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The Effects of Exercise Intensity and Relative Timing of Exercise on Memory Performance

Alex Pennetti University of Windsor

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The Effects of Exercise Intensity and Relative Timing of Exercise on Memory

Performance

By

Alex Pennetti

A Thesis Submitted to the Faculty of Graduate Studies through the Department of **Kinesiology** in Partial Fulfillment of the Requirements for the Degree of **Master of Human Kinetics** at the University of Windsor

Windsor, Ontario, Canada

2015

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The Effects of Exercise Intensity and Relative Timing of Exercise on Memory

Performance

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Alex Pennetti

APPROVED BY:

Dr. Carlin Miller Department of Psychology

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Dr. Kenji Kenno Department of Kinesiology

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Dr. Kevin Milne, Advisor Department of Kinesiology

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October 14, 2015

AUTHOR'S DECLARATION OF ORIGINALITY

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ABSTRACT

When external stimuli cause a physiological response associated with arousal (increased adrenaline and cortisol), human memory is improved. Limited evidence suggests that exercise, a potent physiological stress, can improve memory as well. Consequently, this study aimed to further examine the exercise intensity-induced enhancement in memory and the relative timing of stimulus presentation on this phenomenon. 28 young adults were divided into 3 groups: viewing images before exercise (TG1), viewing images immediately after exercise (TG2) and viewing images 30 minutes post exercise (TG3). Each participant completed either rest, low (40% of VO2peak), moderate (60% of VO2peak), or high intensity (80% of VO2peak) cycle ergometry on separate days as the exercise stress. Correctly recalled images 45min after presentation were observed for memory. No significant differences were found between exercise intensities or timing groups ($p > 0.05$). However, further research is required to establish exercise as a method to improve memory at longer periods.

DEDICATION

This thesis is dedicated to the greatest family this galaxy or any other has produced. First, and foremost this thesis is dedicated to my parents, Mary Lou and Aristide Pennetti. This thesis would not have been possible without their countless sacrifices over the course of the past few decades. You have supported me in a variety of ways, and for that I am eternally grateful. This dedication is a small token of my appreciation but it would be impossible to return to you what you've provided me over the years. I'd also like to make mention of the risk that all of 5 (yes, 5) of my grandparents took. All of my grandparents made the epic journey migrating to Canada, fueled by hopes and dreams of a better life they packed up and left the comforts of their home country of Italy, and arrived with next to nothing but desire, courage and a massive reservoir of motivation. Unmistakably without their massive undertakings I would not be where I am (and probably not alive due to the fact my parents would never have met, but I digress). I also dedicate this thesis to my sister Victoria, my aunts, uncles and cousins who have all helped me immensely throughout my life in a variety of ways that would take up too many pieces of paper to list.

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Firstly, I acknowledge my thesis committee, Dr. Carlin Miller, and Dr. Kenji Kenno. Your time and effort to oversee this project is certainly much appreciated. You've both made significant suggestions and contributions that have improved this project and I again thank you helping me throughout this significant undertaking.

Secondly, I acknowledge and thank the lab volunteers who helped with this project. I am grateful for all of your time, and energy you've given to ensure that the project was run smoothly. My hope is that my passion for research has rubbed off on all of you and that a drive for discovery is a part of your future endeavors. I wish all of you the best in your academic and professional futures and I know that you will all be successful no matter the path you choose.

Lastly and most importantly, I want to acknowledge and apologize to the Milnes. Girls, I'm sorry for taking up so much of your dad's time over the past couple of years and adding to his collection of grey hair. I am leaving the nest now so when he is over worked it'll no longer be (entirely) my fault. Marcia, thanks for all of you've done as well. You've always been so generous to me, and I am truly indebted to you and your family. Finally, Kevin, I cannot do this acknowledgement justice without getting overly mushy and sappy about it, so instead I'll share this quote I saw one day on the internet "Tell me and I forget, teach me and I may remember, involve me and I learn". So, to the greatest teacher: I sincerely thank you from the bottom of my heart (A.K.A the apex).

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ABBREVIATIONS

- CRH: Corticotropin Releasing Hormone
- ACTH: Adrenocorticotropin Hormone
- SAM: Self-Assessment Manikin
- RPE: Rating of Perceived Exertion
- PAR-Q: Physical Activity Readiness Questionnaire
- IAPS: International Affective Picture System
- STAI: State-Trait Anxiety Inventory
- VO2: Volume of oxygen consumed
- HR: Heart Rate

Chapter 1: Literature Review

1.1 Memories connect our past with present

How would you function without memories? You certainly wouldn't be able to comprehend this thesis if you couldn't remember the previous words by the time you've reached the end of this sentence. How could you create lasting bonds with family and friends, without knowing whom you love or hate? Imagine the challenges of a single day if you lost the capacity to store information? Our "selves" are nothing but a collection of memories and our memories are what distinguish us from one another, memories connect our past with our present and memories allow predictions of the future based on past events. Within a memory, we can relive our most significant experiences, however joyful or agonizing they may be. However, memory is still not fully understood. For example, why do we "remember" some things and not others, especially those events that we would rather "forget"? The difficulty in fully characterizing the memory paradigm is due to its complexity. In fact, most theories on memory propose that there are many subtypes and several steps in the formation, storage and retrieval of memories. This complexity is apparent in the very first aspect of the presentation of new information. For example, when presented with new information, there may be a very brief time where there is an almost limitless amount of that new information that can be accessed (Cowan, 2001). However, the ability to retrieve that information is gone in a very short period of time and an individual becomes reliant on the capacities of short-term memory. A typical example of short-term memory is noted when presented with a new phone number. The seven digits are remembered because they are actively being attended to (i.e. attention to the

auditory stimulus). Short term memory typically provides enough time to remember the numbers long enough to write them down, but even within those few seconds, it is easy to forget one or two numbers and they often must be repeated. Without rehearsal or some other consolidating factor, the memory of the number may be lost in minutes and almost certainly in the proceeding hours/days. Consequently, there are other factors responsible for storing a memory in long-term memory. Moreover, it is often taught that in the theory of short term memory, there is a general capacity limit of approximately seven chunks/items of information, however, this limit may be too liberal or too conservative, depending on environmental/personal factors (Cowan, 2001). Consequently, the ability to shift information between initial presentation (or sensation), short-term memory and then longer storage is still an actively studied area. In addition, the temporal distinctions between sensory, short term and long term memory (discussed below) may very well be not as mutually exclusive as the models would suggest. For example, a 45-minute delay would certainly be considered long term memory, however, the mechanisms behind sensory and short-term memory are crucial in the formation of long-term memory. Thus, it is difficult to fully separate these memory subtypes in any investigation of memory.

Nonetheless, a well-accepted general proposal by Baddeley theorizes that when a novel stimulus is presented, it is initially processed using the senses (e.g. sight, smell, touch, etc.). However, attention must be given to any specific stimulus in order for information associated with the stimulus to enter short-term memory for a brief period of time (<30 seconds) (Baddeley, 2000; Baddeley and Hitch, 1974). However, the focus of attention appears to be limited in capacity, thereby limiting the total amount of information that can be stored from any given information set (Cowan, 2001).

Related to, but different, than short-term memory is the working memory or temporary information storage that is used in cognitive tasks. Working memory has been proposed to include executive processing of both auditory and visual information that is needed for current tasks. The process of converting short-term memories into long-term memories is termed memory consolidation or encoding, while the conversion of longterm memories back to usable short-term memory or into working memory is termed memory retrieval or recall (figure 1.1: Modified from (Baddeley, 2000 and Baddeley and Hitch, 1974). Our current understanding of how humans store and retrieve memories is still incomplete and a topic of great interest to many scientists.

Müller and Pilzecker (1900) first proposed the memory consolidation theory at the turn of the $20th$ century. They observed that memories of newly learned information could be interfered with by the introduction of additional information presented shortly after the original information, suggesting that new memories are delicate and consolidate into solidified long-term memories over time (Müller and Pilzecker,1900). This seminal theory has guided the field of memory consolidation for over a century and continues to guide research today.

Expanding upon the memory consolidation theory, researchers in the field of memory and learning have tried to decipher the mechanisms of memory consolidation. In the mid 1990's, Cahill and McGaugh found that participants presented with an emotionally arousing story were able to recall more details about the story than participants presented with a similar yet emotionally neutral story (Cahill and McGaugh, 1995). Their findings preceded further evidence that via increases in glucocorticoid and/or catecholamine concentrations, arousal plays a crucial role in modifying both

human (Andreano and Cahill, 2006; Cahill and Alkire, 2003; van Ast et al., 2013; van Stegeren, 2007), and animal (Roozendaal, 2002; Roozendaal, Okuda, et al., 2006) memory.

 It seems intuitive that emotionally stimulating memories are better remembered, and this is supported through scientific evidence as well (McGaugh, 2003). We are better able to remember the extraordinary, thrilling, or excruciating rather than the mundane, dull, or monotonous. The most well supported hypothesis of why this is the case, is still that of Müller and Pilzecker (Anderson, Wais, & Gabrieli, 2006; McGaugh, 2006), which again suggests that new memories are delicate and consolidate into solidified long-term memories over time, thus the memories that are optimally consolidated into long term memories are those that are likely remembered in the future.

Figure 1.1: General memory paradigm

Figure 1.1: When a novel stimulus is presented it is initially processed using the senses (e.g. sight, smell, touch, etc.). It then enters short-term memory for a brief period of time, (<30 seconds). Often thought to be related, but different than short-term memory, is the working memory or temporary information storage that is used in cognitive tasks. Working memory has been proposed to include executive processing of both auditory and visual information that is needed for current tasks. The process of converting short-term memories into long-term memories is termed memory consolidation or encoding, while the conversion of long-term memories back to short-term memory or into working memory is termed memory retrieval or recall. Both consolidation and recall can be modified by, for example, the physiological state of the individual or the use of different practices. (Modified from (Baddeley, 2000 and Baddeley and Hitch, 1974).

Figure 1.2: Types of long-term memory

Figure 1.2: Explicit long-term and implicit long-term memory differs in the degree that conscious thought is required to access them. Implicit memories are typically accessed as procedural memory (e.g. remembering how to walk). In contrast, explicit memories can be further divided into semantic memory (e.g. remembering the 7 continents) and episodic memory (e.g. remembering a significant life event such as the first day of a new job, or a car accident). As such, the proposed study focused on episodic long-term memory consolidation and retrieval.

1.2 Adrenal stress hormones affect memory

The glucocorticoid, cortisol, and the catecholamines, epinephrine and norepinephrine, are key biochemical regulators of the biological fight or flight response, and consequently, they are significantly increased in the circulation during periods of real and perceived stress (Miller et al., 2007). Cortisol is primarily synthesized and released from steroidogenic cells in the zona fasciculata of the adrenal glands (Simpson and Waterman, 1988). Typically initiated at the hypothalamus with the release of corticotropin releasing hormone (CRH), the anterior pituitary responds to elevated CRH by releasing adrenocorticotropin hormone (ACTH), which in turn stimulates the release of cortisol from the adrenal gland (Dickerson and Kemeny, 2004). Cortisol circulates both free and bound to corticosteroid binding globulin or albumin and has a half-life of approximately one hour. Typically, cortisol signaling involving the glucocorticoid receptor invokes changes in target cell gene expression through upregulated gene transcription.

The catecholamines, specifically epinephrine and norepinephrine are secreted from the sympathetic nervous system and the adrenal medulla. Typically, only secretion from the adrenal medulla results in circulating concentrations of these hormones, but spillover from adrenergic innervation of tissues may also occur during periods of high activation (e.g. during stressful events). The half-life of circulating catecholamines is much shorter than that of cortisol, typically a few minutes, and as such, their effects are normally immediate and fast acting although the modulation of gene expression (i.e. protein building) can occur resulting in slower effects. The catecholamines bind to adrenergic receptors to enact a variety of fight or flight actions including increasing heart

rate, increasing heart contractility and dilating bronchioles (Carrasco and Van de Kar, 2003)

Moreover, during an encountered stress, the catecholamines and cortisol act in concert to increase blood glucose concentration, suppress immune function, induce vasoconstriction, and increase heart rate, thus enhancing an animal's chances of survival (Dickerson and Kemeny, 2004). These homeostatic regulatory functions have no direct impact on memory, however, when cortisol concentrations are high, cortisol can cross the blood-brain-barrier and in conjunction with epinephrine and norepinephrine ultimately influence crucial brain regions (McGaugh, 2004; McGaugh et al., 1996) involved in memory consolidation such as the amygdala and hippocampus (Cahill and Alkire, 2003; Kukolja et al., 2008; McMorris et al., 2011; McGaugh, 2004; McIntyre et al., 2003; Revest et al., 2010; Roozendaal, Okuda et al., 2006; van Stegeren et al., 2007) (Figure 1.3).

Figure 1.3: Modulation of memory consolidation by stress hormones

Figure 1.3: Modulation of memory consolidation by emotional arousal and the subsequent release of adrenal stress hormones (cortisol and catecholamines). Emotional arousal and stressful stimuli (e.g. exercise) activate the release of noradrenaline in the basolateral amygdala and cause the adrenal gland to release stress hormones. In response to the stress hormones, the amygdala increases noradrenergic signaling and modulates memory consolidation in the brain. (Modified from McGaugh, 2006)

From an evolutionary perspective, it is logical that animals that remember a stressful environment or situation may be better able to cope with or avoid repeated exposures to similar stressors in the future, thus making them more fit for survival. As such, it is not surprising that an increase in the stress hormones, cortisol and the catecholamines, would be a potential mechanism by which enhanced memory consolidation would occur during periods of stress.

In fact, treatment with central adrenergic blockers in human (Cahill, Prins, Weber, M., & McGaugh, 1994; van Stegeren, 1998; van Stegeren et al., 2007) and animal models (Roozendaal Okuda et al., 2006) and glucocorticoid blockers in an animal model (Revest et al., 2010) can impair memory performance. The evidence from these studies suggests cortisol and the catecholamines have permissive and/or synergistic actions on memory consolidation. For instance, van Stegeren et al. (2007) found that participants who elicited an increase in endogenous cortisol levels in response to viewing images (ranging from neutral to extremely negative) had increased amygdala activation when given a placebo 90 minutes prior to image presentation, but no difference in amygdala activation when given a beta-blocker 90 minutes prior to image presentation.

Moreover, animal (McGaugh, 2000; Roozendaal, 2000; Roozendaal, Hui, et al., 2006; Roozendaal, Okuda et al., 2006) and human research (Buchanan and Lovallo, 2001; Cahill, Gorski, & Le, 2003; Felmingham et al., 2012; Kuhlmann and Wolf, 2006; Lupien et al., 2005; van Stegeren et al., 1998) have demonstrated the beneficial effects of increased circulating glucocorticoid and catecholamine concentrations on long-term memory performance. The weight of the evidence demonstrates improvements in memory consolidation with an increase in these hormones. However, some evidence has

demonstrated an inverted-U/quadratic dose response pattern of memory consolidation (Andreano and Cahill, 2006; Lupien et al., 2005) suggesting that there is an optimal concentration of cortisol and/or the catecholamines during new information exposure that results in optimal memory consolidation, whereas with further increases in cortisol and/or catecholamines, impairment may ensue (Figure 1.4).

Figure 1.4. Inverted U pattern of recall based on salivary cortisol change in response to stressor.

Figure 1.4. Inverted "U" relationship between cortisol or catecholamine change and subsequent memory (number of items recalled correctly). (Adapted from Andreano and Cahill, 2006)

At the present time, it is not currently known why this quadratic relationship may exist. However, a potential reason may be due to high concentrations of cortisol increasing the binding of low affinity glucocorticoid or other receptors, thus influencing the consolidation processes by decreasing the amount of synaptic long-term potentiation and increasing the amount of synaptic long-term depression (de Kloet, Oitzl, & Joëls, 1999). Long-term potentiation and long-term depression are the processes in which neural synapses strengthen and weaken, respectively. Thus, the initial increases in cortisol which lead to increased binding with high affinity receptors that, increase longterm potentiation and decrease long-term depression could significantly increase the likelihood that a given item or event is remembered sometime in the future while once cortisol concentration is high enough to elicit significant low affinity receptor binding, long-term depression is favoured (Malenka and Bear, 2004).

1.3 Exercise is a physiological stressor

 Physical exercise elicits similar physiological changes as psychological stress. During exercise, there is a need for increased blood flow to working muscle, increased demand/release of metabolic fuels, increased blood acidity, increased temperature, and a demand to clear potentially harmful metabolic by-products. These needs during exercise pose challenges to several aspects of biological homeostasis (i.e. the body is under stress). Exercise elicits significant increases in circulating cortisol (Fryer at el., 2014; Hill et al., 2008; VanBruggen, Hackney, McMurray, & Ondrak, 2011) and catecholamine (Weinberg et al., 2014) concentrations as global responses to many of those stressors. From an evolutionary perspective, the physiological responses to the demands noted

above (i.e. increased cardiac output, glucose output, increased heart rate and blood pressure) are clearly related to the need to engage in exercise (i.e. get away or fight for survival, mating, food, etc.) during stress. Further, the exercise-induced increases in stress hormones are positively correlated with exercise intensity (Crewther, Lowe, Ingram, & Weatherby, 2010; Fryer et al., 2014; Hill et al., 2008; Hough et al., 2011; Kindermann et al., 1982; VanBruggen et al., 2011; Winter et al., 2007). Consequently, because of the aforementioned relationship between these hormones and memory, it has been hypothesized that exercise can improve memory consolidation.

1.4 Acute and chronic exercise improves components of cognitive function

Animal (Berchtold, Castello, & Cotman, 2010; Speisman et al., 2013) and human research (Labban and Etnier, 2011; Roig et al., 2013; Weinberg et al., 2014) provide evidence that exercise may indeed impact memory consolidation, and this enhancement is via the endogenous increase in circulating catecholamine and cortisol concentrations. For example, Weinberg et al. (2014) found that in a randomized controlled trial, participants in the "active" group who performed one leg knee extension/flexion exercise after viewing images were better able to recall these images 48 hours later. Moreover, improved overall physical fitness in children can enhance cognition, memory, and academic achievement (Hillman et al., 2009; Hillman et al., 2014; Loprinzi and Kane, 2015; Pontifex et al., 2010), and physical activity interventions can improve a variety of aspects related to cognition in older adults (Colcombe and Kramer, 2003; Smith et al., 2010). While the exact mechanisms behind these improvements in cognitive function are unknown, that they occur following exercise training suggests chronic neurological adaptations with exercise. Whether these changes are the result of the summation of each

acute bout of exercise or dependent on a chronic adaptation that requires repeated exercise bouts has not been established and certain aspects of this phenomenon have yet to be investigated. Potentially confounding these observations is that exercise is a broad term defining many different frequencies, intensities, durations and types. In particular, the investigation of different exercise intensities on memory consolidation in the same study is rare.

1.5 Effects of stress hormones during memory retrieval

An item of interest within the stress-induced changes in memory is the potential hindering effects of high concentrations of cortisol and catecholamines during memory retrieval. Evidence suggests that high concentrations of these hormones can elicit poorer performance when trying to recall stored memories (Buchanan and Tranel, 2008; de Quervain et al., 2000; Domes et al., 2004; Domes, Rothfischer, Reichwald, & Hautzinger, 2005; Kuhlmann, Piel & Wolf, 2005; Roozendaal, 2002; Smeets et al., 2008; Smeets 2011). Moreover, the mechanism by which cortisol and the catecholamines improves consolidation may be similar to the impairing effects on retrieval. For example, in a study of 42 healthy volunteers, orally administered cortisone (exogenous cortisol) impaired retrieval yet the impairment was attenuated by the concurrent administration of propranolol (a beta adrenergic blocker that blocks the effects of catecholamines)(de Quervain, Aerni, & Roozendaal, 2007).

Another potential similarity between the phenomena of cortisol and the catecholamines improving consolidation and hindering retrieval is related to the dose response action, as an inverted-U pattern may exist in the effects of retrieval hindrance as well (Domes, Rothfischer, Reichwald, & Hautzinger, 2005). However, all but one of the

cited studies of stress-induced impairment in memory retrieval used a form of verbal memory and all but one used a 24-hour delay between presentation and memory retrieval. The present study examined episodic memory (which includes memories of events and episodes and is a component of explicit long-term memory) using images as the material to be remembered with a 45-minute delay between exposure and recall as a representation of long-term memory performance.

1.6 Sex differences in memory consolidation

The examination of sex differences in the stress/memory response has produced equivocal results. Evidence shows no difference between sexes (Weinberg et al., 2014), some sex differences (Andreano and Cahill, 2006; Wolf, 2001) or in most cases, sex differences are not explicitly investigated or reported. In the 2006 study by Andreano and Cahill, it was found that a cold-pressor task (i.e. submersing the hand in ice water) improved memory of a neutral story in men and not in women. It is possible that this sex difference is specific to either the type of stressor, the type of memory or an interaction of the two. Preliminary results from our lab, with a sample of 27 participants (14 male, 13 female) have shown no differences in memory (images recalled 1 week later) between sexes using the same exercise intensities in this study ($p= 0.525$).

1.7 Sex differences in the stress response to exercise

As noted above, no sex differences in the stress response to exercise were evident in the Weinberg et al., (2014) study. However, several studies cited above used all male participants (Fryer at el., 2014; Hill et al., 2008; Van Bruggen et al, 2011). There is a gap in the literature for the investigation of the stress response in both sexes within the same

research study. In preliminary results from our lab, with a sample size of 27 (14 male, 13 female) no sex differences in the stress (cortisol) response to exercise were observed in the response to the same exercise intensities that were used in the present study (p=0.840). The gap in the literature stems from the exclusion of female participants and the underreporting of sex as a variable.

1.8 The effects of the timing of stressor relative to information exposure and memory consolidation or retrieval

It is not currently known how long the potential exercise-induced enhancement in memory consolidation lasts or how exercise after the exposure of material modulates this response. One human study used the relative timing of exercise compared to exposure of memory material (paragraph recall) as a variable and it was found that exercise prior to exposure improved memory in the intervention group versus a control group, but exercise after exposure did not significantly differ from either the exercise before or the control groups (Labban and Etnier, 2011). However, this study used only one exercise intensity and did not use a time delay between the exercise and exposure in the pre-exposure group. In another recent study, the relative timing effects of hydrocortisone administration on long-term memory were assessed (van Ast et al., 2013). Participants (64 men) given 10mg pills of hydrocortisone 210 minutes before encoding outperformed participants that were administered 10mg pills of hydrocortisone 30 minutes before encoding as well as those in the control group that were given placebo pills on a 24 hour delay visual/verbal (words were presented with a corresponding picture in the background) recall test. This may be due to slow acting effects of cortisol or could relate to the inverted-U dose response curve since at the time of encoding the 210-minute group

had significantly lower salivary cortisol concentrations (van Ast et al., 2013). Nonetheless, timing of stressor exposure is an important aspect of the modulation of consolidation and retrieval processes and this requires further investigation.

1.9 Aspects of the exercise and memory field requiring further investigation

Given that the investigation of exercise-induced improvements on memory is a relatively young field, many gaps exist in the literature. Specifically, few studies examine more than one exercise intensity within the same cohort of participants, repeated measures approaches are generally underutilized in memory studies due to challenges related to learning effects, sex is an underreported variable, and the effects of the timing of acute exercise relative to the exposure of the material to be remembered have not been established. The present study attempted to address some aspects of the stress-induced improvement in memory consolidation that have not yet been comprehensively investigated.

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Chapter 2: Manuscript

2.1 Introduction

Why do we remember the things we do, and forget the things that we forget? At times we want this to be a conscious decision (e.g. remembering material for test, where we left our keys, etc.), but often, it seems beyond our control (e.g. remembering the end of a relationship). We don't decide to remember or forget every piece of information the moment that it is presented to us. Human memory is a complex multifaceted matter, which is involved in virtually all of our daily tasks. Although human memory is not fully understood there are several aspects that have been categorized.

 The three major types of memory are sensory, short term and long-term memory. The distinguishing factor between the three types is the length of time that a particular memory is stored in each form. Sensory memory lasts for a very brief period of time, generally not more than a few seconds. The brain processes senses such as sight, smell, taste etc. and if enough significance/attention is given to a particular sensory memory it can then be stored as short-term memory. Long-term memory includes the vast majority of any individual's memories, including names, places, facts, and events. Long-term memories are created from short-term memories through a process called consolidation. In order to be useful in the future, however, long-term memories must be converted back into short-term memories through a process called memory retrieval or recall. Thus, both the process of consolidation and recall are vital to any practical measurement of memory (Baddeley, 2000; Baddeley and Hitch, 1974).

 As humans, we remember the exciting, unique and thrilling as opposed to the boring, repetitive, and monotonous events in our lives. This is supported by a significant

amount of research (Cahill and McGaugh, 1995; McGaugh, 2003; McGaugh, Cahill & Roozendaal, 1996). Likely, life threatening events were more critical to survival, thus remembering these arousing events improved an animal's chances of survival and this trait could be passed on to its progeny. Since it has been repeatedly shown that arousing events and items are more likely remembered, it followed that researchers examined whether external stressors could influence memory. To date, a variety of stressors have been shown to improve memory in humans (Andreano and Cahill, 2006; Smeets et al., 2008; Weinberg, Hasni, Shinohara, & Duarte, 2014) Moreover, the arousal-induced improvement in memory has been linked to the adrenal stress hormones epinephrine, norepinephrine and cortisol in human (Buchanan and Lovallo, 2001; Cahill, Prins, Weber, M., & McGaugh, 1994; Cahill, L., Gorski, L., & Le, K. 2003; Felmingham et al., 2012; Kuhlmann and Wolf, 2006; Lupien et al., 2005; van Stegeren, 1998; van Stegeren et al., 2007) and animal models (McGaugh, 2000; Revest et al., 2010; Roozendaal, 2000; Roozendaal, Hui, et al., 2006; Roozendaal, Okuda et al., 2006). The pattern of the relationship between the stress hormones and memory performance has in some cases been in the shape of an inverted U (Andreano and Cahill, 2006; Lupien et al., 2005;), however, this is still not conclusive. Recently, researchers have tested exercise, one of the most significant stressors on the human body, to examine its effects on memory.

Exercise elicits a variety of physiological responses including the release of the previously mentioned adrenal stress hormones (Fryer at el., 2014; Hill et al., 2008; VanBruggen, Hackney, McMurray, & Ondrak, 2011; Weinberg, Hasni, Shinohara, & Duarte, 2014). Thus, it is logical to suggest that exercise and the concomitant release of endogenous stress hormones could improve memory similar to other stressors. The

investigation of exercise as a method to enhance cognition in general is a relatively young field, but findings suggest that exercise can enhance memory (Berchtold, Castello, & Cotman, 2010; Labban and Etnier, 2011; Roig et al., 2013; Speisman et al., 2013; Weinberg et al., 2014) and other cognitive factors (Loprinzi and Kane, 2015; Hillman et al., 2009; Hillman et al., 2014; Pontifex et al., 2010). The current study aimed to utilize this potential enhancing effect of exercise on memory.

In order to investigate further the effects of exercise on memory, exercise of different intensities were used in a dose response manner between exercise and memory. Multiple exercise intensities have not been typically examined in previous research. Moreover, the timing of exercise relative to the presentation of new information was manipulated in order to establish whether exercise prior to image presentation or exercise after image presentation was more advantageous. Additionally, another timing group involved a 30 minute delay between the completion of exercise and the presentation of images to examine if the memory enhancing effects of exercise were transient or if they could last long enough in order to have an appreciable effect.

2.2 Objectives

The objectives of this study were to a) further investigate the exercise-induced enhancement in memory, and establish a dose response relationship with exercise intensity, b) investigate if the relative timing of stimulus presentation affects this enhancement, and c) attempt to expand the knowledge base of this phenomenon to more applied scenarios.

2.3 Hypotheses

It was hypothesized that:

- i) There would be a dose response effect with respect to exercise and memory consolidation such that higher intensity exercise would result in enhanced recall.
- ii) Viewing images immediately after exercise (timing group 2; see below) would result in the greatest recall.
- iii) Enhanced recall would be positively correlated with salivary cortisol change prior to image viewing.

2.4 Methods

Study Design

This study utilized a repeated measures design (exercise intensity) with a between group factor (timing of image presentation relative to exercise session; Figure 2.1). 28 young adults (10 males and 18 females) were randomly divided into one of three timing of exercise groups consisting of: i) images presented immediately prior to exercise (timing group 1); ii) images presented immediately after exercise (timing group 2); iii) images presented 30 minutes after exercise (timing group 3).

Each participant underwent his or her timing group specific protocol on three of the four image days. The first image day for each participant was a rest/baseline day. On this control day they did not exercise and instead rested for 45 minutes between image viewing and image recall. The order of exercise intensity for the three subsequent image days was randomized for each participant. The three exercise intensities used in this study were low (aimed to elicit 40% of peak oxygen consumption, VO₂ peak), moderate (aimed to elicit 60% VO₂ peak) and high (aimed to elicit 80% VO₂ peak). Image recall occurred exactly 45 minutes after image viewing in each instance. Saliva samples were collected

on all days at baseline, immediately prior to image recall, immediately prior to and post exercise, and prior to image recall. Note that some saliva samples served as dual samples. For example, the post exercise sample for those in timing group 2 was also the pre imageviewing sample. On the rest day and for timing group 1 the baseline saliva sample also served as the pre image-viewing sample. Additionally, for those in timing group 1, the post exercise sample served as the pre image recall sample. For timing group 2, the post exercise sample also served as the pre image-viewing sample. Thus, on exercise days for timing group 1 and on the rest/control day, 2 samples were collected, on exercise days for timing group 2, 3 samples were collected per day and 4 saliva collections were made on exercise days for timing group 3. Thus a total of 8 salivary samples were collected from those in timing group 1, 11 salivary samples from participants in timing group 2 and 14 samples from participants in timing group 3. Salivary samples were used to measure cortisol due to the reduced invasiveness compared to blood collection and the potential of blood or injection phobias that could have invoked a significant stress response in some participants (Ritz, Meuret, & Ayala, 2010). In addition, salivary cortisol levels reliably reflect serum cortisol concentrations (Dorn et al., 2007). In addition to saliva collection at the times noted above, heart rate was monitored during all exercise sessions.

Figure 2.1. Study design. After recruitment (A), all participants performed a baseline (B) image viewing and recall test prior to performing a maximal exercise test. Participants were randomized into one of three timing groups (C) in which image viewing (IV) was varied. Imaging viewing occurred immediately prior to, immediately after or 30 minutes after exercise for Timing Group 1, 2 and 3, respectively. Salivary samples (SS) were taken immediately prior to, and immediately after exercise, as well as immediately prior to IV, and Image recall (IR). The time between IV and IR was exactly 45 minutes in all circumstances. Immediately after each IV, participants were required to fill out an image day questionnaire that also served as a distractor from rehearsal or other strategies. At least seven days after each testing day, participants completed another full session dictated by their respective timing group at an exercise intensity of 40, 60 or 80% of VO2peak until that subject had completed all exercise intensities over three separate days. The order of the exercise intensity was also randomized. Each exercise bout consisted of a 5-minute warm-up (WU), 22 minutes at either; 40%, 60% or 80% of VO2peak and a 3 minute cool down (CD).

Recruitment

Healthy (answer of "yes" to all questions on the physical activity readiness questionnaire, see below), young adult (18-30 years of age) participants were recruited from the University of Windsor using email, and by word of mouth. Using these recruitment methods, 47 people expressed interest in participating in the study. After initial contact, 32 individuals subsequently volunteered to participate in the study and attended the Physical Activity and Cardiovascular Research (PACR) Lab in the Faculty of Human Kinetics for baseline assessment. Three participants did not return to the lab after the baseline assessment, and one participant did not return after completing both the baseline assessment and one exercise day. Consequently, 28 individuals (18 females, 10 males; 20.07 ± 2.28 years of age) fully completed the study and were used in final analyses. This resulted in an 87.5% retention and completion rate. Participant characteristics are outlined in Table 2.1.

Group	Sex	n	Age (y)	SD	Height (cm)	SD	Weight (kg)	SD	BMI	SD	VO ₂ Peak (ml/kg/min)	SD.	
Timing Group	Female	6	18.7	0.8	165.8	6.3	62.2	7.6	22.7	3.4	31.3	5.6	
	Male	3	21.3	2.5	177.0	\cdot .7	77.7	11.6	24.8	3.4	44.1	3.3	
	Total	9	19.6	1.9	169.6	7.5	67.3	11.4	23.4	3.4	35.5	8.0	
Timing Group 2	Female	6	21.8	3.5	165.5	5.6	65.0	9.3	23.7	\mathbf{r} $\overline{2}$	35.1	7.5	
	Male	$\overline{4}$	20.0	2.2	176.5	4.4	77.8	7.3	24.9	$\overline{8}$	49.7	13.6	
	Total	10	21.1	3.1	169.9	7.5	70.1	10.4	24.2	2.4	40.9	12.3	
Timing	Female	6	18.8	0.4	163.5	6.6	57.3	$^{\prime}.8$ ⇁	21.4	\mathbf{r}	39.0	7.6	
Group	Male	3	20.7	0.6	180.3	4.6	75.3	4.0	23.2	2.3	45.0	3.0	
3	Total	9	19.4	1.0	169.1	10.2	63.3	11.1	22.0	2.0	41.0	6.9	
Total	Female	18	19.8	2.5	164.9	5.9	61.5	8.4	22.6	2.7	35.1	7.3	
	Male	10	20.6	1.8	177.8	3.9	77.0	7.2	24.4	2.4	46.6	8.6	
	Total	28	20.1	2.3	169.5	8.1	67.0	10.9	23.2	2.7	39.2	9.5	

Table 2.1: Descriptive Statistics for Participants divided by Timing Group

Table 2.1: Descriptive Statistics for Participants divided by Timing Group. Timing group 1 (image viewing prior to exercise) Timing group 2 (image viewing immediately post exercise) Timing group 3 (image viewing 30 minutes post exercise).

Procedures

Participants who responded to the call for participants were asked to complete the Physical Activity Readiness Questionnaire (PAR-Q, Appendix A). The PAR-Q is a standard pre-exercise questionnaire recommended by the Canadian Society of Exercise Physiology. Subsequently, participants were asked to report to the Physical Activity and Cardiovascular Research (PACR) Lab in the Human Kinetics building in appropriate exercise attire (e.g. shorts, gym shoes, t-shirt, etc.). The intent and procedures of the project were verbally explained to each participant, and subsequently, he/she read and signed a written informed consent form. As part of this procedure, participants were then asked to read, complete and sign the PAR-Q in the presence of the investigator to ensure that they understand and were indeed able to partake in the exercise study. Once enrolled in the study, participants were given a random identification code to ensure confidentiality of any personal information recorded.

Day 1/Baseline

 On each participant's first visit, after signing an informed consent form, and completing the PAR-Q questionnaire (Appendix A) a memory performance test was conducted. A salivary sample was collected both prior to image viewing and image recall based on the collection procedure for all samples as follows:

Salivary Collection Procedure

Participants were asked to rinse their mouths with a cup of water and a salivary sample was obtained using a commercially available saliva collection swab (Salimetrics, USA) placed under the tongue for 2 minutes. After removal of the swab from the

participant's mouth, it was placed in a collection tube and centrifuged for 15 min at 1500rpm. Typically, approximately 250 – 2000 μl was collected in this fashion. Collected saliva was then stored in the collection tube in an ultra-low temperature $(-70^{\circ}C)$ freezer for future analysis (see cortisol analysis below).

On the baseline-testing day, immediately after saliva collection, image viewing took place. In all image-viewing instances, participants were escorted to a designated image viewing area within 1 minute of other events. Once in the image viewing area, participants were asked to sit comfortably in an adjustable cushioned office chair in front of a desk and standard computer widescreen monitor positioned at approximately eye level. Prior to the presentation of images, all participants were read the following script:

"You are about to be shown 15 images. You will likely find some of the images pleasant, some unpleasant and some neutral. Each image will be presented to you for 10 seconds. When I cue you by saying, "go ahead" you should name the slide (orally) using a word or short phrase. For example, if there is a woman holding a tennis racquet, you might say "tennis, or tennis player" when cued. After 10 seconds of viewing a black screen, the images will be presented one after another. Your image viewing session will begin shortly."

Subsequently, a set of 15 images rated for valence, arousal, and dominance by the International Affective Picture System (IAPS) were presented in semi-random order (i.e. first and last images remained the same to account for order effects) on the computer monitor. The participant was separated from the experimenter by an office wall, but communication could occur verbally.

On all days, 45 minutes after image viewing was completed, participants were given a pen and booklet of paper and asked to recall as many images as possible in as much time as needed, and were told that the order in which they wrote the images did not matter. Once participants indicated that they could not recall any further images, the booklet was returned to the experimenter.

The sets of images that were shown on each day were different, but standardized based on ratings of valence, arousal and dominance. Moreover, using redundant images was avoided (i.e. presenting a picture of a dog on more than one image day). Image IDs, valence, arousal and dominance scores from the IAPS are presented in Table 2.2

	Day 1					Day 3				Day 4					
Image															
ID	Val	Aro	Dom	Image ID	Val	Aro	Dom	Image ID	Val	Aro	Dom	Image ID	Val	Aro	Dom
8465	5.96	3.93	5.97	7150	4.72	2.61	5.55	8206	6.43	6.41	5.19	1850	6.15	4.06	5.94
2314	7.55	4.00	6.17	2384	5.92	3.41	6.32	2395	7.49	4.19	6.31	2398	7.48	4.74	6.18
5300	6.91	4.36	4.14	5593	6.47	3.98	5.89	7472	6.25	4.00	6.31	2341	7.38	4.11	6.44
9830	2.54	4.86	4.96	7060	4.43	2.55	5.85	2580	5.70	2.79	5.88	7175	4.87	1.72	6.47
7224	4.45	2.81	6.26	8600	6.38	4.26	5.54	7217	4.82	2.43	6.25	7234	4.23	2.96	5.73
7240	6.02	5.51	6.37	7220	6.91	5.30	5.80	7165	6.09	3.50	6.30	5611	7.05	3.99	6.04
8230	2.95	5.91	4.05	9400	2.50	5.99	3.78	9184	2.47	5.75	3.86	9291	2.93	4.38	4.75
8499	7.63	6.07	5.51	8496	7.58	5.79	6.33	8370	7.77	6.73	5.37	8185	7.57	7.27	5.47
9405	1.83	6.08	3.40	9921	2.04	6.52	3.57	9908	2.34	6.63	2.79	9930	3.12	5.71	2.97
9331	2.87	3.85	4.72	9341	2.85	4.49	4.22	9415	2.82	4.91	4.22	9180	2.99	5.02	4.52
9445	3.87	4.49	4.51	1270	3.68	4.77	5.25	1280	3.66	4.93	5.05	2206	4.06	3.71	4.46
1610	7.69	3.98	6.77	1650	6.65	6.23	4.29	5725	7.09	3.55	6.23	2151	7.32	4.37	5.90
1903	5.50	4.25	6.01	2382	5.67	3.75	5.97	2682	3.69	4.48	4.02	2446	4.70	3.79	5.51
3005.2	5.98	4.84	5.97	2890	4.95	2.95	5.99	2850	5.22	3.00	5.87	3213	2.96	6.82	3.92
7031	4.52	2.03	6.14	1947	5.85	4.35	5.77	2389	6.61	5.63	5.90	2102	5.16	3.03	5.80
Mean	5.08	4.46	5.40	Mean	5.11	4.46	5.34	Mean	5.23	4.60	5.30	Mean	5.20	4.38	5.34
SD	1.96	1.15	1.02	SD	1.71	1.30	0.92	SD	1.84	1.41	1.10	SD	1.82	1.43	1.01

Table 2.2: IAPS Standardized Emotional Ratings

Tabl $\frac{\omega}{\infty}$ 2. Standardized Ratings of the 60 images selected for use for this study from IAPS. Standard scores are included in the user manual for the IAPS and are based off of ratings from a modified SAM (ranging from 1-9). Image sets were selected in order to be relatively close with one another based on the standardized ratings for valence (val), arousal (aro), and dominance (dom).

Immediately after image viewing on each day, participants completed the Image Day Questionnaire (Appendix D), which asked the participant to recall in writing:

- a) The approximate total time of sleep on the night immediately preceding the current visit
- b) Whether the participant had exercised in the 48 hours prior to the current visit
- c) Food and drink consumption since waking on the morning of the current visit
- d) Whether the participant had consumed any stimulants in the 24 hours prior to the current visit.

The questionnaire was used solely as a method to justify exclusion of potential outlying data. Since no outliers were observed, no participant had data excluded.

On the baseline testing day after completing the Image Day Questionnaire, participants underwent maximal exercise testing. Prior to beginning the test, participants were fitted with a telemetric heart rate monitor (Cosmed, Italy) and asked to mount an electronically braked cycle ergometer (Ergoline, Germany). The cycle seat height was adjusted for comfort and proper positioning of the participant. A head strap was used to secure a mouthpiece for gas (expired oxygen and carbon dioxide) analyses. Prior to exercise, it was explained to participants that the RPE is a scale from 6-20 with a rating of 6 being equivalent to no effort exerted and a rating of 20 equated with maximal exertion. Further, participants were told that the Self-Assessment Mannequin (SAM-Appendix C) requires participants to point to one of 5 pictures in each row (3 total rows) to assess their emotional state at a given time. The first row rated the emotion of valence, the second arousal, and the third dominance. The valence rating ranges from pleasant to unpleasant. It includes pictures of a smiling, happy figure to a frowning unhappy figure.

The second row is for arousal, and the ratings range from calm to excited. The pictures for this rating range from an excited, wide-eyed figure to a relaxed, sleepy figure. Lastly, the ratings for dominance range from feeling dominant to feeling dominated. The pictures for this rating range from a large/powerful and in control figure to a small and dominated figure. While seated on the bike prior to the maximal exercise test, participants were told what each row of figures in the SAM represented and then the participants were given synonyms to describe the polar ends of each row. Participants were given the examples of "annoyed" to "pleased" for valence, "relaxed" to "stimulated" for arousal and "influenced" to "influential" for dominance. Then, participants were asked to point to one picture in each row that represented how they felt at that particular time. Thus, the first SAM score recorded for each participant represents his or her emotions at the time of resting on the cycle ergometer.

Once ready, participants were asked to start pedalling at a rate of 60 rotations per minute (rpm) and to try to maintain this pace throughout the entire test. Physiological data was recorded until the end of the testing procedure. After 2 minutes of cycling at a resistance of 30W (note: for most young healthy individuals, 30W resistance is very easy and could be the equivalent of riding a bike on a flat or slight downhill), the resistance on the cycle was increased in a step incremental fashion (30W/2 min stage) until volitional exhaustion. Throughout the test, verbal encouragement was given in an attempt to help the participant achieve maximal effort. During the final 30 seconds of each stage participants were asked to physically point out their ratings of perceived exertion (RPE-Appendix B) and self-assessment on a printed RPE scale and SAM pictogram, respectively.

Maximal effort in the exercise test was determined if the participant exhibited at least 3 of the following 5 criteria: voluntary cessation of testing; a heart rate within 10 beats of age predicted maximum; an inability to maintain 60rpm on the cycle ergometer; a plateau in VO2 even though resistance had been increased; a respiratory exchange ratio greater than or equal to 1.1. After the test had been completed, the participant was required to remain on the cycle, pedalling against little resistance (30W) until heart rate returned to within 10 beats of the initial stage (typically within 5 min). Subsequently, the mouthpiece was removed, and the participant stopped pedalling and dismounted the cycle. This initial fitness assessment served 2 purposes. First, it acted as a familiarization with the exercise equipment thereby reducing emotional responses associated with a novel setting during future tests. Second, the initial fitness assessment was used to set the workload intensities for the future exercise sessions.

At the conclusion of maximal testing, a date and time for the next testing day was established. All image days began between 11am – 4:30pm. This time restriction was set to account for diurnal patterns of cortisol concentrations. Participants were asked, but not required, to come in on the same day of the week and the same time of day for each exercise test.

Participants repeated the protocols specific to their timing group on the 3 subsequent days requiring exercise. All image days were separated by at least 7 days and they were informed that they should try to refrain from caffeine consumption and advised to consume a small meal 120 to 60 minutes prior to the start of their visits.

After the baseline testing day, participants were randomly (accomplished using IBM PASW random number generator) assigned to Timing Group 1, 2 or 3. Within each

timing group and for each participant, the order of exercise intensity (low, moderate or high) was also randomly determined.

Exercise/Image Days

On all exercise days, participants completed the STAI (State-Trait Anxiety Inventory) version Y1 for state anxiety only. The STAI has been validated as a reliable measure for anxiety in a diverse population (Spielberger, 1983). While trait anxiety (Y2) is stable over time, including retest periods of one hour to months, state anxiety as measured by the STAI varies, expectedly, with the degree of stress or anxiety (Spielberger, 1983). However, the internal consistency of state anxiety is indicated by high Cronbach's alpha coefficients (>0.90), a measure of the reliability of psychometric tests in a normal and stressed population (Spielberger, 1983). Subsequent to the STAI-Y1, the participants completed an initial rest period and saliva collection as noted above. Then, depending on the timing group assigned, participants proceeded according to the following:

Timing Group 1: After initial saliva collection, participants were escorted to the image viewing area and image viewing took place as described above (note that a different set of 15 images matched for valence, arousal and dominance ratings was presented on each day within each timing group such that the 15 images shown on day 2 were different than day 3 and 4). Immediately after image viewing, participants completed the image day questionnaire followed by 30 minutes of exercise at either a low, moderate (mod) or high intensity (approximately 40, 60 or 80% of VO₂peak-described below). A saliva sample was then obtained using the methods described above and the participant was required to rest for the necessary additional time to sum up to 45 minutes since they completed

image viewing. At 45 minutes after image viewing, participants were asked to recall the images they had viewed that day according to the procedures described above. At the conclusion of image recall, participants were asked to return to the PACR lab 7 days later to repeat the activities but at one of the other exercise intensities. Testing followed by 7 days was repeated until the participant had exercised all 3 exercise intensities.

Timing Group 2: After initial saliva collection, participants completed 30 minutes of exercise at 40, 60 or 80% of VO₂peak (described below). A saliva collection was obtained immediately following exercise and then participants proceeded to image viewing as described (i.e. within 5 minutes). A questionnaire followed image viewing and image recall occurred 45 after the image viewing completion. At the conclusion of image recall, participants were asked to return to the PACR lab 7 days later to repeat the activities but at one of the other exercise intensities. Testing followed by 7 days was repeated until the participant had exercised at each exercise intensity.

Timing Group 3: After initial saliva collection, participants underwent 30 minutes of exercise at 40, 60 or 80% of VO2peak (described below). A saliva sample was obtained immediately after exercise and then participants were ask rest (seated) for 30 minutes prior to image viewing as described. The image day questionnaire was completed immediately after image viewing and then the participant was asked to rest (seated) for 45 minutes prior to image recall. At the conclusion of image recall, participants were asked to return to the PACR lab 7 days later to repeat the activities but at one of the other

exercise intensities. Testing followed by 7 days was repeated until the participant had exercised at each exercise intensity.

Exercise Bouts

 Each exercise bout consisted of a 5 minute warm up period at 30W followed by 22 minutes of continuous cycling at a predetermined wattage corresponding with 40%, 60% or 80% of their VO2peak. The order of exercise intensity for exercise/image viewing days was randomized such that participants exercised once at low (40%), moderate (60%) and high (80%) intensity, but only viewed and recalled images according to their respective Timing Group protocol.

SAM measurements were taken at 2.5 and 17.5-minute marks of each exercise session to assess each participant's emotional status. Heart rate was monitored throughout the exercise bout. It was determined a priori that if participants cycled for longer than 20 minutes total (15 minutes of the 22 minute exercise portion) then the day would follow accordingly. The exercise portion was then followed by a 3 minute cool down period at an output of 30W.

After completing image recall on each participant's fourth and final visit to the lab, they rated each of the 60 images that were shown to them using the same SAM that they used to rate their emotions during exercise.

Salivary cortisol EIA

Saliva samples were analyzed for cortisol concentrations using a commercially available Enzyme Immunoassay (EIA) Kit (Salimetrics, USA) according to the manufacturer's guidelines. In the EIA, cortisol in standards and unknown concentrations compete with cortisol linked to horseradish peroxidase for the antibody binding sites on a

coated 96-well microplate. After incubation, unbound content is washed away. Bound cortisol peroxidase is measured by the reaction of the peroxidase enzyme on the substrate tetramethylbenzidine. The reaction produces a blue colour, but a yellow colour is formed once the solution is stopped using sulfuric acid. Optical density was read on a standard plate reader at 450 nm. The amount of cortisol peroxidase detected, as measured by the intensity of colour is inversely proportional to the amount of cortisol present. The minimal detection limit of the cortisol assay is 0.007 μg/dL. The correlation of salivary cortisol with serum cortisol is reported to be $r = 0.91$, $p < 0.0001$. The antibody is reported to be highly specific for cortisol with only minimal (i.e. <1%) cross-reactivity for other glucocorticoids except dexamethasone (19.2% cross-reactivity), which is a synthetic glucocorticoid.

Recall scores

Total correct, incorrect and redundant items were tabulated and used for analyses. Two graders assessed written recall responses from participants. Graders had written down the word that the participant had stated aloud that corresponded to each image during image viewing. If the participant wrote that word during recall it was considered a correct recall. Likewise, if the graders deemed that the participant accurately described the image using another word or phrase, then that response was deemed correct as well. If no word corresponded to an image it was marked as a missed image. Additionally, if a word was written that did not correspond to any images it was marked as an incorrect recall (5 instances). Redundant recalls were also tracked, however there were no instances of a redundant recall. Participants typically wrote down the word they said

aloud for correct answers, or if they did not remember a word they most often did not guess.

Statistical Analyses

SPSS (IBM, U.S.A) Version 21 was used to conduct all of the following statistical analyses. For all tests an alpha level of p<0.05 was considered significant.

2 factor (intensity x sex) Repeated Measures ANOVAs were conducted to assess the physiological responses to exercise, including salivary cortisol change, RPE, and the three emotions of valence, arousal, and dominance captured in the SAM. Exercise intensity (low, moderate and high) was used as the independent variable within subjects while sex (male and female) was used as a between group independent variable. For these tests, sex was included to show that there were no differences in the physiological responses between men and women. The dependent variables were in each case salivary cortisol (ug/dl), RPE (rating from 6-20), valence rating of 1-5, arousal rating from 1-5, and dominance rating from 1-5.

To assess the effects of exercise intensity and relative timing of exercise on memory scores, a 2 factor Repeated Measures ANOVA (4 levels of exercise intensity) with between groups factors (3 timing groups) was conducted. Upon finding significant main effects or interactions, a Tukey's post hoc test was conducted in order to determine significant differences between variables. An alpha level of $p<0.05$ was considered significant. For this analysis the independent variables were exercise intensity (rest, low, moderate, high) and timing group (timing group 1, timing group 2, timing group 3). The dependent variable being assessed was correct recalls.

To assess the effects of visit day and relative timing of exercise on memory scores, a 2 factor (day x timing group) Repeated Measures ANOVA with between groups factors was conducted. Upon finding significant main effects or interactions, a Tukey's post hoc test was conducted in order to determine significant differences between variables. An alpha level of $p<0.05$ was considered significant. For this analysis, the independent variables were the within subjects factor of day (day 1, day 2, day 3, day 4) and between subjects factor of timing group (timing group 1, timing group 2, timing group 3). The dependent variable being assessed was correct recalls.

Pearson correlation tests were conducted to examine the relationship between salivary cortisol prior to image viewing and image recall and memory scores. Moreover, a Pearson correlation was conducted to assess the correlation between pre mage viewing salivary cortisol and pre image recall cortisol on each day of different exercise intensities. In all Pearson correlations, r-values and p values are reported.

 Sleep from the previous night, and caloric intake of that day, collected from the Image Day Questionnaire, was assessed using 2 factor (intensity x timing group) Repeated Measures ANOVAs with four levels of exercise intensity and timing group as a between groups independent variable. In these cases, the independent variables were exercise intensity (rest, low, moderate, high) and timing group (timing group 1, timing group 2, timing group 3). The dependent variables were number of hours slept and calories consumed, respectively. Additionally to assess the STAI questionnaire a 2 factor (intensity x timing group) Repeated Measures ANOVA with three levels of exercise intensity (low, moderate, high) and timing group (timing group 1, timing group 2, timing group 3) as a between groups independent variable was conducted. If any questionnaire

was incomplete or missing responses, that participant's data was not included in the analysis for that particular portion of the study.

Figures are reported as means and standard deviation unless otherwise noted. Effect sizes [partial eta² (η ²)] and observed powers are reported for selected variables.

2.5 Results

Responses to exercise

Descriptive statistics for each timing group are presented in table 2.1. Participants had no difficulty completing either the low or moderate intensity exercise protocols (40% and 60% of VO2peak, respectively). However, on the high exercise protocol (80% VO2peak) day, the intensity of exercise (i.e. power elicited on the cycle ergometer) was reduced by 10 watts for 6 participants because they found the exercise too challenging to complete. On 4 occasions, participants could not complete the entirety of the exercise bout. In those 4 instances, at least 20 minutes were completed and consequently, their data was used in analyses.

Heart rate and $VO₂$ responses to exercise are presented in figure 2.2. The low, moderate and high exercise intensities that were set elicited distinct $VO₂$ and HR responses`. Due to data loss during recording, only 15 complete sets of HR data and 22 complete sets of VO2 data were available for graphing. As such statistics were not run for these data, but the figures do indicate that the exercise intensities were within range of the desired 40, 60 and 80% of VO2peak.

Salivary cortisol responses to exercise for all participants are presented in figure 2.3. There was no significant main effect for time (pre versus post) or intensity (low

versus mod versus high intensity; p>0.05). Moreover, there were no significant differences between sexes (p>0.05).

Figure 2.2. Physiological Responses to Exercise Sessions

Figure 2.2. Physiological Responses to Exercise Sessions in Males (n=10) and Females (n=18). Shown as mean values of 10-second intervals. A, percent maximum heart rate and B, percent of peakVO2. Exercise sessions consisted of a 5-minute warm up at 30W followed by 22 minutes at low (aimed to elicit 40% of peakVO₂), moderate (aimed to elicit 60% of peakVO₂), or high intensity (aimed to elicit 80% of peakVO₂).

Figure 2.3. Salivary Cortisol Response to Exercise

Figure 2.3. Salivary Cortisol Response to Exercise in Males (n=10) and Females (n=18) shown as mean values + standard deviation. Salivary samples were collected prior to and post exercise. Exercise sessions consisted of a 5-minute warm up at 30W followed by 22 minutes at low (aimed to elicit 40% of peakVO₂), moderate (aimed to elicit 60% of peakVO₂), or high intensity (aimed to elicit 80% of peakVO₂). No significant differences were observed between pre and post exercise(p >.05)(partial η ² = 0.023; observed power $= 0.118$) nor exercise intensity(p>.05)($\eta^2 = 0.071$); observed power: 0.390).

Subjective ratings of exercise (i.e. RPE and SAM scores) for all participants at the 17.5 minute time point of the exercise protocols are presented in figure 2.4. There was a significant main effect for intensity such that RPE during high intensity exercise was reported to be significantly greater than moderate and low intensity exercise $(p<0.05)$ and RPE during moderate intensity exercise was significantly greater than that during low intensity exercise (p<0.05; figure 2.4A). In all SAM scores (i.e. valence, arousal and dominance) there was a significant main effect for intensity such that participants in the high intensity group reported significantly different scores (i.e. less pleasant, less calm, less dominant) than the low and moderate intensity groups (p<0.05; figure 2.4B, C and D).

Figure 2.4. Subjective Ratings of Exercise Intensities

Figure 2.4. Subjective Ratings of Exercise Intensities in Males (n=10) and Females $(n=18)$ shown as mean values + standard deviation. All subjective ratings of exercise were taken all at once (using the RPE and SAM) at the 17.5-minute mark of the exercise session. A: rating of Perceived exertion is a number from 6-20 given by the participant to reflect their personal rating of exertion $(p< 0.001)(\eta^2 = 0.885)$; observed power = 1.000). B: Rating of valence from 1-5 where a lower number represents more satisfaction/happiness $(p=0.014)$ $(\eta^2=0.291)$; observed power = 0.774). C: Rating of Arousal is a rating from 1-5 where a lower number represents higher arousal (p <0.001)(η ² = 0.564; observed power = 0.999) D: Rating of dominance from 1-5 where a higher number represents increased feeling of dominance ($p = 0.038$)($p^2 = 0.230$)(observed power = 0.630) Significant differences ($p<0.05$) are denoted by $*$.

Image Recall – Correct Images

The means of correct image recalls by timing group and exercise intensity are presented in table 2.3. There were no significant differences observed in the number of images recalled correctly either due to exercise intensity $(p>0.05)$ or between timing groups ($p > 0.05$).

In order to observe whether there was an order effect, correct recall scores were grouped by day of presentation within each timing group. A significant main effect of order was observed $(p<0.001)$ and post hoc analysis revealed that participants remembered significantly more images on the final testing day than any other day (table 2.4).

Group	N	Baseline	Low	Mod	High
			Timing Group 1 9 10.0 (1.9) 10.1 (2.3) 10.1 (1.8) 10.3 (1.8)		
			Timing Group 2 10 10.1 (1.7) 11.0 (2.4) 10.5 (2.4) 11.1 (1.7)		
			Timing Group 3 9 9.4 (1.7) 11.2 (2.1) 10.4 (3.0) 10.9 (2.8)		

Table 2.3: Mean correct image recalls by timing group and exercise intensity

Table 2.3. Mean (SD) correct image recalls by timing group and exercise intensity.

Exercise sessions consisted of a 5-minute warm up at 30W followed by 22 minutes at low (aimed to elicit 40% of peakVO₂), moderate (aimed to elicit 60% of peakVO₂), or high intensity (aimed to elicit 80% of peakVO₂). Timing group 1 (image viewing prior to exercise) Timing group 2 (image viewing immediately post exercise) Timing group 3 (image viewing 30 minutes post exercise). There were no significant differences observed in the number of images recalled correctly either due to exercise intensity $(p>0.05)$ ($\eta^2 = 0.205$)(observed power = 0.442) nor interaction between timing groups $(p>0.05)$ ($\eta^2 = 0.041$)(observed power = 0.137).

Table 2.4: Mean correct image recalls by day.

Group	N	Day 1	Day 2	Day 3	Day 4*
Timing Group 1 9 10.0 (1.9) 9.9 (2.0) 9.6 (2.3) 11.1 (1.1)					
Timing Group 2 10 10.1 (1.7) 10.2 (2.3) 10.6 (2.2) 11.8 (1.7)					
Timing Group 3 9 9.4 (1.7) 9.8 (2.6) 11.1 (2.7) 11.7 (2.3)					

Table 2.4. Mean (SD) correct image recalls by day. Day 1 was a baseline/rest day for all participants. Days 2-4 consisted of exercise sessions at low (aimed to elicit 40% of peakVO₂), moderate (aimed to elicit 60% of peakVO₂), or high intensity (aimed to elicit 80% of peakVO2). Each day was assigned a consistent set of 15 images that were standardized based on IAPS standard scores for arousal, valence, and dominance. A significant main effect of order was observed (p <0.001)(η ² = 0.483; observed power: 0.960) and post hoc analysis revealed that participants remembered significantly more images on the final testing day than any other day.

Image Recall – Incorrect Images

There were very few incorrect images recalled. In fact, a total of 5 incorrect recalls were observed among all participants and these incorrect recalls came from only 2 individuals. In no instance were any of those incorrect recalls deemed to be images from prior testing days (redundant images).

Recall and Salivary Cortisol

Given that there was no significant difference in salivary cortisol either pre or post exercise or between intensity days, change in cortisol was not correlated with total correct images recalled. In order to determine whether salivary cortisol prior to image viewing or image recall was related to image recall regardless of prior exercise intensity, a Pearson correlation (displayed in figure 2.5) was run on pre image viewing salivary cortisol, pre image recall salivary cortisol and total number of images recalled. Pre image viewing cortisol was significantly correlated with pre image recall salivary cortisol ($r =$ 0.865, p <0.001), however, neither salivary cortisol measure was correlated with the correct number of images recalled ($r = 0.112$, $p > 0.05$ and $r = 0.086$, $p > 0.05$) for pre image viewing and pre image recall, respectively.

Figure 2.5 Salivary Cortisol Correlations

Figure 2.5. Salivary Cortisol Correlations. Capital letters represent correlations with correctly recalled images, while small letters represent correlations between salivary cortisol at image viewing and at image recall (i.e. 45 min apart). A: Baseline day pre image viewing and pre image recall salivary cortisol vs. correct images recalled. a: pre image viewing salivary cortisol vs. pre image recall salivary cortisol. B: Low intensity exercise day pre image viewing and pre image recall salivary cortisol vs. correct images recalled. b: Low intensity exercise day pre image viewing salivary cortisol vs. pre image recall salivary cortisol.

Figure 2.5 Salivary Cortisol Correlations

Figure 2.5. Salivary Cortisol Correlations. C: Moderate intensity exercise day pre image viewing and pre image recall salivary cortisol vs. correct images recalled. c: Moderate intensity exercise pre image viewing salivary cortisol vs. pre image recall salivary cortisol. D: High intensity exercise day pre image viewing and pre image recall salivary cortisol vs. correct images recalled. d: High intensity exercise day pre image viewing salivary cortisol vs. pre image recall salivary cortisol.

Sleep, STAI, and Caloric Intake

 The Image Day Questionnaire (Appendix D) asked participants about the amount of sleep (in hours) they had the previous night and what food they consumed that day. The number of hours slept the previous night was recorded and the food/drinks consumed were inputted into a calorie calculator (EATracker.com) to estimate the number of calories consumed. Moreover, on exercise days, participants filled out an STAI – Y1 (Appendix E) as a means of standardizing the initiation of each visit to the lab by having participants fill out the questionnaire while seated. The answers to the questionnaire were recorded and tabulated to provide a score for each day. The results are outlined in Table 2.5.

Table 2.5 Image Day Questionnaire and STAI – Y1 Data.

Table 2.5. Image Day Questionnaire and STAI – Y1 Data. The image day questionnaire was filled out each visit following image viewing and provided the data for the number of hours slept the previous night and the food/drink the participant had consumed that day. The STAI – Y1 was filled out at the beginning of all exercise days and answers from this questionnaire produced a score which is refle $\sum_{n=1}^{\infty}$ in the table. Timing group 3 was significantly different in STAI – Y1 scores from both timing group 1 (p<0.05) and timing group 2 ($p < 0.05$)

2.6 Discussion

This study attempted to further establish the arousal-induced enhancement on long term memory, using a practical stimulus (exercise). This study did not support the hypothesis that exercise would improve memory performance (Table 2.3). There are several potential reasons that may have contributed to these findings. First, the study parameters of this study varied with the previously published data related to arousal and memory. For instance, this study used a repeated measures approach to assess memory. The repeated measures aspect may have had implications on the results of the study by allowing a training effect to occur. Additionally, this study used 45 minutes between image viewing and image recall which is less time than much of the published work [e.g. 1 week (Andreano and Cahill, 2006) or 2 day (Felmingham et al., 2012) delay between presentation and recall]. These parameters were constructed in order to comprehensively assess the potential effects of exercise on long-term memory while still being able to fulfill the requirements of the procedure in a time efficient manner. While a 45-minute delay assesses long-term memory, other factors could certainly influence the number of images remembered in each instance. A longer delay between image viewing and image recall would likely increase the number of images forgotten during that designated course of time due to the deterioration of those neural connections storing the memories images, particularly those not subject to any benefit from the arousing stimulus. The potential underlying memory enhancement from arousal/exercise may be accomplished by extending the life of a given memory by prolonging the deterioration process of said memory. Thus, it is possible that arousal would not influence memory performance with a delay of 45 minutes but could influence memory performance a day or a week later, as

fewer memories would have deteriorated due to enhanced consolidation stemming from the arousal/exercise. Indeed, this has been shown in stress enhanced recall after more than a week (Andreano and Cahill, 2006).

Additionally, only 15 images were shown each day, and in terms of memory performance, typically all participants were able to remember 10 of 15 images (Table 2.3). Due to the short time delay in combination with only using 15 images each day, it is possible that a ceiling effect had manifested. For instance, on 4 occasions a participant recalled all 15 images presented to them that day (2 of these instances were from the same participant). While no significant differences were found between the exercise intensities, the day1/baseline day was associated with the lowest memory performance of all image-viewing days (Table 2.4). Thus, the three exercise days tended to improve memory compared to baseline. However, this certainly may be due to the order effect of the rest day being the first of 4 days or due to the nature of the 15 images in set 1. Similarly, that Day 4 showed the best memory performance could be attributed to an order effect or the inherent nature of the 15 images in set 4. Further investigation is still warranted to determine if exercise can enhance memory recall.

Another difference between this study and previous literature relates to the lack of a significant difference in cortisol response between exercise intensities. This study followed a very similar exercise routine, in terms of time and intensity, as used in previous research (VanBruggen et al. 2011). That study observed elevated cortisol both immediately and 30 minutes post high intensity $(80\% \text{ of peak VO}_2)$ exercise (VanBruggen et al., 2011). The high intensity exercise in this study was certainly more challenging than the other intensities as reflected in RPE scores, heart rate measurements,

and the fact that some participants were unable to complete the 22 minute protocol at the assigned ergometer resistance. It is possible that the salivary samples may have been collected too early and did not catch a potential latent increase in salivary cortisol.

It is also worth noting that in terms of assessing exercise intensity as the sole contributor to improving memory performance, the effect size of 0.081 was very small and the observed power of 0.537 was less than the desired power of 0.8. Consequently, further research involving a much larger sample size of participants is warranted.

As noted previously, human memory is an extremely complex paradigm that is not fully understood, nor easily assessed. Very small environmental or personal factors can have large implications on the likelihood that a given image or of a set of images is remembered. Although efforts were made to control these variables through randomization of images, scripting of experimental procedures, etc., uncontrolled variables could have significantly impacted memory performance. Subtle changes between image days, such as changes in the smell of the room or the number of experimenters present could have influenced the likelihood of an image being recalled, or personal association with a particular image could have inflated recall of certain image sets. Moreover, having participants say the word aloud has implications to memory performance. It forces them to have some connection/reference to the image, thus influencing their chances of recalling the image and provides a second stimulus (auditory) in a brief time after the first stimulus, which is the stimulus of the image itself (visual). Thus, the memory could take different paths while in the form of a short-term memory (i.e., using the visuo-spatial sketchpad as a visual stimulus and/or the phonological loop as an auditory stimulus). Given that most participants simply recalled

the word they associated with the image, it is possible that image became secondary to the word for storage. The type of memory that is formed could change based on the image, the environment and/or the given participant. This adds another complex layer to the assessment of the effects that arousal/exercise had on memory performance. Based on these reasons, further research on this topic is warranted to determine the role arousal/exercise has on memory performance.

2.7 Further Research

As mentioned previously, on 4 occasions a participant recalled all 15 images presented to them that day, further studies that employ a same day recall test should increase the number of images that are shown to participants as a method of further parsing out and assessing memory performance. Another method to further assess memory performance is to have participants describe details of the images instead of only having them name the images. Additionally, other types of memory assessments can be administered such as verbal memory of key words, or assessing participants' memories of a story that is read to them. Moreover, although 45 min after information presentation would be considered long term memory, it is possible that exercise (or physiological stress) has a more pronounced effect on limiting the decay (i.e. more stably consolidating) of memories. Consequently, a longer time frame between information presentation and recall should be employed. The use of post exercise glucocorticoid and/or catecholamine blockers would elicit more information related to the mechanisms of stress-induced memory enhancement. Further research could study female participants across the menstrual cycle to examine if female sex hormone levels influence the stress/memory relationship. Another key variable to investigate would be academic

achievement. This study used university students however there is still natural differences between people's memory and this may be reflected in their academic performance. By including this as a covariate it could potentially elicit further information about the potential effects of arousal/exercise on memory. Additionally, exercise in a lab setting is vastly different from going for a morning run or attending a basketball practice. Thus, a major challenge is translating lab results to more real world applications. Therefore, further research of different exercise settings and environments would be necessary as well.

2.8 Conclusion

In conclusion, this study did not support the hypotheses that exercise can i) improve long-term memory nor that ii) the improvement would be dependent upon exercise intensity and relative timing of exercise nor iii) the memory performance would correlate with increases in salivary cortisol. Additionally, no sex differences were present in the effects of exercise on memory performance. However, further investigations are warranted to a) determine if exercise can improve memory at longer intervals for recall (e.g. 24 h versus 45 min), b) more comprehensively understand the mechanisms and influence behind the potential enhancement, and c) determine if exercise can be used as a practical technique to enhance memory. These further investigations may one day have a significant impact in populations that desire improved memory performance such as students in academic settings, and those with memory disorders that would treasure any and all help that could allow them to remember the precious memories the majority of us take for granted.

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Appendices

Appendix A: PAR-Q

PAR-Q & YOU

Regular physical activity is fun and healthy, and increasingly more people are starting to become more active every day. Being more active is very safe for most people. However,
some people should check with your doctor be

ne participates in a physical activity program or a fitness appraisal, this section may be used for legal or NOTE: If the PAR-Q is ladministrative purposes. **"I have read, understood and completed this questionnaire. Any questions I had were answered to my full satisfaction."**

Appendix C: Self Assessment Manikin

FIGURE 1 The Self-Assessment Manikin (SAM)

5) Have you consumed any over the counter (e.g. benadryl) or other stimulants in the past 24 hours prior to your visit today?

YES If "YES", please identify the product. ____________________ NO

Appendix E. STAI-Y1

For Dissertation and Thesis Appendices:

You cannot include an entire instrument in your thesis or dissertation, however you can use up to five sample items. Academic committees understand the requirements of copyright and are satisfied with sample items for appendices and tables. For gustomers needing permission to reproduce five sample items in a proposal, thesis_p or dissertation, the following page includes the permission form and reference information needed to satisfy the requirements of an academic committee.

Sample Items:

Appendix F: Ethics Approval

Kevin Milne

From: Sent: To: Cc: Subject: ethics@uwindsor.ca Friday, December 19, 2014 2:57 PM Mr. Alex Pennetti (Primary Investigator); Dr. Kevin Milne (Supervisor) ethics@uwindsor.ca **REB** Clearance

W University

Today's Date: December 19, 2014 Principal Investigator: Mr. Alex Pennetti RFR Numher 32098 Research Project Title: REB# 14-255: The Effects of Exercise Intensity and Relative Timing of Exercise on Memory Performance Clearance Date: December 19, 2014 Project End Date: August 31, 2015 Milestones: Renewal Due-2015/08/31(Pending)

This is to inform you that the University of Windsor Research Ethics Board (REB), which is organized and operated according to the Tri-Council Policy Statement and the University of Windsor Guidelines for Research Involving Human Subjects, has granted approval to your research project on the date noted above. This approval is valid only until the Project End Date.

 $\,$

A Progress Report or Final Report is due by the date noted above. The REB may ask for monitoring information at some time during the project's approval period.

During the course of the research, no deviations from, or changes to, the protocol or consent form may be initiated without prior written approval from the REB. Minor change(s) in ongoing studies will be considered when submitted on the Request to Revise form.

Investigators must also report promptly to the REB:

a) changes increasing the risk to the participant(s) and/or affecting significantly the conduct of the study;

b) all adverse and unexpected experiences or events that are both serious and unexpected;

c) new information that may adversely affect the safety of the subjects or the conduct of the study.

Vita Auctoris

Alex Pennetti was born in 1991 in Windsor Ontario and has continuously lived in the Windsor area. He earned a Bachelor of Human Kinetics degree from the University of Windsor in 2013.