a single bout of exercise may influence not just emotional memory or association memory, but their combination. It would be expected that emotional or associative memory is influenced by acute exercise in some manner. This expectation is based on the effect that acute exercise has been demonstrated to have on the hippocampus (via exercise-induced factors) and the overall increase in physiological arousal, which has previously been shown to influence amygdala-mediated memory. In my extensive review of the literature, no study has examined this question. Theoretically this research question could yield interested results given the demand that association memory tasks place on the hippocampus, the modulating effect emotional stimuli have on amygdala and hippocampal function, and the potential influence acute exercise may have on arousal and the hippocampus. Beyond the novelty of examining emotional association memory with respect to exercise, as discussed in this background section, many previous exercise-cognition studies have methodological shortcomings including missing control groups, lack of physiological measurements, and no experimental controls to avoid potential placebo effects. Thus, my study aims to address a variety of these methodologically potentially influential factors.

2. Study Aims and Hypotheses

The general aim of this study was to investigate the effect of acute exercise on associative memory for pairs of negative and neutral images. Using three groups, a very light intensity exercise intervention group (low intensity group), hard intensity exercise intervention group (high intensity group), and a no-activity control, I examined how varying intensities of exercise may influence a participant's memory for emotional association memory. I used the task by Madan et al. (2017), Exp. 3, due to its consistent outcomes across multiple studies (Caplan et al., 2019; Madan et al., 2012; Madan et al., 2017), along with neuroimaging data confirming this task's recruitment of the hippocampus (Madan et al., 2017).

I expected that high intensity exercise will alter emotional association memory compared to both the light-intensity exercise group and the no-activity control group. Hypothetically, high intensity exercise should increase arousal and therefore amygdala-based processes related to emotional memory (Arent & Landers, 2003; Bass et al., 2014; Basso & Suzuki, 2017; Bernstein & McNally, 2017; Griffin et al., 2011; Heuer & Reisberg, 1992; Hotting et al., 2016). Furthermore, high intensity exercise should increase hippocampal-mediated processes related to association memory (Chua, Schacter, Rand-Giovannetti, & Sperling, 2007; Erickson et al., 2011; Griffin et al., 2011; Holmes et al., 2004; Newman et al., 2017). Based on the previously discussed findings of exercise effects on association memory and emotional item-memory, as well as the extant literature on emotional association memory, I had three main hypotheses:

1) Assuming an increase in hippocampal function (e.g., blood flow) after high intensity exercise, the normally observed decrease in association memory for negative information will dissipate and result in equal association memory for negative information compared to

neutral information. The same prediction results from assuming exercise-induced arousal may supersede any arousal-mediated effects from the negative materials themselves, as observed in some previous studies (Basso & Suzuki, 2017; Wunsch et al., 2019). Again, this would nullify arousal effects of the materials and results would show equal association memory for negative and neutral materials after high intensity exercise (but not low intensity or no-activity).

2) Alternatively, assuming an increase in arousal after high intensity exercise intensifies the normal discrepancies between neutral and negative association memory, I will observe an even stronger deficit for negative association memory compared to neutral association memory in the high intensity exercise group compared to both control groups.

3) Based on relatively consistent effects of exercise on association memory (see section 2.2.1), high intensity exercise may increase overall association memory performance, irrespective of any differential effects of exercise on emotional versus neutral association memory.

Exploratory aims: Although not the focus of the current study, the task I used also included a measure of subjective memory confidence. Owing to previous placebo effects regarding cognitive improvement in exercise studies (Desharnais et al., 1993; Szabo, 2013), I explored whether exercise intervention would influence associative memory confidence (for neutral information, negative information or both) as well as the link between subjective memory confidence and objective memory accuracy. People tend to overestimate the memorability of emotional over neutral materials (Zimmerman & Kelley, 2010). If exercise acts to increase any effects of emotional arousal by the materials, subjective memory confidence should be amplified by exercise, and in that case de-coupled more from actual memory performance. However, if exercise-induced arousal supersedes arousing effects of the materials, there should be less of a difference in subjective memory confidence between negative and neutral materials after exercise.

3. Methods

This study was approved by the University of Alberta Research Ethics Board (PRO00077772). All participants provided written informed consent. The consent process included a brief description of the study including a warning to expect some level of physical exercise, as well as some example pictures to illustrate the nature of the materials that participants would encounter (some pictures were negative in valence, see below). The post-study debriefing included a list of mental health resources in case participants experienced negative aftereffects.

3.1. Participants

A total of 105 undergraduate students from introductory psychology courses in fall 2019 at the University of Alberta participated in this study in exchange for partial course credit. Participants were recruited via an online portal delivered by the Department of Psychology. Age of participants ranged from 16 to 35 years. Of the original 105 participants, data from a total of 10 were excluded for the following reasons: Six did not adhere to the exercise protocol and/or achieved the desired heart rate changes in response to the exercise, three participants had below-chance memory performance, and one participant experienced an external interruption (fire alarm). The final sample consisted of 95 participants (53 females, 42 males) of whom 31 were in the high-intensity exercise condition (17 females, 14 males), 33 in the low-intensity exercise condition (20 females, 13 males), and 31 in the control condition (16 females, 15 males).

3.2. Materials

The experiment had three blocks (see Figure 3.1). In block 1, participants completed the consent process, filled out a mood survey, completed a practice memory task and then performed the pre-intervention memory task (List 1). In block 2, the exercise (or control) intervention took place including heart-rate monitoring and a fitness-level survey. In the last block, participants performed the post-intervention memory task (List 2). The experiment ended with a 5-minute debriefing phase. The length of the experiment averaged 100 minutes.

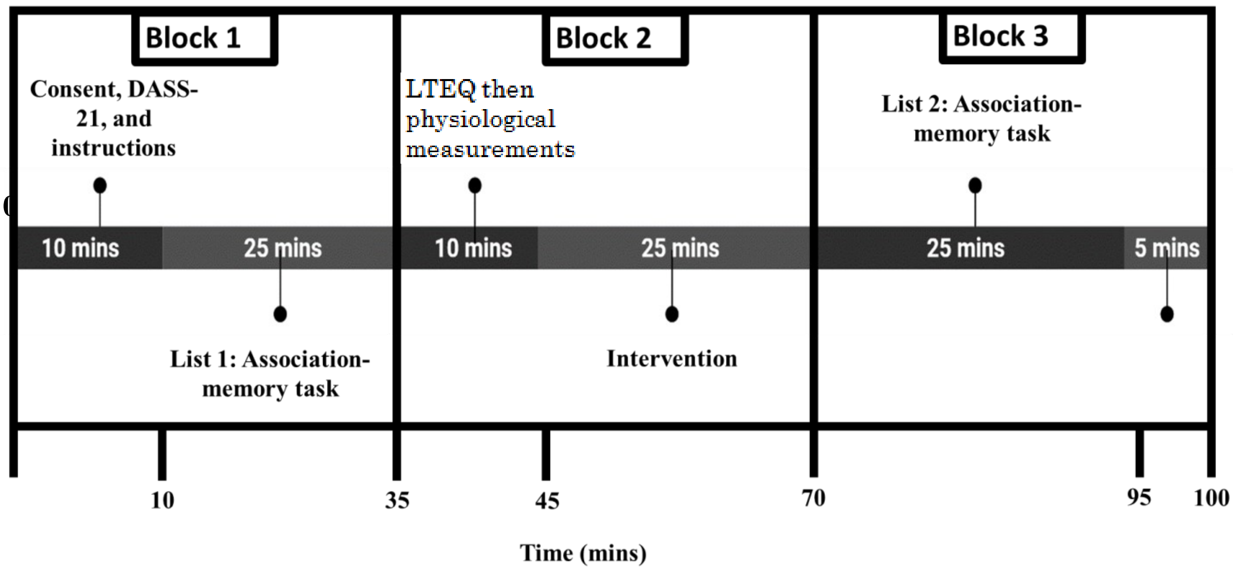

Figure 3.1. Elements and timeline of the experiment.

3.2.1. Surveys

Two surveys were administered: the Depression, Anxiety, and Stress Scales (DASS-21) to measure mood/mental health, and the Godin Leisure-Time Exercise Questionnaire (LTEQ) to determine average physical activity levels.

- ***The Depression, Anxiety, and Stress Scales (DASS-21):*** Exercise can result in mood changes (Basso & Suzuki, 2017), which could potentially moderate effects of exercise as well as effect on emotional memory specifically. Thus I measured mood with the DASS-21, the 21-item short version of the original DASS (Lovibond & Lovibond, 1995). The

DASS-21 is a self-report scale which measures the extent to which depression, anxiety, and stress has been experienced in the past 7 days. There are 7 items per sub-scale and questions are measured on a 4-point Likert scale from on a scale from 0 (did not apply to me at all) to 3 (applied to me very much) (Henry & Crawford, 2005). Sum scores are computed by adding the scores on the items (total and per subscale), multiplying the result by 2, and arriving at a DASS-21 total score range between 0 and 120. A cut-off score of 60 was used for the total DASS score as proposed by (Lovibond & Lovibond, 1995). DASS-21 total scores ≥60 score are considered as “high” or “severe” burden of depression, anxiety, and stress within the last week. The DASS-21 is widely used and has good reliability (range of Cronbach alpha = .82 to .97 across studies (Henry & Crawford, 2005; Lovibond & Lovibond, 1995). In the current study, the DASS-21 produced a similarly high Cronbach alpha of .896.

- ***The Godin Leisure-Time Exercise Questionnaire (Rowe, Mahar, Raedeke, & Lore, 2004) LTEQ:*** The Leisure-Time Exercise Questionnaire (LTEQ; Shephard, 1997) was used to evaluate the frequency of vigorous, moderate, and light-intensity exercise activity that is performed on a weekly basis by allowing researchers to calculate a total metabolic equivalent score (MET). More specifically, the LTEQ asked participants to self-report how many times per week they engage in a particular intensity of exercise for more than 15 minutes. Participants are given examples of each level of intensity of exercise activity; for example, a leisurely walk is an example of light-intensity exercise. Participants’ provided weekly numbers were summed using the formula: (9x strenuous exercise hours) + (5x moderate exercise hours) + (3 x mild exercise hours) = MET (Shephard, 1997).

Additionally, self-reported physical fitness measured with the LTEQ is moderately correlated to objective physical fitness levels, eg., VO2max scores (r = .56) using (Copeland, Kowalski, Donen, & Tremblay, 2005).

3.2.2. Association Memory Task

The association memory task (programmed in Presentation ®, Neurobehavioral Systems) was identical to the task in experiment 3 of Madan et al. (2017), and similar to the task used in Caplan et al. (2019). The task is composed of a set of 208 pictures (104 negative, arousing pictures and 104 neutral, non-arousing pictures), from the International Affective Picture System (IAPS) (Lang et al., 2008) and the internet. The images contain people, objects and animals in both indoor and outdoor settings. The negative images are often graphic and distressing, for example mutilated bodies, sick children, and decaying food items. Neutral images depict mundane scenes such as a plate or someone watching tv. Each picture has previously (Madan et al., 2017) been rated for level of arousal on a 9-point modified version of the Self-Assessment-Manikin (Bradley & Lang, 1994). A score of '9' indicating low arousal, negative pictures were rated higher in arousal ($M \pm SD = 5.09 \pm 0.85$) than neutral pictures ($M = 7.70 \pm 0.35$; $t(212) = 35.74$, $p < .001$) (Madan et al., 2017). As shown in Figure 3.2, participants performed the memory task twice, before the intervention (List 1) and after the invention (List 2). Each list was comprised of 52 same-valence pairs (26 negative-negative pairs, 26 neutral-neutral pairs). There was no repetition of images between List 1 and List 2.

Each list contained an encoding phase and a retrieval phase. In the encoding phase, pairs were presented one at a time, with both pictures (each picture measured 450×300 pixels) adjacent to one another on a computer screen for 2000 msec preceded by a fixation cross for

1000 msec. Pairs were always of the same valence, either two negative pairs, or two neutral pairs. Participants were explicitly instructed to study the pairings and informed that their memory for each pair would be tested later. Following the presentation of each pair, participants completed two trials of a motor task in which, using a mouse, they were asked to click on the image of a star in one of five different screen locations (as seen in Figure 3.2 C). This task had originally been included in Madan et al. (2017)'s functional MRI study (exp. 3) to control baseline hippocampal activity, but was irrelevant for the current study and not further analyzed. These cycles of encoding and motor task repeated until all 52 pairs had been displayed. The encoding phase concluded with a visual 2-back task to interrupt memory rehearsal (see (Madan et al., 2017)] for additional details).

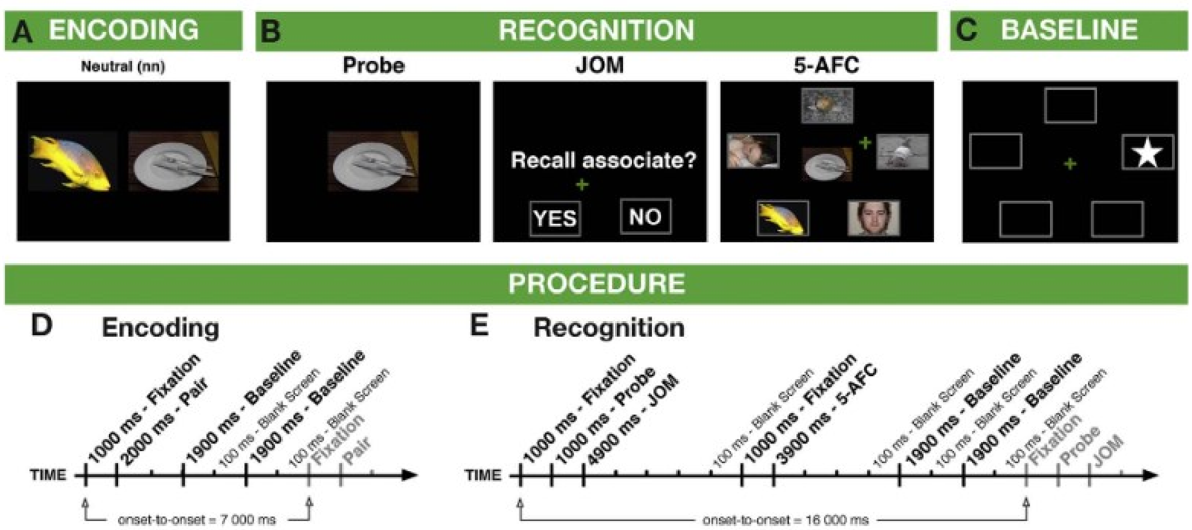

Figure 3.2: *Example of association memory task: sourced from* (Madan et al., 2017)

Following the encoding phase, in the retrieval phase each pair was first probed with a judgment of memory (JoM) task and a 5-alternative forced choice (5-AFC) association recognition task (as seen in Figure 3.2. A probe image was presented from one the 52 pairs shown in the encoding phase, followed by the JoM task intended to emulate cued recall of the pictures. During the JoM task, participants were prompted by the question: "Recall associate?" and presented with the options "Yes" or "No". Participants were instructed to be "conservative" with their memory judgments and to only select a 'yes' response if they were confident that they correctly remembered the picture that was previously associated with the probe picture. One trial of JoM lasted 4900 ms, followed by a 100-ms blank screen and 1000-ms fixation-cross. Following the JoM task, participants were presented with the 5-AFC association recognition task. The same probe picture as in the JoM task was presented in the center of the screen (225 × 150 pixels), surrounded by an array of five pictures (one correct target, four lures, all lure pictures were of the same emotional valence and selected from other pairs in the encoding phase) in fixed screen positions. Participants were given 3900 ms to select the correct target picture, followed by a 100-ms blank screen. The retrieval phase concluded with the same 3-minute n-back task as was used after the encoding phase.

3.2.3. Intervention

Participants were randomly assigned to one of three conditions: High-intensity exercise, low-intensity exercise, and control.

- ***Randomization of participants to conditions and blinding:*** Awareness of an upcoming exercise task can increase physiological arousal (Desharnais et al., 1993; Lindheimer et al., 2017) and cognitive awareness of an exercise intervention may produce expectations of benefits to cognition, subjecting participants and experimenters to potential placebo effects (Desharnais et al., 1993; Szabo, 2013) To ensure blinding and avoid pre-intervention expectation and other biases as much as possible, details on the upcoming exercise intervention were minimal in the beginning of the experiment. Both participants and experimenters were unaware of the experimental condition until the pre-intervention memory test (minute 35) had concluded. At that time, the experimenter drew from one of two boxes (divided by gender to ensure equal representation of men and women in each condition) a folded piece of paper which contained the condition name (high-intensity exercise, low-intensity exercise, or control) and they then explained the intervention protocol to the participant.

- ***High-intensity exercise:*** The high-intensity exercise consisted of a 5-minute warmup phase on a stationary spin bike, 5 minutes of "ramp-up" to increase their heart rate to 85% of the participant's calculated maximum, followed by 15 minutes of cycling at 85-90% of their maximum heart rate. Along with gear changes, subjects were encouraged to maintain constant revolutions per minute (RPM) around 65-75. Exercise intensity was controlled by the experimenter via the adjustments of the bike gears accordingly to the participant's heart rate.

- ***Low-intensity exercise:*** The low-intensity exercise condition consisted of 25 minutes of cycling at or below a heart rate of 100 bpm. Again, exercise intensity was controlled by the experimenter via the adjustments of the bike gears accordingly to the participant's heart rate. Throughout both, high-intensity exercise and low-intensity exercise conditions, the same nature video (see below) was shown to match the no-activity control and exercise conditions.

- ***No-activity control condition:*** The control condition included sitting while viewing the video "David Attenborough Desert Seas National Geographic" (Wild Nature TV, "David Attenborough Desert Seas National Geographic", 2017, 0:00-25:00) via YouTube for 25 minutes, i.e., the same duration as the two exercise conditions. The movie showed various marine activities and contained no graphic or violent scenes (animal death/killings, etc.) to avoid any physiological arousal that may be caused by the movie.

3.2.4. Assessment of heart rate, blood pressure, and perceived exertion

We measured all participants' resting heart rate and blood pressure. For participants in either of the two exercise conditions, I measured heart-rate changes during and after the intervention as well as their perceived exertion.

- ***Heart rate and blood pressure:*** Blood pressure and heart rate were measured using the Omron BP742N 5 Series Blood Pressure Monitor. Using participants' age, I calculated maximum heart rate using the calculation: 220 – age (Nes, Janszky, Wisloff, Stoylen, & Karlsen, 2013). The calculated maximum heart rate was divided into three sections: 85% of maximum heart rate (max. heart rate), 90% of max. heart rate and 95% of max. heart rate in order to evaluate the effects and effectiveness of the exercise intervention. During the intervention, participants in the high-intensity and the low-intensity conditions were given an electrocardiographic chest strap heart rate monitor (Garmin 'DUAL' chest heart rate monitor) and instructed on how to apply it. Via Bluetooth, participants' heart rate was displayed on a Garmin Forerunner 35 watch, which only the experimenter would see throughout the exercise task (Gillinov et al., 2017; Labban & Etnier, 2011). Heart rate was manually recorded every two minutes during the entirety of the exercise (Gillinov et al., 2017).

- ***Rate of Perceived Exertion (RPE):*** For the high-intensity and low-intensity exercise conditions, participants' perceived exertion was monitored throughout the intervention using a 10-point rating scale describing and visually illustrating increasing levels of exertion. The scale was shown to participants every 2-4 minutes (high-intensity exercise) or every 4-7 minutes (low-intensity exercise), with participants indicating their current state according to the images and their descriptions. This measure served as a manipulation check and safety measure to avoid overexertion (levels 9 or 10 on the scale), along with close monitoring of other physical signs of exhaustion such as shortness of breath, dizziness, and extreme perspiration to ensure participants' well-being, providing water or terminating the session if necessary (no participant was deemed to or asked to terminate the session).

3.3. Statistical Analyses

Statistical analyses were carried out with IBM SPSS for Windows, Version 26.0 and JASP, Version 0.12.2. Participant characteristics including age, sex, resting heart rate, and calculated maximum heart rate, as well as answers in the questionnaires (DASS-21; LEQT) across the three experimental conditions (high-intensity exercise, low-intensity exercise, no-activity control) were compared using univariate analyses of variance for numerical variables or chisquare tests to compare frequency counts. Post-hoc tests were Bonferroni-corrected across groups but not across analyses. The effectiveness of the manipulation was evaluated by summarizing average heart-rate changes over three blocks: baseline heart rate (minute 0), block 2 (minutes 0-5), block 3 (minutes 6-15) and block 4 (minutes 16-25). Resting heart rate was compared between all three conditions using univariate ANOVA. In addition, a 2*4 repeated-measures ANOVA tested whether heart rate changes were different between high- and low-intensity exercise groups, as a function of the task blocks (rest, blocks 1-3). For all repeated measures ANOVA with factors that had more than 2 levels, degrees of freedom were corrected using Greenhouse-Geisser estimates of sphericity.

In order to test the core hypothesis (1) and its alternative (2), I conducted a series of 3 x 2 x 2 repeated measures ANOVA with between-subjects factor CONDITION (high-intensity exercise, low-intensity exercise, no-activity control), and within-subject factors LIST (List 1 – pre-intervention, List 2 – post-intervention) and EMOTION (negative pairs, neutral pairs). Dependent variables were 5-AFC recognition accuracy (hits) and a d'-prime equivalent to account for guess rates (Hacker & Ratcliff, 1979). Briefly, each person's probability of accurate associative recognition performance was adjusted based on the number of choice alternatives (in my case, 5), using Hacker and Ratcliff (1979) tables. To illustrate, a person with a 0.5 probability of retrieval in a 2-alternative forced-choice recognition memory task would have a d-prime score of 0, indicating that their performance would be identical to guessing. The same 0.5 probability in a 5-alternative forced-choice task would yield a better outcome with a d-prime score of 0.84. Thus, higher d-prime scores indicate better memory, adjusted for the guess rate of 20% in this 5AFC task. Inherent in these analyses was a test of hypothesis 3, assuming main effects of

CONDITION, but no interactions between CONDITION x LIST x EMOTION. This was analyzed using a 3 x 2 x 2 ANOVA with factors CONDITION x LIST x EMOTION.

Exploratory analyses on subjective memory confidence were equivalent in structure but used judgements of memory (JoM) instead of accuracy/d-prime as dependent variables. In order to probe whether exercise influenced the relationship between objective memory accuracy and subjective memory (JoM), I used Yule's Q (Yule, 1922). Briefly, Yule's Q is the so-called coefficient of colligation and represents a measure of association between two binary variables. Because individuals could either be correct (assigned a number '1') or incorrect (assigned '0') in their JoM, the resulting 2 x 2 contingency table had four possible outcomes (Tab. 3.1):

Table 3.1: Possible outcomes between recognition memory accuracy and JoM, analyzed with Yule's Q coefficient of colligation.

	5AFC Correct	**5AFC recognition Incorrect**
JOM **"Yes"** - I remember the previously associated picture	1/1 ➔ match	1/0 ➔ mismatch
JOM **"No"** - I don't remember the previously associated picture	0/1 ➔ mismatch	0/0 ➔ match

The resulting odds are typically log-transformed to scale these outcomes similar to a correlation coefficient with score from -1 (here this would be complete non-match between JOM and accuracy, see Table 3.1 'mismatch') and 1 (JOM and accuracy are perfectly overlapping; see

Table 3.1 ‘match’). Importantly, the size of Yule’s Q does not speak to average levels of accuracy or JoM, but to the strength of their relationship, i.e., how precisely one’s subjective memory is matched (or not) by actual memory accuracy.

Furthermore, in order to test whether memory (objective: 5-AFC accuracy, d-prime; subjective: JoM) showed differential outcomes with respect to emotional valence at all, two bias scores were calculated: a) the difference between accuracy (hit rate, d-prime) for neutral pairs minus accuracy for negative pairs; b) the difference between JoMs for neutral minus negative pairs. A bias score of zero would indicate no bias against or towards differential retrieval of negative or neutral pictures. The size of these bias scores was tested against zero using one-sample T-tests.

Finally, since hypothesis 1 predicted a null-effect I included Bayesian statistics to probe the size of the ANOVA outcomes. Briefly, the Bayesian framework (Gelman & Robert, 2014; Quintana & Williams, 2018) offers an alternative approach to classic ‘frequentist’ statistics, as it allows to quantify how much more likely outcomes are under the null hypothesis compared to an alternative hypothesis, given a prior probability. The so-called “Bayes factor” (BF10) quantifies the degree to which the outcomes favour either of the two hypotheses by considering their prior odds. Hypothesis testing in psychology/life sciences typically yield Bayes factor values between 0.01 and 100 (Wetzels et al., 2011). The classification scheme in the JASP software by Lee and Wagenmakers (2014) proposes a series of labels for which ranges of specific Bayes factor values can be considered “anecdotal”, “moderate”, “strong”, “very strong”, or “extreme” relative evidence for a hypothesis (Fig. 3.3). I followed this classification scheme here and considered B10 values smaller than 0.33 as moderate or stronger evidence for the null hypothesis, B10 values larger than 3 as moderate or stronger evidence for the alternative hypothesis and treated B10 values between 0.33 and 3 as uncertain.

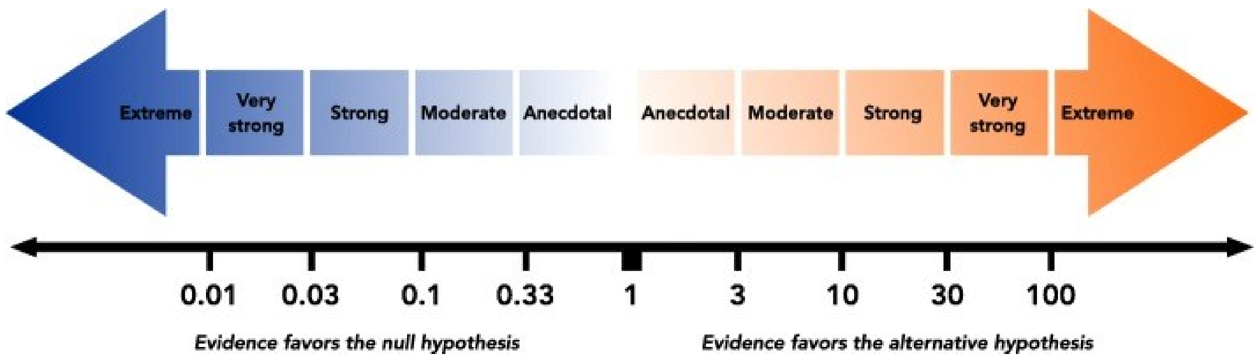

Figure 3.3: This classification scheme is included in JASP (Lee & Wagenmakers, 2014) and assigns interpretations for a range of Bayes factors.

4. Results

The results section will first outline background variables across conditions, followed by manipulation check outcomes, before presenting the core results of this study. The chapter will close with exploratory outcomes.

4.1. Overview on Participants

Table 4.1 displays the characteristics of the study population across the three conditions: low-intensity exercise, high-intensity exercise, no-activity control. On average, participants were around 19 years of age, with 55.8 % of the sample (N=95) being female. Conditions did not differ in participant age, gender distribution, baseline resting heart rate, self-reported fitness level in the LTEQ, and mood in the DASS-21. The only significant difference between groups was in the time of day in which they were assessed. As shown in Table 4.1, proportions of individuals tested in the morning were larger in the Low-intensity exercise group than in the high-intensity group and vice versa, more participants from the high-intensity group were tested in the afternoon compared to the low-intensity group.

Table 4.1: Characteristics of the participants in the three conditions.
Data are means (SD) or frequencies (percentages).

	Low Exercise (n = 33)	High Exercise (n = 31)	Control (n = 31)	Test Statistic	p-value
Age (years)	19.33 (1.85)	19.71 (1.92)	19.13 (1.38)	F(2,92)=0.89	.41
Gender (male)	14 (42.42%)	14 (45.16%)	15 (48.39%)	$\chi^2(2)= 0.54$	.76
Test time					
before 12 pm	19 (57.58%)$_a$	8 (25.81%)$_b$	12 (38.71%)$_{a,b}$	$\chi^2(2)=6.71^a$	.03
after 12 pm	14 (42.42%)$_a$	23 (74.19%)$_b$	19 (61.29%)$_{a,b}$		
Resting heart rate (bpm)	71.76 (12.14)	72.42 (13.14)	69.53 (10.28)	F(2,91)=0.49	.62
Fitness: LTEQ	56.76 (24.95)	59.26 (22.21)	61.10 (27.77)	F(2,92)=0.24	.79
Mood					
DASS-21 total	39.03 (28.37)	50.71 (33.18)	46.45 (27.14)	F(2,92)=1.27	.29
DASS-21 ≥ 60	11 (33.3%)	11 (35.5%)	12 (38.7%)	$\chi^2(2)= 0.20$	.90

[a,b]: Different superscripts indicate significant differences between conditions in Bonferroni-corrected post-hoc tests.
bpm: beats per minute; DASS-21: Depression Anxiety Stress Scales; LTEQ: Godin-Leisure Time Exercise Questionnaire

4.2. Manipulation check

Resting heart rate showed no differences between conditions (see Table 4.1). A 2 x 4 repeated-measures ANOVA was conducted on heart rate changes as a function of CONDITION (low-intensity exercise, high-intensity exercise) and BLOCK of time during the intervention (block 1: rest, block 2: warm-up during 0-5 minutes, block 3: exercise during 6-15 minutes, block 4: exercise during 16-25 minutes). There was a main effect of CONDITION ($F(1,62)=285.29$, $p=.000$, $\eta^2_{part} = .99$) and a main effect of BLOCK ($F(1.97,121.83)=625.73$, $p=.000$, $\eta^2_{part} = .91$), qualified by an interaction between CONDITION and BLOCK ($F(1.97,121.83)=145.70$, $p=.000$,

η^2_{part} = .70). These outcomes are illustrated in Figure 4.2, with means and standard deviations provided in Table 4.2.

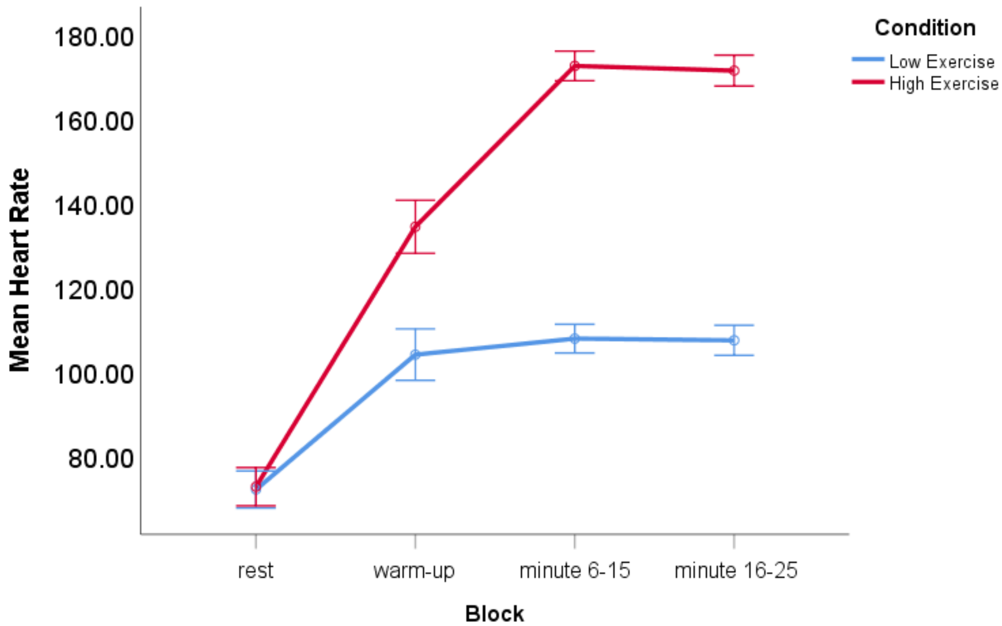

Figure 4.2: Mean heart rate of the two intervention groups by blocks of time. Error bars are 95% confidence intervals around the mean.

Table 4.2: Mean heart rate (SD) in the two intervention groups across time blocks during the study.

	Low Exercise	**High Exercise**
Block 1: Resting	71.76 (12.14)	72.42 (13.14)
Block 2: Warm-up (minute 0-5)	103.74 (15.55)	134.08 (19.43)
Block 3: Exercise (minute 6-15)	107.54 (10.94)	172.22 (8.32)
Block 4: Exercise (minute 16-25)	107.14 (11.81)	171.11 (8.21)

Post-hoc t-tests showed significant differences between conditions in all time points after the resting phase, with higher heart rates in the high exercise condition than the low-intensity exercise condition (all p's <.001). Within conditions, average heart rates were elevated during the warm-up period compared to rest in both groups (low exercise: t[32]=9.25, p<.001; high exercise: t[30]=17.29, p<.001). In the low exercise condition, no further changes in heart rate were seen between warm-up and later times (block 3: t[32]=1.58, p=.12; block 4: t[32]=1.37, p=.18), whereas in the high exercise condition, heart rate was substantially further increased after the warm-up period (warm-up vs. block 3: t[30]=15.40, p<.001; warm-up vs. block 4: t[30]=14.55, p<.001), staying similarly elevated throughout the intervention (block 3 vs. block 4: t[30]=1.15, p=.26).

Thus, as intended, our high intensity exercise intervention yielded a significant change in heart rate compared to resting heart rate, which continued to increase past the warm-up period after which it remained elevated and stably high throughout the rest of the exercise. Further, the low exercise condition remained at a lower and stable rate from the beginning of the warmup until the end of the experiment.

4.3. Association memory accuracy

In order to test whether the intervention had an effect on associative memory, I conducted a 3 x 2 x 2 repeated measures ANOVA on recognition hits in the 5-AFC association recognition task with between-subjects factor CONDITION (high exercise, low exercise, control), and within-subjects factors LIST (List 1, List 2) and EMOTION (negative, neutral). We observed a main effect of LIST (F(1,92)=13.7, p=.000, η^2_{part}=.13) and a main effect of EMOTION (F(1,92)=14.2, p=.000, η^2_{part}=.13). These main effects indicated better associative memory for pairs from List 2

(M= 63.0%, SD= 0.18) than List 1 (M= 58.1%, SD= 0.16), and for neutral pairs (M= 62.7%, SD= 0.18) compared to negative pairs (M=58.4%, SD = 0.16). The main effect of CONDITION was not significant ($F(2,92)=.26$, $p=.77$) and there were also no significant interactions involving CONDITION. Bayes factors for the main effect of LIST ($BF_{10}=209.20$) and EMOTION ($BF_{10}=34.62$) were in clear support of the significant main effects. Bayes factors for the non-significant main effect of CONDITION ($BF_{10}=0.083$), and the non-significant interactions involving CONDITION (CONDITION x EMOTION: $BF_{10}=0.03$; CONDITION x LIST: $BF_{10}= 0.02$; CONDITION x EMOTION x LIST: $BF_{10}=0.000133$) were all definitively supportive of null findings (Figure 4.3 A).

These analyses were repeated with the d'-prime accuracy measure, correcting for guess rates. Similar to the results with simple recognition hits, d'-prime outcomes yielded a main effect of LIST ($F(1,92)=19.2$, $p=.000$), and a main effect of EMOTION ($F(1,92)=12.8$, $p=.001$). Bayesian statistics confirmed the robust main effects of LIST ($BF_{10}=6205.20$) and EMOTION ($BF_{10}=34.21$). Bayes factors for the non-significant main effect of CONDITION ($F(1,92)=.45$, $p=.64$, $BF_{10}=0.08$), and interactions that involved the group factor, i.e., CONDITION x EMOTION ($BF_{10}=0.04$), CONDITION x LIST ($BF_{10}= 0.03$), as well as the three-way interaction CONDITION x EMOTION x LIST ($BF_{10}=3.31 \times 10^{-4}$) were all definitively supportive of null findings (Figure 4.3 B).

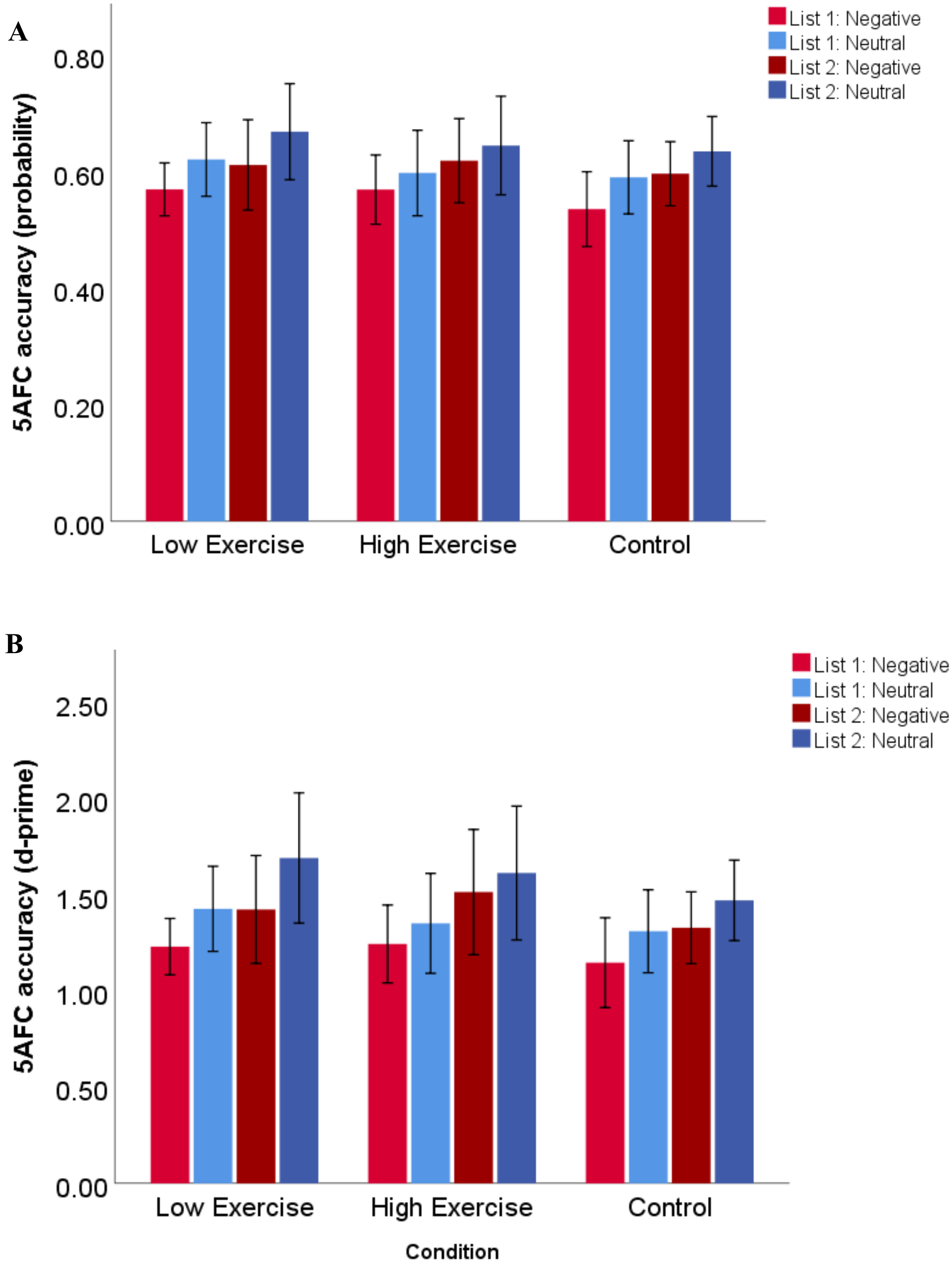

Figure 4.3: Associative recognition accuracy. A) proportion of recognition hits, B) d-prime. Error bars are 95% confidence intervals around the mean.

Thus, our outcomes supported no effect of the high-intensity (or low-intensity) exercise intervention on association memory performance in this task. Similar to previous studies with this paradigm (Caplan et al., 2019; Madan et al., 2017), I replicated a small advantage of association memory for neutral pairs over negative pairs, represented in the main effects of EMOTION, in the entire sample. Probing whether the memory advantage for neutral pairs was present at all, overall as well as within each list and condition, memory bias scores were calculated where recognition hits (or d-prime) for negative pairs were subtracted from recognition hits (or d-prime) for neutral pairs. Thus, positive bias scores would indicate better memory for neutral pairs than negative pairs. I then conducted one-sample t-tests comparing these bias scores against zero (no memory bias) for each list, both in the entire sample and within conditions. Results on accuracy bias scores are illustrated in Figures 4.4-4.5.

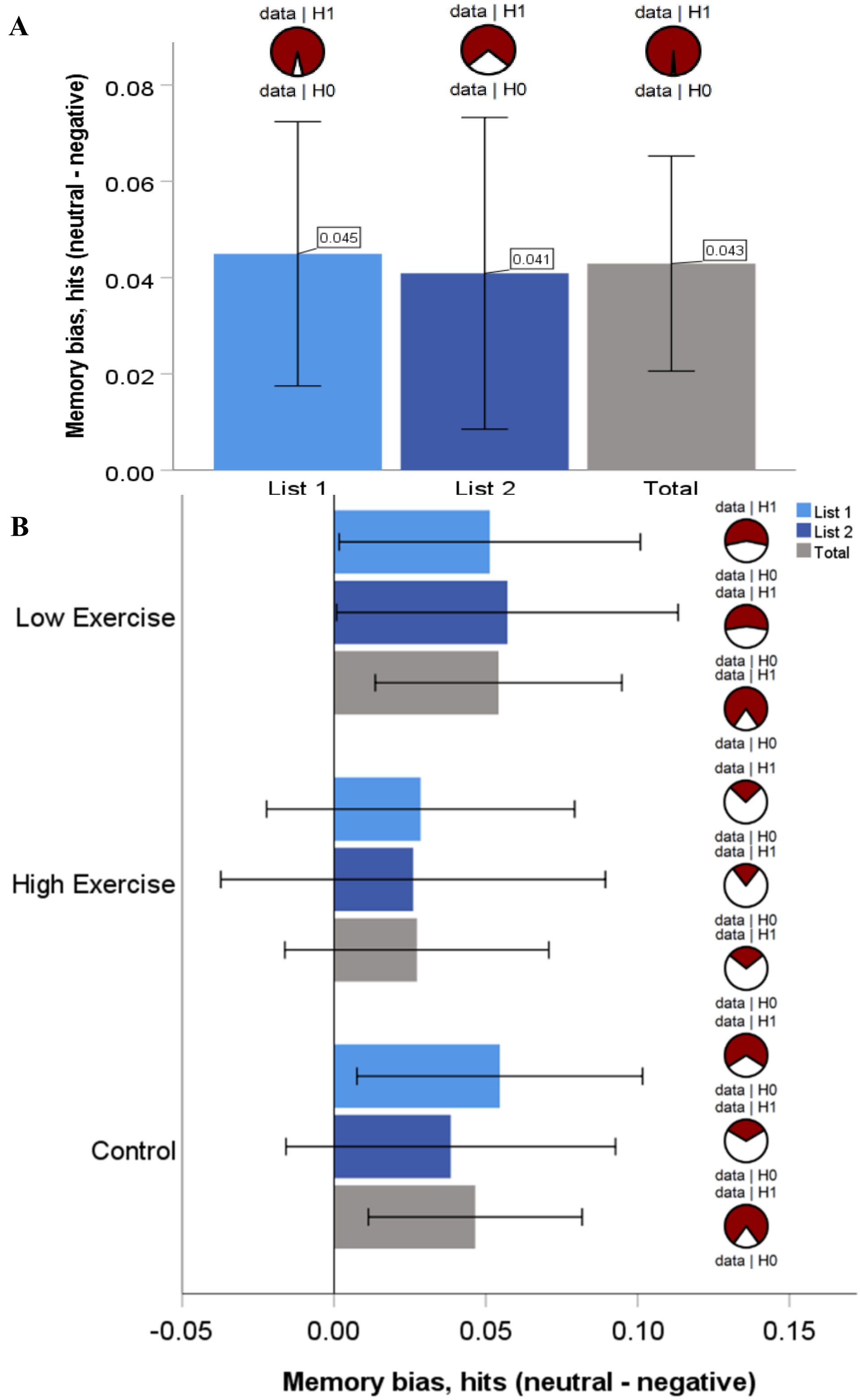

Figure 4.4: Accuracy bias (recognition hits for negative minus neutral pairs) for A) in the entire sample, B) in each condition

Across all groups (Figure 4.4 A), the accuracy bias using recognition hits was significantly larger than zero in List 1 ($t(94)= 3.25$, $p= .00$, BF=14.87) and in List 2, although weaker ($t(94)=2.51$, $p =.01$, BF = 2.19). Thus, overall, memory for neutral pairs was better than memory for negative pairs, in particular in List 1. The magnitude of this neutral-pair memory advantage was small; around 4.5% in List 1 and 4.1% in List 2 (cf. Figure 4.4 A).

Within each condition (Figure 4.4 B), the low-intensity group demonstrated a significant bias in both List1: $t(32)=2.11$, $p=.04$, $BF_{10}=1.29$, and in List 2, $t(32)=2.07$, $p= .04$, $BF_{10}=1.21$, but the Bayes factors were largely inconclusive. The high-intensity exercise group had no bias in either list (List 1: $t(30)=1.15$, $p =.26$, $BF_{10}=0.35$; List 2: ($t(30) = 0.84$, $p = .40$, $BF_{10}=0.27$), with moderate support for the null finding already in List 1. The control group demonstrated a just significant bias in List 1 ($t(30)=2.37$, $p=.02$, $BF_{10}=2.11$), but not in List 2 ($t(30)=1.45$, $p=.15$, $BF_{10}=0.49$). Bayes factors in the control group all fell within the ‘inconclusive’ range but showed more support for the effect than a null finding in List 1, and more support for a null finding than an effect in List 2.

These analyses were repeated with d’-prime (Figure 4.5).

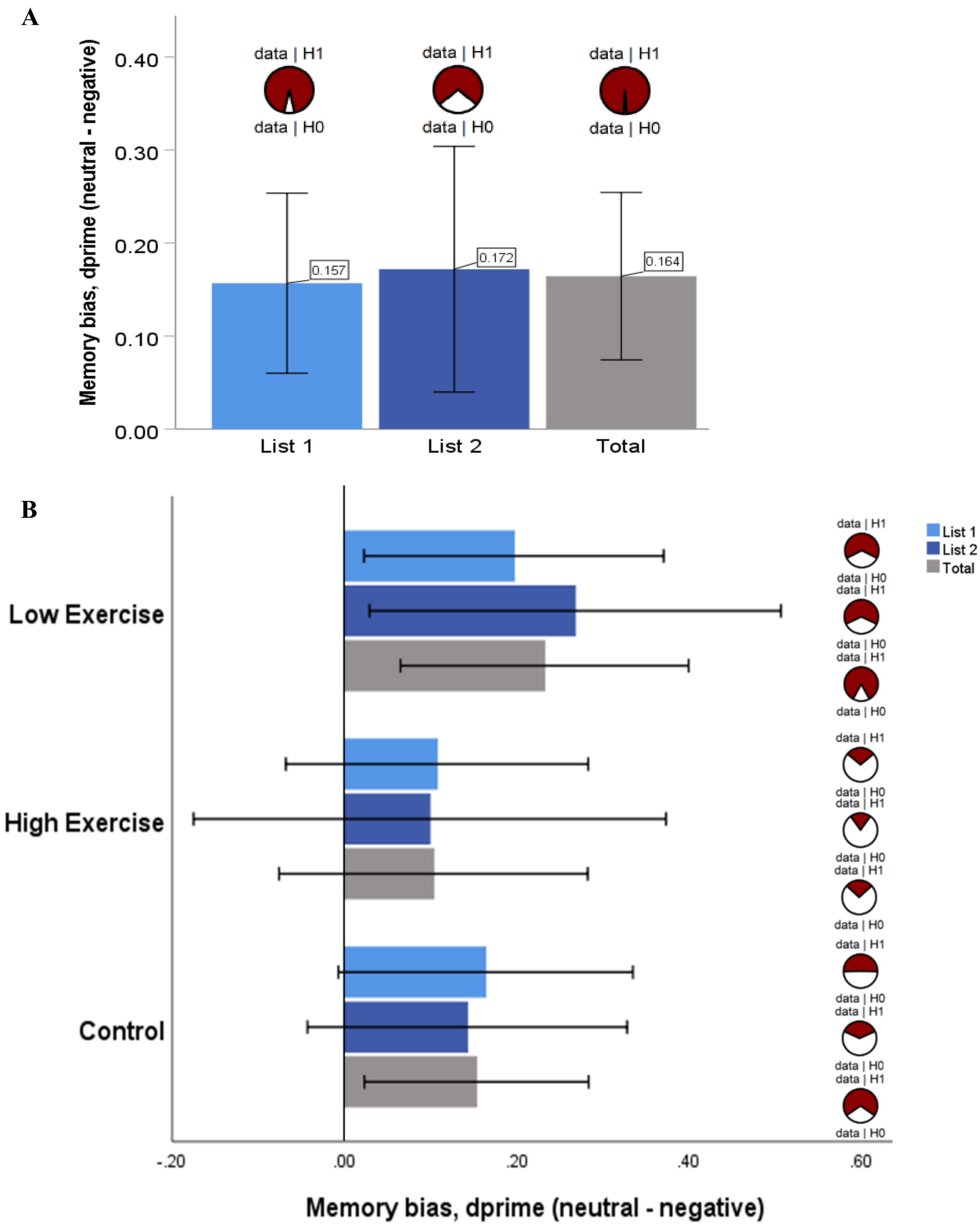

Figure 4.5: Accuracy bias (d-prime for negative minus neutral pairs) for A) in the entire sample, B) in each condition.

Results on d-prime bias scores were largely identical to those on recognition hits bias scores, I observed a significant memory bias in d-prime overall (Figure 4.5 A) across groups in List 1 ($t(94)=3.22$, $p=.002$, $BF_{10}=13.50$) and in List 2 ($t(94)=2.58$, $p=.01$, $BF_{10}=2.68$). Bayes factor for List 1 provides strong evidence in favour of the alternative hypothesis, while Bayes factor for List 2 was inconclusive. The low-intensity group demonstrated a significant bias in both List 1 ($t(32)=2.30$, $p =.02$, $BF_{10}=1.85$) and List 2 ($t(32)=2.28$, $p=.04$, $BF_{10}=1.78$), but with inconclusive evidence from the Bayes factors (Figure 4.5 B). The high-intensity group did not have any significant bias in List 1 ($t(30)=1.25$, $p=.22$, $BF_{10}=.38$) or List 2 ($t(30)=0.73$, $p=.46$, $BF_{10}=.25$). Again, Bayes factors for the high-intensity group indicate moderate support for the null hypothesis for List 1 and was inconclusive for List 2. The d-prime bias score of the control group in List 1 failed to reach significance ($t(30)=1.95$, $p=.06$, $BF_{10}=1.02$) and was absent in List 2 ($t(30)=1.57$, $p=.12$ $BF_{10}=.57$). Again, Bayes factors in the control group fell within the 'inconclusive' range but showed more support for an effect than a null finding in List 1, and more support for a null finding than an effect in List 2.

4.4. Exploratory analyses: Subjective judgements of memory

As part of our exploratory analyses I also evaluated how acute exercise influenced subjective judgements of memory for neutral and negative pairs, regardless of objective memory performance. As a reminder, in the retrieval portion of the memory task each trial first presented a probe picture, then asked participants to judge (subjectively) whether they had retrieved the picture that had previously been paired with the probe picture. "Yes" responses in these subjective Judgements of Memory (JoM) were analyzed using a 3 x 2 x 2 ANOVA with factors CONDITION x LIST x EMOTION. We found a main effect of EMOTION ($F(1,92)=7.04$, p=.009, BF_{10}=2.18) and a main effect of LIST (F(1,92)=3.9, p=.049, BF_{10}=.48), and again no significant main effect of CONDITION (F(2,92)=.84, p=.435, BF_{10}=0.14). These main effects indicated better memory across groups for neutral pairs (M=46.5%, SD= 5.69) over negative pairs (M=42.9%, SD= 5.66) and higher subjective memory in List 2 (M=21.2%, SD= 5.81) compared to List 1 (M= 20.1%, SD= 5.51). Whereas the Bayesian statistics were inconclusive regarding the main effects for LIST (BF_{10}=.48) and EMOTION (BF_{10}=2.18), I observed evidence in favour of a null effect of CONDITION (BF_{10}=0.14).

In order to determine if exercise may have influenced the relationship between objective memory hits and subjective JoMs, I measured their degree of association using Yule's Q coefficient. A high score indicates concordance between objective (hits) and subjective (JoM) performance. Log-odds of the Yule's Q coefficients were subjected to a 3 x 2 x 2 repeated measures ANOVA with factors CONDITION, LIST, and EMOTION. We found no significant main effects of CONDITION (F=2.15, p=.12, BF10=.04) or LIST (F=1.43, p=.24, BF10=205.75), but there was a robust main effect of EMOTION (F(1,92)=16.21, p=.0001, BF10=.15). The relationship between subjective and objective memory performance was significantly stronger for neutral pairs (M=1.98, SD=0.81) than negative pairs (M=1.62, SD=0.66).

4.5. Correlations

Finally, in the two exercise groups, I also conducted exploratory correlation analyses relating core outcomes of the memory task (d-prime in both lists) with participants' reactivity to the intervention, i.e., their mean heart rate during the exercise. In order to keep the number of correlations small, I averaged d-prime across both negative and neutral pairs. Heart rate was averaged across the entire exercise intervention (minutes 6-25). The outcomes are shown in Table 4.3 and illustrated in Figure 4.6.

Table 4.3: Pearson correlations between hits/d-prime and heart rate in the two exercise conditions

	Low Exercise		High Exercise	
	HR warm up	**HR exercise**	**HR warm up**	**HR exercise**
List 1 d-prime	.27	.18	.30	.37*
List 2 d-prime	.28	.12	.22	.41*
Total d-prime	.29	.15	.27	.42*

*: p-value < .05

In the high-intensity group only, mean heart rate during the exercise intervention was positively correlated to memory hits, in both lists. The scatter plot in Figure 4.6 illustrates both groups' correlations between d-prime in List 2 and heart rate during exercise, showing the difference in their correlation patterns. Of note, these correlations were not driven by outliers as can be seen in the scatter plot.

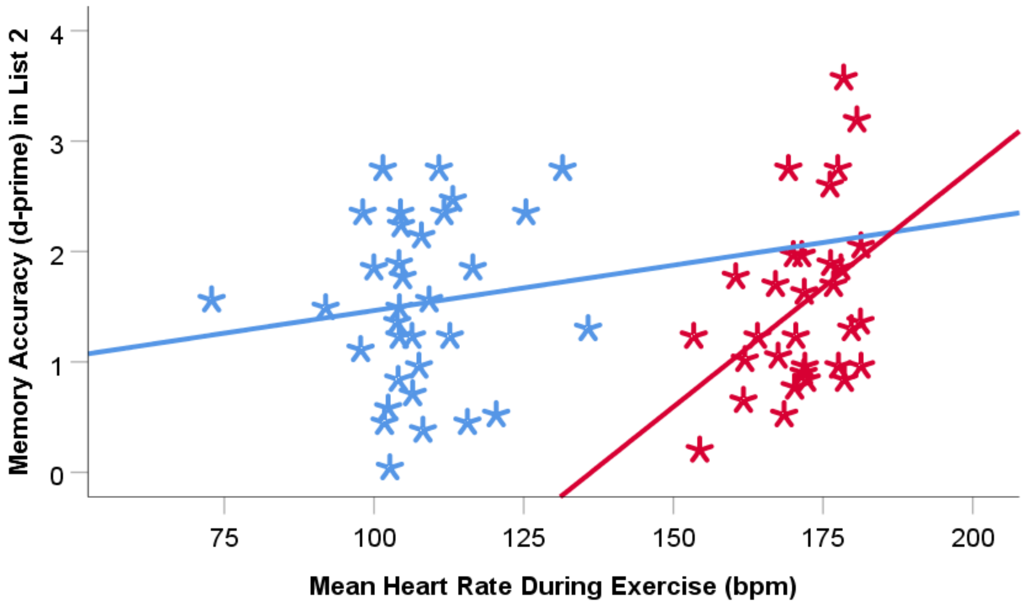

Figure 4.6: Correlations between memory (d-prime) in List 2 and average heart rate during exercise in the low exercise (blue) and the high exercise (red) group.

Since more people from the low-intensity exercise group compared to the high-intensity exercise group were tested in the morning, I also examined whether test-time was related to memory hits and heart rate changes due to exercise. Point-bi-serial correlations between test time (0=morning, 1=afternoon) and d-prime showed a trend correlation in the low-intensity group, with individuals who were tested in the morning having slightly better memory: $r(33)= -.32$, $p =.07$. None of the other correlations (see Table 4.4) were significant.

Table 4.4: Correlations between memory accuracy (d-prime) and time of testing (0=morning, 1=afternoon), heart rate during exercise

	Low Exercise	**High Exercise**	**Control**
Time of day	.26	-.21	.05
Heart rate during exercise	-.32	.07	n/a

Because test time and intervention were confounded by this sampling error, the correlations between heart-rate changes and memory (in the high exercise group only) could instead have been an effect of being predominantly tested in the afternoon. Thus, I also tested:

A) Whether time-of-day substantially influenced the correlation between heart rate increase and memory performance using partial correlations controlling for test-time
B) Whether correlations between heart rate increase and memory performance were substantially different in subgroups of people tested in the morning or in the afternoon.

The outcomes of the partial correlations are shown in Table 4.5, showing that controlling for test-time left the original correlations (cf. Table 4.3) virtually unchanged, I still observed significant relationships between heart-rate and memory in both lists only for the high exercise group, although the low exercise groups' correlation for List 1 now became a trend effect (r_{part} = .33, p= .058). Thus, the positive relationship between memory and heart-rate changes in the high exercise group seemed uninfluenced by test-time.

Table 4.5: Partial correlations between memory accuracy (d-prime) and heart rate during exercise, controlling for time of testing

	Low Exercise	**High Exercise**
List 1	.34	.42*
List 2	.19	.42*

As can be seen in Table 4.6, all correlations between heart rate and memory split by test time were positive, with the correlation for List 2 for people in the high exercise condition tested in the afternoon passing statistical threshold: r(22)= .42, p=.04, an effect likely due to larger sample size.

Table 4.6: Correlations between memory accuracy (d-prime) and heart rate during exercise, split by condition and time of testing

	Low Exercise		High Exercise	
	Morning (n=19)	Afternoon (n=14)	Morning (n=8)	Afternoon (n=23)
List 1	.34	.38	.69	.47
List 2	.19	.21	.35	.42*

Inspecting the scatter plots of these relationships did not reveal any substantial differences in the relationships between heart rate changes and memory between morning-tested and afternoon-tested individuals' either (see Figures 4.7 – 4.10). Thus, even though there were differences between the two exercise groups' test times, these did not seem to influence the outcomes.

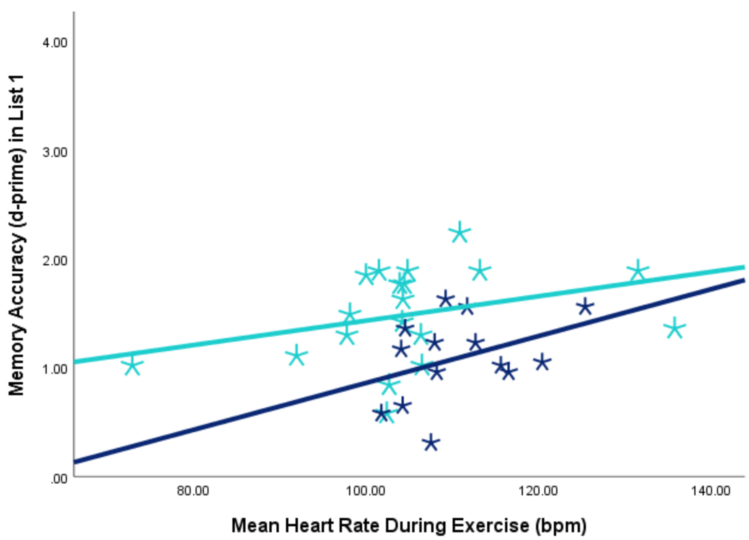

Figure 4.7: Correlations between memory (d-prime) in List 1 and average heart rate during exercise in the low exercise separated by tests done in the morning (light blue) versus afternoon (dark blue)

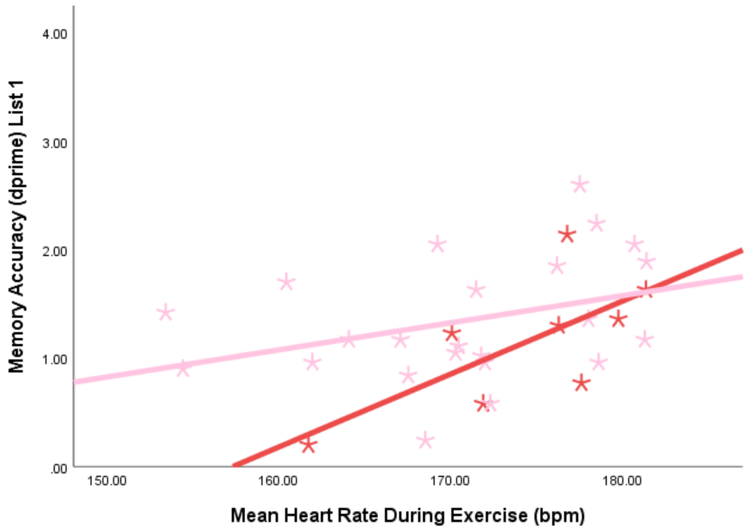

Figure 4.8: Correlations between memory (d-prime) in List 1 and average heart rate during exercise in the high exercise separated by tests done in the morning (light pink) versus afternoon (dark pink)

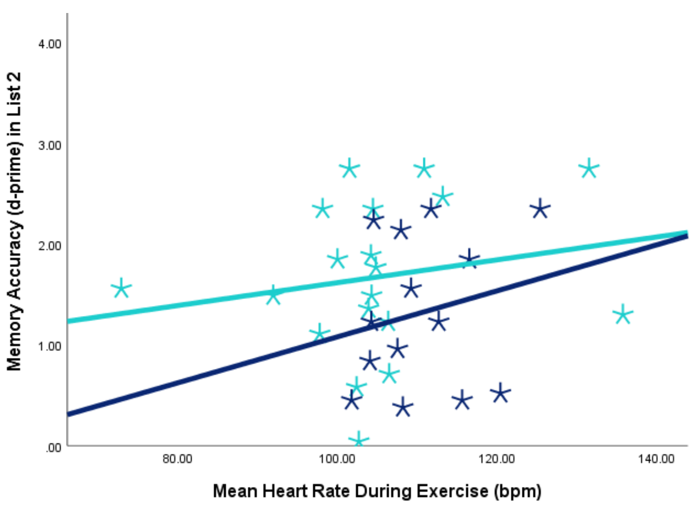

Figure 4.9: Correlations between memory (d-prime) in List 1 and average heart rate during exercise in the low exercise separated by tests done in the morning (light blue) versus afternoon (dark blue)

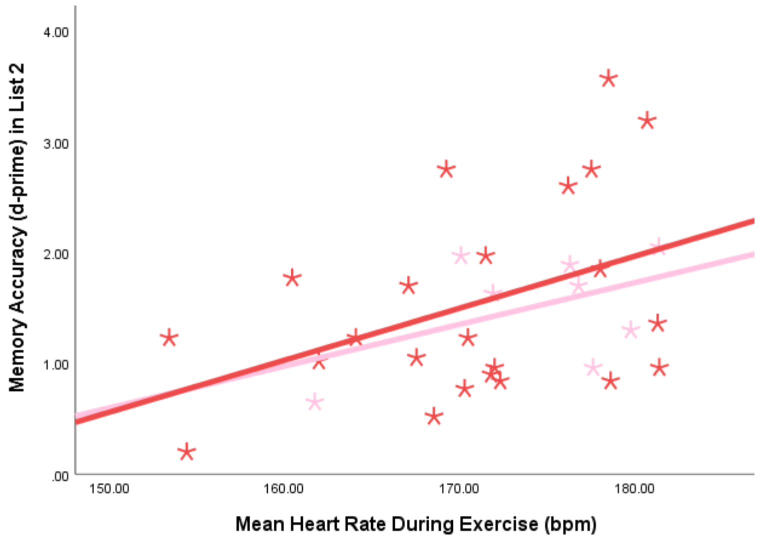

Figure 4.10: Correlations between memory (d-prime) in List 1 and average heart rate during exercise in the high exercise separated by tests done in the morning (light pink) versus afternoon (dark pink)

5. Discussion

Does acute exercise influence emotional association memory? The results of my study confirmed several null-findings: Acute exercise at high-intensity or low-intensity had no effect on memory accuracy, memory bias, and also did not influence subjective judgements of memory. Despite a successful exercise intervention and replication of the non-exercise-related outcomes of the task, I conclude that acute exercise did not influence emotional or association memory in this study.

Irrespective of exercise, I replicated a main effect of emotion in the memory task, indicating that association memory accuracy for neutral information was better overall than for negative information, as intended and shown in previous studies from our group (Caplan et al., 2019; Madan et al., 2012; Madan et al., 2017) and others (Bisby & Burgess, 2014; Bisby et al., 2016; Zimmerman & Kelley, 2010). Specifically, previous studies with variants of the same task have reported better memory for neutral picture pairs over negative picture pairs, in the magnitude of 7.9% (Caplan et al., 2019), 8.6% (experiment 1 of (Madan et al., 2017), 6.8% (experiment 2), and 6.2% (experiment 3), with an average of 7.4%. Across both lists and all conditions, I observed an overall advantage of 4.3% for neutral over negative pair memory, which overall was significantly different from zero although somewhat smaller than in the previous studies. I had expected the bias to be present for all groups before the intervention in List 1, and had alternative hypotheses about how such a bias could change after exercise.

To reiterate, my first hypothesis predicted that the neutral-pair bias would dissipate in the high-intensity exercise group compared to the low-intensity and the no-activity control condition. My alternate hypothesis stated that the bias would get stronger following high-intensity exercise. Given the evidence that the task I used directly recruits the hippocampus and prior research implicating the positive responsiveness of the hippocampus to acute exercise, theoretically, the physiological changes produced through exercise may act on the hippocampus and alter association memory performance (Basso & Suzuki, 2017; Budde et al., 2010; Carro et al., 2003; Chang et al., 2012; Coutts et al., 2009; Egan et al., 2003; Erickson et al., 2013; Goekint et al., 2008; Griffin et al., 2011; Hakansson et al., 2017; Hegberg et al., 2019; Jeanneteau et al., 2012). Regarding the particular memory task here, experiment 3 in Madan et al. (2017) reported that the more difficult successful encoding of negative pairs required increased hippocampal activity, relative to the easier and extra-hippocampal encoding of neutral pairs. If hippocampal functions are improved via exercise, encoding of negative and neutral pairs could have been equally difficult, resulting in no bias in the high-intensity group. Alternatively, having to perform a difficult exercise in front of an experimenter could have made the participants in the exercise condition more stressed compared to the other conditions, and hence exaggerated the emotional memory bias (Buchanan & Lovallo, 2001; Schlemmer & Desrichard, 2018). Clearly, I observed no support for the alternate hypothesis - the bias did not become stronger after high-intensity exercise. Regarding the first hypothesis' null-prediction, although there was no bias in the high-intensity exercise group in List 2, this group already showed no sizable memory bias in List 1 (see Figures 4.4B and 4.5B). Thus, the high-intensity exercise group was the only one that started out without a neutral-pair memory bias and therefore exercise-induced changes to the balance between neutral and emotional pair memory are difficult to evaluate as a result of the intervention. Interestingly, the control group showed a pattern of outcomes we expected to observe in the intervention: Using conventional statistics the control group demonstrated a significant memory bias toward neutral pictures in List 1 ($t(30)=2.37$, $p=.02$, $BF_{10}=2.11$), but not in List 2 ($t(30)=1.45$, $p=.15$, $BF_{10}=0.49$). This change in bias follows my prediction (hypothesis 2) for the high-intensity exercise group. Although the reasons for this findings are unclear, perhaps this could be due to boredom with the 'intervention' (i.e., watching a relatively unengaging nature video) and causing a drop in motivation to perform the memory task to the best of their ability. However, I would like to note that the change in bias was small, the control group barely had a significant bias in List 1 and the Bayes Factor for List 2 indicates more support for the null (see Figure 4.4). Further, when analyzed using d-prime (Figure 4.5), the memory bias in List 1 was no longer significant ($t(30)=1.95$, $p=.06$, $BF_{10}=1.02$) and remained non-significant in List 2 ($t(30)=1.57$, $p=.12$ $BF_{10}=.57$). Thus, there was a small change in bias in the control group resembling the prediction I had for the high intensity exercise group, but the size and stability of the bias findings in this study overall are difficult to interpret. If the control groups' bias in List 1 is taken seriously, perhaps boredom with the control intervention may have led to participants disengaging from the experiment and therefore eliminated the bias in List 2.

More importantly, I expected all three groups to start out with a memory bias (i.e., before they had participated in any intervention). Thus, the following section speculates about potential reasons for the unexpected lack of bias in List 1 for the high-intensity group.

No memory bias in the high-intensity exercise group prior to the intervention

There are several potential reasons for pre-exercise differences in performance. First, I would like to note that in an extensive pilot phase for the current study, I had also observed a lack of bias in the high-intensity group in List 1 *prior* to the exercise intervention, Briefly, in a separate, non-blinded pilot study with 50 participants (16-17 in each group) I had also observed no significant memory bias in List 1 in a high-intensity exercise condition (mean bias: 2.1%, $p=0.53$ compared to zero), unlike significant neutral-pair biases in both a low-intensity exercise group (12%, $p<0.001$) and a control group (6.2%, $p=0.046$). The high-intensity exercise group also had (non-significantly) higher accuracy in List 1 (mean recognition hits: 57.24%), compared to participants in the low-intensity exercise (51.08%) or control condition (51.36%).

In the pilot phase of this study, I had interpreted that these memory differences prior to any intervention may have been due to a placebo effect and/or an increase in arousal in anticipation of the expected high-intensity exercise. As discussed in Section 1.2, a potential issue with exercise-cognition research is the current public opinion that exercise is beneficial for brain function and cognition, and this prevailing belief may cause expectancy-driven placebo effects if not controlled by experimental design (Lindheimer et al., 2017). Additionally, simply knowing that one will have to soon be engaged in rigorous exercise may cause physiological stress and anxiety. This potential increase in anxiety could also theoretically alter memory performance on the first list due to increases in cortisol, epinephrine, or noradrenaline (Robinson, Sünram-Lea, Leach, & Owen-Lynch, 2008). Lastly, when the experimenter is aware of the experimental condition, they could themselves experience and convey more anxiety; knowing they are about to run a participant through the high-intensity exercise condition may be anxiety-inducing as it is much more complicated and intensive compared to the low-intensity or no-activity control conditions. Experimenter anxiety may become apparent to the participant and influence their mood and/or performance. Thus, the outcomes of our initial prompted us to implement the current randomization and blinding such that neither the experimenter nor the participant were aware of the condition until after the participant had completed the association-memory task for the first time (List 1). This process, in theory, should have eliminated any differences in List 1 performance across groups. However, although the accuracy differences between the high-intensity and the other groups were addressed by this change, the absence of a memory bias in List 1 in the high-intensity group remained.

The most obvious reasons for these outcomes are methodological - the memory bias in this task might simply be too small and too variable. Inspecting the size of the biases against zero by Bayes factors indicated most of the within-group outcomes to be in the 'undetermined' range - not in support of the null hypothesis or the alternative hypothesis. In other words, even though by conventional statistics, the low-intensity and control groups may have had significantly better memory for neutral pairs than negative pairs before the intervention (whereas the high-intensity exercise group did not), the Bayes factors for these within-group tests were largely inconclusive. Further in support of this interpretation is the large variability across subjects as apparent in the large error bars on Figures 4.4 and 4.5. In fact, only when collapsing across the entire sample (N=95) was the memory bias reasonably supported by Bayes factors (Figures 4.4A, 4.5A). None of the previous studies with variants of this paradigm (Caplan et al., 2019; Madan et al., 2012; Madan et al., 2017) reported Bayes factors but based on the current outcomes, a future study with about three times larger sample sizes *per group* would be required to confirm or refute the presence of a memory bias. In this instance, each group would consist of at minimum 90 participants and such a study may then be able to evaluate any changes to emotional memory biases after exercise using this paradigm.

Furthermore, I did not ask participants when they last exercised prior to testing (or if they commuted to testing by bike…etc). Thus, it is possible that some participants who had engaged in exercise prior to the study were (by chance) randomized to the high-intensity group and therefore already started out with different performance than participants in the other two groups. Additionally, a higher number of participants coincidentally participated in the high-intensity exercise condition in the afternoon (after 12 pm) compared to the low-intensity group and the non-active control. Given the effects of circadian rhythm on cortisol, with lower levels of cortisol and memory performance in the afternoon, this could have possibly influenced average memory performance as well as any exercise-memory links disproportionately for the high-intensity exercise group (Hwang, Castelli, & Gonzalez-Lima, 2016; Potter & Keeling, 2005). Future studies should test all participants either around the same time of day or at least ensure an even distribution across groups.

Heart-rate in the high-intensity exercise group was related to better association memory

Beyond effects on emotional memory/memory bias, my third hypothesis suggested that high-intensity exercise may increase overall association memory performance, i.e., irrespective of differential effects of exercise on emotional versus neutral association memory. This hypothesis was motivated by some previous studies reporting better association memory after exercise (see also discussed in section 2.2.1 (Coleman et al., 2018; Griffin et al., 2011; Hotting et al., 2016; Schmidt-Kassow et al., 2013; Schmidt-Kassow et al., 2014; Van Dongen et al., 2016; Winter et al., 2007)). We saw no significant differences in association memory accuracy memory between the high-intensity exercise compared to low-intensity exercise and the control group. However, when I conducted exploratory correlation analyses relating memory accuracy (using d-prime in both lists) with participants' reactivity to the intervention, I found that in the high-intensity group only, greater reactivity was positively correlated to memory accuracy, both pre-and post-intervention. Simply put, those who were high responders to exercise (achieving higher average heart rates after the warm-up phase until the end of the 25-minute exercise) demonstrated better memory performance overall, compared to low responders.

Several of previous studies examined relationships between association memory and individual differences in various biological/physiological parameters related to reactivity to the exercise intervention. For example, Keyan and Bryant (2017) found that participants with a stronger salivary cortisol response to exercise also demonstrated better associative memory than those who had a weaker response. Furthermore, Griffin et al. (2011) found that the blood serum levels of BDNF produced in response to exercise were related to better associative memory performance in face-name learning. Winter et al. (2007) measured peripheral catecholamine plasma levels (dopamine, epinephrine, and norepinephrine), blood lactate, and serum BDNF. They found that exercise-induced BDNF increases improved immediate learning speed of picture-novel-word pairs and dopamine/epinephrine increases were positively related to delayed retention of associative memory. In Hotting et al. (2016), BDNF increases after hard-intensity exercise were positively correlated to retention of vocabulary (word-novel-word pairs) after 24 hours, and in this case unrelated to immediate learning. Thus, it is possible and in line with previous findings that associative memory changes after exercise are not equally observed in all participants but exclusively or especially in those with higher reactivity to the intervention. The findings by Griffin et al (2011) and Winter et al. (2007) also indicate that such effects could have been stronger if I had tested memory retrieval at a longer delay. Exercise will induce changes to neural (hippocampal), molecular (BDNF), endocrine (cortisol), and physiological (heart-rate) systems at a different time courses (Buchanan & Lovallo, 2001; Hotting et al., 2016; McMorris, 2016; McMorris & Hale, 2015), but at the very least, measuring additional biological parameters could uncover further relationships to associative memory also in the current task. Since in the current study, correlations between heart-rate changes during high-intensity exercise and memory performance were already observed in List 1 (i.e., prior to the exercise) and not just in List 2, some feature of the participants in the high-intensity exercise condition rather than, on in addition to, effects of exercise per se may have been at play here, similar to factors discussed in the context of the absent memory bias in List 1 in the high-exercise group (e.g., differences in the test time).

In general, what determines heart-rate responsiveness to high-intensity exercise? Typically if the target heart rate is relatively high, as it was in my study (90% of calculated maximum heart rate), those with higher fitness levels tend to stay at a more consistent heart rate once they have reached the target heart rate, as they would have adapted to greater autonomic cardiac regulation (Fronchetti, Nakamura, De-Oliveira, Lima-Silva, & De Lima, 2007). In contrast, participants with lower fitness levels cannot as easily regulate their heart rate to stay at a high target level consistently (Fronchetti et al., 2007; Kwon et al., 2016). In my study, higher average heart rates in the high intensity exercise group may indicate better fitness level because less fit participants struggling to maintain the taxing target heart rate may show more fluctuations in heart rate just below the target, averaging to lower heart rate increases on average (Fronchetti et al., 2007; Lewis, Kingsley, Short, & Simpson, 2007). Figure 5.1 illustrates this concept for my study with a high target heart rate of 90% of maximum. Conversely and also hypothetically, if I had chosen a lower target heart rate, heart rates of those with lower fitness levels would fluctuate both above and below a lower target heart rate and their average heart rate increases may be more similar to those with high fitness levels (see Figure 5.2).

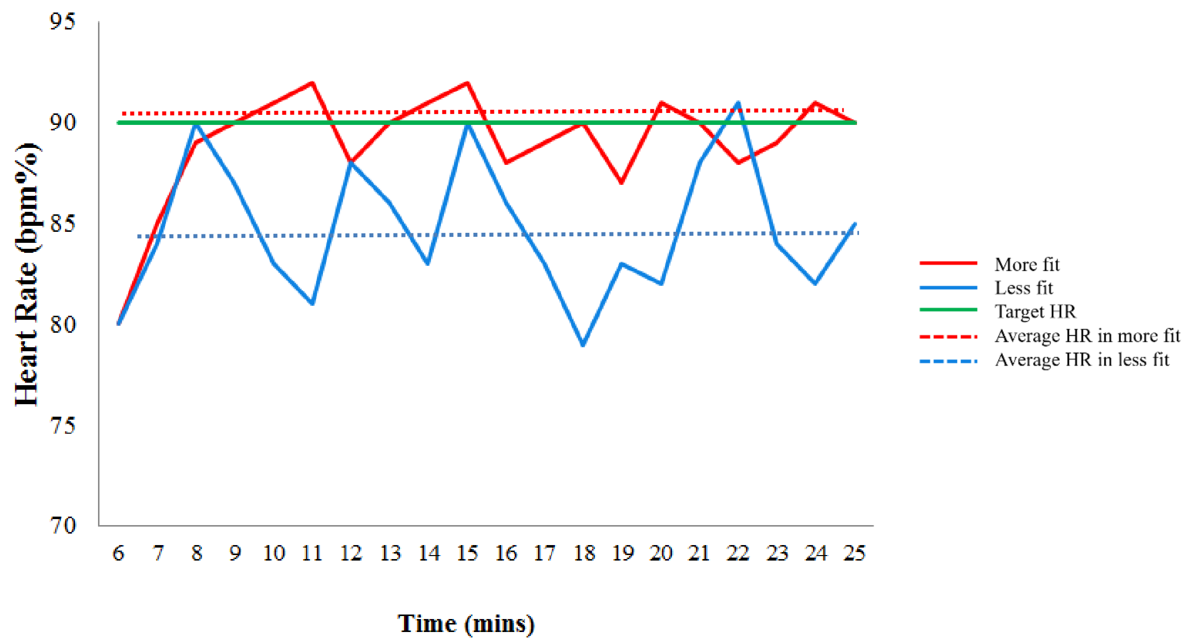

Figure 5.1: Theoretical heart rate response (bpm% of calculated max heart rate) of high exercise group (red), and the low exercise group (blue) where the target heart rate is 90% of max (green).

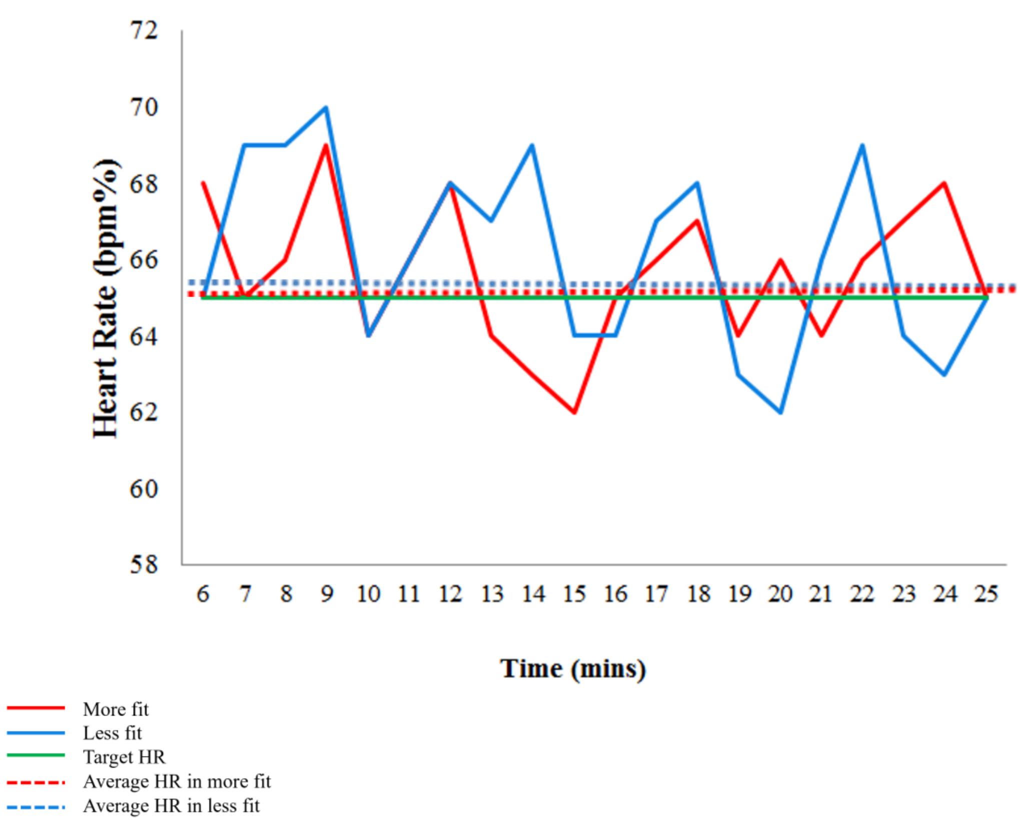

Figure 5.2: Theoretical heart rate response (bpm% of calculated max heart rate) of high exercise group (red), and the low exercise group (blue) where the target heart rate is 65% of max (green).

Thus, individuals with better ‘responsiveness’ (higher average heart rate) in the current study are theoretically more likely to be the more fit participants, as they seemingly struggled less to keep their heart rate at 90% of max. In contrast, those who had, on average, a lower heart rate may have struggled to maintain the goal of 90% and would have hovered closer to our minimum expectations of ~85% of maximum heart rate. However, with our current heart rate data, it is impossible to assess variance in the heart-rate changes between participants as data collection points were only done roughly every two minutes but not consistently so across all participants and I therefore did not analyze the heart rate measure any further. Furthermore, in the current study, we found no statistical relationship between the fitness-levels we measured using the LTEQ scale, and the exercise-induced heart-rate changes. If average heart rate indicated fitness levels, it would mean that those who are more fit performed better on our memory task, even prior to the exercise intervention. This result would not be unexpected, as individuals who exercise regularly tend to have greater vascularization of the body and parts of the brain compared to their less fit counterparts, and increased vascularization allow for better delivery of both centrally and peripherally produced factors (lactate, dopamine, epinephrine, cortisol, BDNF) to the brain, including memory-critical hippocampal regions (Erickson et al., 2013). Given that the current memory task has been shown to involve hippocampal activity (Madan et al. 2017), dispositional physical fitness levels of the participants could have influenced their physiological/biological responsiveness to the exercise intervention, hippocampal function and subsequently, their memory performance (Alfini et al., 2016; Erickson et al., 2011; Holmes et al., 2004; Redila & Christie, 2006). The LTEQ-scale I used here is a self-report measure and due to the desirable nature of being considered a "fit person". there are limitations in self-report of fitness-levels (Jensen, Rosthøj, Linneberg, & Aadahl, 2018; Piasecka, Kolmetz, Kotyśko, & Stankiewicz, 2018; Van Heuvelen, Kempen, Ormel, & de Greef, 1997). However, in some previous studies both subjective and objective physical fitness levels have been found to influence links between acute exercise and cognition (Chang et al., 2012; Tomporowski, 2003). Nevertheless, in future research, an objective measurement of fitness levels such as a measurement of VO2 maximum may better evaluate the role of dispositional fitness in influencing what factor (if any) may have influenced the relationship between heart-rate and memory performance in the high-intensity exercise group.

No effect of exercise on association memory accuracy

Why was association memory accuracy - on average - not influenced by exercise? Subtle methodological differences between the relevant previous studies and my own study could have played a role and are discussed in the following section, starting with the type and intensity of the interventions, followed by the experimental order of exercise and memory testing, the memory tasks/materials, as well as the cohorts.

Type and intensity of exercise: As reviewed in section 1.2.1, four of the twelve association memory studies used interventions that would classify as at least 'hard' intensity, similar to my own, and these studies had shown that exercise improved some aspects of association memory (Griffin et al., 2011; Hotting et al., 2016; Van Dongen et al., 2016; Winter et al., 2007), see Table 5.1.

Table 5.1: Exercise protocols in the current study and previous studies with hard- to maximum exercise intensity and positive association memory outcomes.

Authors	**Exercise Intensity**	**Exercise Duration**
Current study	**Hard (90% max HR)**	**25 mins**
Hotting et al., (2016)	Hard (80% max HR)	30 mins
Van Dongen et al., (2016)	Hard (80% max HR)	35 mins
Winter et al., (2007)	Maximum (~94% max HR)	10 mins
Griffin et al., (2011)	Maximum (up to max HR/failure)	10 mins – 30 mins (average: 15-20 mins)

Using maximal intensity exercise (Griffin et al., 2011) also used cycling and had participants exercise to maximum intensity (only 7% greater than the heart rate intensity used in my study) However, the duration of their intervention ranged from ~12 minutes to maximum 30 minutes (average 15-20 mins), whereas our exercise intervention lasted always 25 minutes. Griffin et al. (2011) had such a wide time range since they used a “ramp up” protocol in which participants exercised to their maximum heart rate, or until they could not maintain a minimum cadence while cycling. The other maximum intensity exercise intervention study (Winter et al., 2007) also had participants work out for only 10 minutes total. The two remaining studies using high-intensity exercise had similar exercise durations to ours (30 minutes at 80% of maximum heart rate (Hotting et al., 2016); 35 minutes at 80% of max heart rate (Van Dongen et al., 2016). However, both studies kept participants at a minimum heart rate that was 10% lower in our study, with 80% instead of 90% of maximum heart rate). Thus, the lack of overall association memory improvement in List 2 in the high-intensity exercise group may have been due to our intervention being too intense and too long, leading to lack of motivation, exhaustion, fatigue and/or boredom to perform the memory task a second time.

Interestingly, in the meta-analysis by Chang et al., (2012), studies with similar protocols (exercise followed by cognitive task) found that shorter exercise bouts (less than 20 minutes) negatively affected cognitive performance while longer bouts (more than 20 minutes) had positive effects on cognitive performance. In theory, this effect is observed because the physiological mechanisms which respond to acute exercise require time to build to minimum levels needed to benefit cognition (Chang et al., 2012; Tomporowski, 2003). However, in exercise protocols lasting longer than 20 mins, fatigue and dehydration may negatively impact the benefits incurred from the exercise itself, leading to an intricate balance between potential benefits and detriments of exercise on cognition (Chang et al., 2012; Cian, Barraud, Melin, & Raphel, 2001; Cian et al., 2000; Tomporowski, 2003). Simply performing the task twice (which none of the other twelve association memory studies did) may have added to boredom/fatigue or habituation with the task. While we made water readily available to participants, we did not measure water intake, nor fatigue following exercise and prior to List 2 encoding.

The order of administration of the exercise intervention and the memory task differed from most of the previous association memory studies. Our participants performed the entire memory task twice (encoding and retrieval of two different lists) with an exercise intervention between lists, whereas most previous studies only had one list, with encoding and retrieval administered once (Coleman et al., 2018; Hotting et al., 2016; Johnson et al., 2019; Loprinzi, Day, et al., 2019; Loprinzi, Koehler, et al., 2019; McNerney & Radvansky, 2015; Schmidt-Kassow et al., 2013; Schmidt-Kassow et al., 2014; Van Dongen et al., 2016; Wingate et al., 2018; Winter et al., 2007). Similarly, all four of the emotional memory studies included only one list with encoding and retrieval (Bruhl et al., 2019; Keyan & Bryant, 2017; Wade & Loprinzi, 2018b; Weinberg et al., 2014). Only one of the twelve association memory studies had a similar protocol like mine: encoding→ retrieval → exercise → encoding → retrieval (Griffin et al., 2011). To reiterate my previous interpretation, the repetitiveness and duration of the memory task, in combination with other time-consuming elements of the protocol (testing took on average 90 mins to 120 mins total), may have contributed to loss of motivation, especially considering that the memory task was done twice (~50 minutes total of memory testing). However, it should also be noted that (Griffin et al., 2011)'s protocol was very similar with their memory task taking approximately 25 minutes each time as well.

Memory task and materials: The current study is the first to test exercise effects on emotional association memory such that this exact combination of features in a memory task cannot be directly compared to previous findings. None of the other twelve associative memory studies used picture-picture pair learning as I did here. Some studies used object-location learning (Coleman et al., 2018; Loprinzi, Koehler, et al., 2019; Van Dongen et al., 2016). Object-location learning has been extensively linked to hippocampal function in animals (DeVito & Eichenbaum, 2010; Eichenbaum, 2017)and given the prominent role of the hippocampus in spatial cognition beyond memory also in humans (Burgess, Maguire, & O'Keefe, 2002; Cornwell, Arkin, Overstreet, Carver, & Grillon, 2012), perhaps, exercise-induced changes in hippocampal function have a better chance to affect spatial association-memory tasks. However, this is difficult to conclude based on the inconsistent findings of the three relevant studies, reporting positive effects in (Van Dongen et al., 2016), no effects in (Loprinzi, Koehler, et al., 2019), and positive effects only in men (Coleman et al., 2018). It should be noted that object-location learning is a *within*-object association memory task since the location and the object coincide. Our task was purposefully designed to probe the effects of emotion on *between*-object association memory, following Mather's (2007, 2011) framework. In within-object association tasks, emotional aspects of the object would necessarily enhance learning of the location due to unitization processes (the location and the object become 'one') and result in better, not worse, association memory for emotional versus neutral associations.

Other association-memory exercise studies (Johnson et al., 2019; Loprinzi, Day, et al., 2019; McNerney & Radvansky, 2015; Schmidt-Kassow et al., 2013; Schmidt-Kassow et al., 2014) used verbal paired associates with variable list length of 10 pairs (Johnson et al., 2019; Loprinzi, Day, et al., 2019), 20 pairs (McNerney & Radvansky, 2015), or 40 pairs (Schmidt-Kassow et al., 2013; Schmidt-Kassow et al., 2014). (Griffin et al., 2011) participants learned 10 face-name pairs, and (Winter et al., 2007) presented 120 picture-nonword pairings over five learning blocks. Although my list length was higher than most of these, with 52 pairs, the list length in verbal paired associates tasks is typically low. As a side note, (Schmidt-Kassow et al., 2013; Schmidt-Kassow et al., 2014) presented 40 word-nonword pairs, which is arguably too high, and they achieved rather low memory accuracies between 10%-20%. A direct comparison of "memory load" cannot be drawn relative to my study, using pictures rather than verbal pairs. The learning procedure was explicitly instructed in all studies but in Winter et al. (2007) in which exposure to the pairings was also repeated five times. Taken together, these rather pronounced experimental differences make a direct conclusion based on materials/tasks difficult, both comparing the previous studies to each other in this regard as well as the comparing them to my study.

Participants: While most similar to the current study in terms of exercise intervention, both Winter et al, (2007) and Griffin et al, (2011) sampled only male volunteers who received no monetary or other benefits (such as course credit). This differs from our population, who were male (~40%) and female (~60%) undergraduate students who gained course credit in a introductory psychology course in exchange for their participation. This may present a difference in motivation and may be another reason for differences in outcomes between the current study and Griffin et al, (2011) who had a similar design and protocol. Another observation from our pilot study in which I recruited both volunteers and students who received course credit for their participation was that memory accuracy of volunteers (n=22) was on average 3.5% better than performance of student participants (n=38), and anecdotally, volunteers were much more eager to participate and perform well. These sampling differences in sex, recruitment and potential motivation to participate should also be considered.

No effect of exercise on emotional memory

Although I did not find that exercise influenced emotional memory specifically, this was not entirely unexpected given the negative results from the four previous emotional memory-exercise studies (Bruhl et al., 2019; Keyan & Bryant, 2017; Wade & Loprinzi, 2018b; Weinberg et al., 2014). Notably, two of the four studies took additional biological measurements and one study found some aspects of memory performance related to those.

Keyan and Bryant (2019) assessed salivary cortisol and BDNF genotype. Slightly less than half of their participants were carriers of the valmet66 allele, a genetic variant which significantly disrupts the activity-dependent secretion of BDNF; more specifically, carriers of this common variant have been observed to have reductions of BDNF in both the hippocampus and the amygdala (Egan et al., 2003; Marosi & Mattson, 2014), brain regions involved in emotional memory (amygdala) or episodic memory (hippocampus). Keyan and Bryant (2019) also measured salivary cortisol levels as an indirect measure of BDNF production, as cortisol increases the expression of BDNF (Jeanneteau et al., 2012). Both cortisol and BDNF concentrations typically increase in response to increasing exercise intensity (Basso & Suzuki, 2017; Maass et al., 2016). In Keyan and Bryant (2019), within the exercise group, individuals with the val66met polymorphism showed episodic memory improvement (not specifically memory for emotional pictures but all pictures) if they also had a significant increase in cortisol in response to the exercise. That is, in val66met carriers with assumed lower BDNF levels, episodic memory improvements after exercise may have been mediated via cortisol increase and – hypothetically – BDNF increase. However, this link was non-specific to *emotional* memory changes. The results of my research support the findings that exercise intervention does not significantly affect emotional aspects of an episodic memory task.

Weinberg et al. (2014) measured salivary alpha amylase, a biomarker for sympathetic nervous system activity (produced in response to exercise) that is often assessed in acute stress induction paradigms (Nater et al., 2006; Nater & Rohleder, 2009; Rohleder, Nater, Wolf, Ehlert, & Kirschbaum, 2004). Participants in their exercise group had overall higher level of salivary alpha amylase compared to participants in the resting group, indicating that they did have a physiological response to the exercise intervention. However, higher levels of alpha amylase in the exercise group were unrelated to memory performance overall and also unrelated to memory for the emotional pictures.

I would like to point out that in the current study, all ANOVA outcomes involving the interaction between 'emotion' and 'condition' were true null findings and not due to the small sample size/lack of experimental power, as confirmed with Bayes factors around BF_{10}=0.03 (recognition hits) and BF_{10}=0.04 (d-prime). Given the current and previous negative outcomes related to acute exercise effects on association memory versus emotional memory, it appears more promising to concentrate on association memory rather than emotional memory in future exercise studies.

Exploratory analyses: No effect of exercise on subjective memory

Finally, I also explored how acute exercise may influence subjective judgments of memory for neutral and negative pairs, regardless of objective memory, as well as the relationship between subjective and objective memory. Previous studies from my lab observed positive relationships between subjective judgements of memory or judgements of learning and actual memory accuracy (Caplan et al.; Madan et al., 2017) - participants tend to be accurate in their judgements that they can learn and retrieve neutral pairs better than the negative pairs in this paradigm. Given previous meta-memory findings pointing to overconfidence of people when they judge their ability to memorize emotional materials (e.g., Zimmermann and Kelley, 2010), and assuming arousal effects on people's mood when they exercise (Basso & Suzuki, 2017), I thought that perhaps individuals in the high-intensity exercise condition may become less accurate in their subjective memory judgements. However, our JoM outcomes supported prior findings with this task and indicated that participants seem to have a good concept of what they remember. The exercise intervention played no role in this effect, with moderate support for the null hypothesis from Bayesian statistics (BF_{10}=.14). Finally, the strength of the relationship between objective memory hits and subjective JoMs could have been influenced by exercise but it was not - participants were more accurate in their memory judgements for neutral pairs than they were for negative pairs, irrespective of the intervention, with support for the null hypothesis from Bayesian statistics (BF_{10}=.04).

Strengths and limitations

Several strengths of this study should be pointed out. First, I took many precautions to avoid common limitations of previous cognition-exercise research (Etnier & Chang, 2009; Etnier et al., 1997). For example, a common problem is the lack of proper control groups (Chang et al., 2012; Etnier & Chang, 2009) and to avoid this problem, I included both a low-intensity exercise group as well as a no-activity control group. Being able to compare results from the low-intensity exercise group (<50% of max heart rate) with those from the no-activity control group would have theoretically allowed us to control for the issue of a placebo effect from doing some exercise at all. Furthermore, a unique feature I added to our protocol was that the high and low-intensity exercise group viewed the control group's nature video while exercising, to avoid any possible confounding influence the video may have on mood (Alvarsson, Wiens, & Nilsson, 2010). Furthermore, to address a previous inconsistency in the literature, I chose to follow standardized categories to determine and stage exercise intensity. When examining exercise-cognition research, it can be difficult to understand the *true* intensity of the exercise based on the descriptions of the authors alone. That is, "hard", "moderate", "easy", "light" can have different meanings across studies. We chose to follow the standards set by the American College of Sport's Medicine (ACSM) which labels intensity based on what percentage of a calculated maximum heart rate is being achieved. This standard has been used by other reviewers when comparing the literature for systematic reviews/meta-analyses (Chang et al., 2012). Furthermore, I used heart rate as an objective measure of physiological response which is more precise than subjective measures (e.g., 'perceived exertion') used by some studies (Whaley, Brubaker, Kaminsky, & Miller, 1997).

Finally, blinding and randomization the way I used it here allowed for a cleaner interpretation of our findings and none of the relevant studies examining effects of acute exercise on association or emotional memory used any form of blinding. Although the high-intensity exercise group unexpectedly demonstrated different memory patterns even prior to intervention, at least this cannot have resulted from any expectation biases of the experimenter or the participant. The reasons for this unexpected effect are not clear and therefore solution to this imbalance are speculative. However, for future studies it would be important to require that participants not exercise within 24 hours prior to testing, to ensure experimenters are equally confident administering any of the three conditions, and to test participants around the same time of day across the three conditions.

With regard to limitations, due to the high demand of the emotional association memory task, its duration (~25 mins x 2), the duration of intervention/control (~25 mins), along with the high physical demand of the exercise interventions, I believe our protocol may have been too demanding on participants and may have caused mental, physical, or boredom and fatigue. To elaborate further, our control participants watched 25 minutes of a mundane nature video while passively sitting in a chair. Anecdotally, many participants expressed boredom with this task, possibly affecting how they performed on List 2 of the memory task. Similarly, the high-intensity exercise condition was physically demanding, and participants had to work very hard to maintain a heart rate of 90% of their maximum heart rate. This type of physical demand is also emotionally/mentally demanding (J. Thomas, Adler, Wittels, Enne, & Johannes, 2004), so this may have affected motivation to perform the memory task. Participants in the low-intensity exercise group often voiced that the exercise task was quite boring as they had to bike very slowly to keep their heart rate below 50% of their maximum heart rate. Just as proposed with the control group, boredom may have affected their memory performance and/or motivation.

A shortcoming of my study design was my lack of balance in testing participants evenly in the morning and the afternoon in each condition. Both the low exercise group and the high exercise group had positive correlations between memory accuracy and average heart rate when time of day was controlled although these were mostly non-significant due to small subsample sizes except in the afternoon-tested high exercise group ($r(31)= .42$, $p=.04$). Cortisol levels are well known to be lower in the afternoon and higher in the morning (Hwang, Castelli, & Gonzalez-Lima, 2016; Potter & Keeling, 2005). Assuming high intensity exercise stimulated cortisol release more than low-intensity exercise, when general levels of cortisol were at their lowest (i.e., in the afternoon), our high exercise intervention should theoretically have the biggest impact on memory performance in people tested in the afternoon (Hwang, Castelli, & Gonzalez-Lima, 2016; Potter & Keeling, 2005).However, due to the unequal subsample sizes ($n=23$ of the high intensity group were tested in the afternoon, $n=8$ in the morning), this remains speculative.

Another limitation was the observation of rather profound practice effects in the memory task, with robust and large main effect of LIST in all analyses (see Figures 4.3 A and 4.3 B). . Thus, the size of these practice effects could have overshadowed any intervention-related changes in memory or memory bias from List 1 to List 2. One way to address this caveat in the future would be to overtrain participants prior to the experiment to eliminate any practice effects (e.g., add in longer and more difficult practice tests prior to the actual experiment). Conversely, the effect of List could be eliminated entirely by only having participants complete the memory task once. I describe an example of such a between-subject design below.

A future between-subjects design with six groups but only one list, administering the exercise intervention either pre- or post-encoding may be beneficial. This would shorten the experiment, and likely keep participants in any of the three conditions more motivated. Although I would no longer be able to compare performance before and after the intervention within the same subject, this change, given enough participants in each group, i.e., ~n=90 without changes to the study design, would likely lead to lower variability of the memory outcomes within each group. This larger number of participants per group would address the issues with experiment power, although by changing the experiment into a between-subject design might make these sample size increases redundant.

6. Conclusion

The present results provide no evidence that an acute bout of high-intensity or low-intensity physical exercise leads to changes in emotional association memory for pairs of images. There was some correlative evidence that higher physiological responsiveness to high intensity acute physical exercise may be linked to better association memory performance generally. However, it remains an open question what influences whether a participant will have a greater physiological response to exercise, be it physical fitness or other. Altering the experimental approach such as: limiting memory testing to a singular session following exercise intervention, measuring more physiological parameters such as heart rate variability, heart rate fluctuations, and assessment of each participant's dispositional physical fitness level using VO2 max testing may be promising for future studies exploring the effects of exercise on memory.

Regardless of the outcomes, my study addressed many prior methodological issues with exercise-cognition research such as lack of control groups, and possible error sources like placebo effects. This also was the first study to examine how acute exercise would influence emotional association memory, an important question in the context of psychiatric conditions like Post-traumatic Stress Disorder. As such, if exercise had an effect on arousal-based memory distortions, e.g., elicitation of fear memories based on innocuous cues such as in PTSD (Morey et al, 2020), this knowledge could help optimize treatment for these conditions. Therefore, further research using emotional association memory paradigms in conjunction with exercise interventions would still be informative. Overall, this information is important to the field of exercise cognition research as it touches on a previously unanswered question with a highly controlled study design and the first data on influences of exercise on emotional association memory.

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