ACUTE EXERCISE CAN PROTECT A NEWLY ACQUIRED PROCEDURAL SKILL

A Thesis

by

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ABSTRACT

The present study was designed to evaluate if an acute bout of moderate intensity exercise could provide some protection to a newly formed memory for procedural skill. Congruent with previous work, test performance for a target motor sequence practiced 6-hr earlier exhibited minimal forgetting. Inclusion of additional practice with an alternative motor sequence 45-min after the original practice significantly increased forgetting of the target motor sequence. Inserting a bout of exercise between practice with the two motor sequences, reduced the extent of forgetting of the target motor sequence. Using a 6-hr retention interval, which occurred across a wake period, verified that this protection of new procedural skill knowledge was exercise-not sleep-dependent. These data are consistent with the claim that exercise can expedite the employment of consolidation leading to more rapid stabilization of a labile motor memory that provides greater resiliency to interference from new learning. The benefit in procedural skill test performance following exercise was localized to execution rather than the concatenation process, the latter of which has been implicated in sleep-dependent memory improvements. Finally, the exercise-mediated memory benefit was not associated with increase peripheral lactate concentration resulting from the exercise bout. This may in part be due to the use of moderate rather than more vigorous intensity exercise being used in the present work.

DEDICATION

This thesis work is dedicated to my wife, Suna Choi, who has always been a source of encouragement and support during my graduate life.

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The E-Prime program used for Motor Sequence Tasks in Chapter 2 was provided by Ph.D. student Jing Chen of the Department of Health and Kinesiology.

All other work conducted for the thesis was completed by the student independently.

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TABLE OF CONTENTS

LIST OF FIGURES

LIST OF TABLES

CHAPTER I

INTRODUCTION

Regular cardiovascular exercise has positive effects on human physiological fitness. In response to physical training, muscle protein synthesis increases in both older and younger individuals (Short, Vittone, Bigelow, Proctor, & Nair, 2004). Bone mass which is normally attenuated with aging, is increased by physical activities in adult and senior citizens (Guadalupe-Grau, Fuentes, Guerra, & Calbet, 2009). Regular exercise also reduces the likelihood of developing diseases such as obesity, cancer, and diabetes (Warburton, Nicol, & Bredin, 2006). Importantly for the present work, exposure to physical activity is also beneficial for human cognition (Hillman, Erickson, & Kramer, 2008). Improvement in cognitive function is closely correlated with changes in cerebral function and structure (Berchtold, Castello, & Cotman, 2010; Cotman, Berchtold, & Christie, 2007). According to Colcombe and Kramer (2003), aerobic physical training impacts brain regions related to executive control including parietal and prefrontal regions.

To date, most of the studies addressing exercise-dependent cognitive benefits have focused almost exclusively on neuropsychological tasks that target cognitive operations related to attention, decision-making, and processing speed (Roig, Nordbrandt, Geertsen, & Nielsen, 2013). Less is known about the effects of cardiovascular activity on memory and learning (Erickson et al., 2011; Roig, Skriver, Lundbye-Jensen, Kiens, & Nielsen, 2012). Studies that have considered the impact of physical activity on learning and memory have focused on the influence of either an acute bout of exercise or chronic exercise (Roig et al., 2013). The former is defined as performing only a single bout of exercise, whereas the latter considers the efficacy of multiple bouts of exercise executed over several weeks or months (Roig et al., 2013).

Currently, the literature includes far greater investigation of the importance of chronic exercise as opposed to the benefits of single exercise session for human memory (Rhee et al., 2015; Roig et al., 2013). This is interesting given a recent meta-analysis from Roig et al. (2013) reported more robust effects following acute as opposed to chronic exercise for memory performance (Mang, Snow, Wadden, Campbell, & Boyd, 2016; Roig et al., 2013). Of the studies evaluating acute exercise and human memory, most have focused on declarative memory. Declarative memory involves recall and/or recognition of facts, lists, as well as episodes of everyday life which are often assessed using traditional memory tasks involving verbal-auditory and visuo-spatial span or long-term episodic memory (Lambourne & Tomporowski, 2010; Mang et al., 2016; Roig et al., 2013). The present work focused explicitly on the role of acute exercise for procedural skill learning. Procedural learning has been central to our understanding of motor skill acquisition, and has frequently involved the acquisition and retention of motor sequences or adaptation to visual or dynamic perturbation (Doyon et al., 2009).

Only a few studies have asked if an acute bout of exercise positively impacts long-term memory for procedural skills (Roig et al., 2013). A number of these have focused on the potential benefit of a single bout of exercise prior to a bout of motor learning. For example, Roig et al. (2012) assigned individuals to one of three experimental conditions consisting of experiencing no exercise, exercise-before or exercise-after practice of a visuomotor accuracy-tracking task. Exercise consisted of a 20-min bout of moderately intense activity on a cycle ergometer. Performance during training was unaffected by a preceding bout of exercise. Memory for the tracking task was evaluated after 1-hour, 24-hour, and 7-day delay following the initial practice bout. Exposure to exercise either before or after training, when compared to the no-exercise control condition, resulted in superior retention after both 24-hours and 7-days. However, after 7 days, the individuals that experienced exercise following practice exhibited the largest retention benefit (Roig et al., 2012). The long-term efficacy of exercise following practice led Roig and colleagues to conclude that exercise-dependent memory gains were localized to consolidation processes engaged shortly after a learning episode (Diekelmann & Born, 2007; Korman et al., 2007). Other studies have revealed some limited benefits of moderate-intensity aerobic exercise when administered prior to motor skill training on acquisition and retention (Mang et al., 2016; Statton, Encarnacion, Celnik, & Bastian, 2015).

While the impact of an acute bout of exercise prior to the training of a motor skill has received some attention (Mang et al., 2016; Roig et al., 2012; Statton et al., 2015), minimal effort has been exerted to explore Roig et al.'s (2012) observation that exercise following motor training facilitates post-practice consolidation. Rhee et al. (2015) noted that the impact of post-practice exercise on the development of motor memory may have been underestimated in the work of Roig et al. because the motor skill learned was more dependent on visual guidance than memory. Recall that Roig et al. (2012) used a visual-motor tracking task which requires a motor response continuously track a visual signal. To address this shortcoming, Rhee et al. evaluated the influence of post-training exercise for the acquisition and retention of motor sequence task which has a rich history of use in studies addressing motor memory and learning (Abrahamse, Ruitenberg, de Kleine, & Verwey, 2013; Doyon et al., 2009).

Specifically, Rhee et al. examined the efficacy of a short bout of moderately-intensive cycling as a means of protecting a newly acquired motor sequence. Rhee et al. focused on the reduced overnight gains in motor sequence skill that occurred from practicing a novel motor sequence in close temporal proximity to the practice of a target sequence (Walker, Brakefield, Seidman, et al., 2003). Rhee et al. proposed that inserting a brief bout of exercise between practice of a to-be learned motor sequence and the interfering practice with a novel sequence that occurred 2-hours later might offer some protection to the newly acquired motor memory. The rationale was that exercise would facilitate post-practice consolidation which would in turn more rapidly stabilize the newly acquired knowledge, thus rendering it less susceptible to the interfering influence of practice with a novel motor sequence (Roig et al., 2012). As predicted, Rhee et al. revealed that an acute bout of exercise did reduce the negative impact of the later practice.

The data from Rhee et al. (2015) in conjunction with those of Roig et al. (2012) highlight post-practice consolidation as a candidate process that is modifiable by a brief bout of moderate-intensive aerobic exercise. It is important to note that the studies of

Rhee et al. and Roig et al. revealed exercise-dependent memory benefits for tests that occurred after a night of sleep. This is critical because there is an extensive literature detailing the positive contribution of sleep to post-practice consolidation (Diekelmann & Born, 2007; Walker, Brakefield, Hobson, & Stickgold, 2003). Indeed, evidence exist revealing significant procedural skill enhancement following sleep but not equivalent wake periods for motor sequences such as those used by Rhee et al. (2015). As a result, one cannot be sure that the benefit of acute exercise for improved motor memory, reported by Rhee el al. and Roig et al., is a consequence of an independent contribution from post-practice exercise or exercise interacting with sleep-dependent processes that function to enhance motor skill performance.

In light of this issue, the primary objective of the present work was to directly assess if there is an independent contribution from post-practice exercise to memory for a motor sequence. To accomplish this objective, all participants were exposed to practice with a pre-structured eight-element motor sequence that was followed by a test session conducted 6 hours later. Thus, the retention of the motor skill was determined following a temporal interval that did not include sleep. A control condition (CON condition) involved practice of a target motor sequence and a test administered 6-hours later. It was expected that participants in the CON condition would exhibit stabilization or minimal forgetting of the newly acquired motor sequence knowledge reflected in test performance being equivalent to that observed at the end of training (Walker, Brakefield, Hobson, et al., 2003). A separate group of individuals (INT condition) was administered additional practice of an alternative eight-key motor sequences 45-min after completion of the initial practice with the target sequence prior to their 6-hr delayed test. It was hypothesized that test performance for the target motor sequence would be poorer than that observed for individuals assigned to CON condition as a result of practice with the alternative motor sequence (see Walker et al., 2003). Finally, a separate group of individuals (EXE+INT condition) experienced practice with both the target and interfering motor sequences but were administered a brief bout of moderate intensity aerobic exercise between practice bouts. It was anticipated that the loss of performance at the 6-hr delayed test due to interfering practice (i.e., INT condition) would be attenuated with the inclusion of the acute exercise session.

The motor sequences used in this study have been characterized as discrete sequence production (DSP) tasks (Abrahamse et al., 2013). The use of a DSP task in the present study offered a unique opportunity to examine the locus of any facilitation from the acute bout of exercise for motor skill acquisition and/or retention. Specifically, Abrahamse et al. (2013) suggested that the execution of a DSP task involves three distinct processes critical to successful execution of a sequence skill. The first process, sequence *initiation*, is reflected in the time to complete the first key-press. This process is traditionally much slower than subsequent key-presses because it is presumed to include the selection and preparation of the sequence including readying the initial motor chunk of a sequential motor skill. The *concatenation* process is manifest as a relatively slow key-press observed in the middle of a set of elements that constitute the sequence, reflects a cost of transition from one motor chunk to the next that are included in the sequential action. Finally, all other key-presses are assumed to only involve an *execution* process, typically reflected in rapid responding often less 100 ms, as elements within a single motor chunk are implemented. This latency indexes the cost of executing the most primitive element (i.e., key-press) contained in a motor chunk.

It has been reported that sleep-dependent enhancement of sequence performance results from facilitating the concatenation process. For example, Kuriyama, Stickgold, and Walker (2004) reported that offline performance gains resulting from being exposed to sleep-filled rather than waked-filled retention intervals were localized to the formation of motor chunks and/or amalgamating separate motor chunks into larger functional units. Kuriyama et al. revealed that the transitions that were the slowest and most difficult at the conclusion of the training period demonstrated the largest benefit from sleep. Sleep key transitions during motor sequence production have been interpreted as demarcations of the beginning of a motor chunk and reflect delays associated with the concatenation process (Abrahamse et al., 2013). If exercise operates in a similar manner to sleep, with respect to facilitating consolidation, one would anticipate exercise-dependent benefits to be linked to an improvement in concatenation of the motor chunks. This is possible as there has been speculation as to a central role for an upregulation in brain-derived neurotrophic factor (BDNF) for central nervous system improvements from both sleep and exercise (Knaepen, Goekint, Heyman, & Meeusen, 2010; Roig et al., 2013; Skriver et al., 2014). It is of course plausible that role of exercise for post-practice consolidation is more broad-based and might positively influence other sequence production processes such as initiation and execution.

In addition to a role of BDNF for exercise-induced procedural memory enhancement (Roig et al., 2013; Skriver et al., 2014), Skriver et al. (2014) reported a significant relationship between the elevation in lactate concentration following exercising and the eventual memory improvement. Lactate is a metabolic substrate that has been considered an important component for neuronal functioning (Costalat, Aubert, Magistretti, & Pellerin, 2006; Skriver et al., 2014; Wyss, Jolivet, Buck, Magistretti, & Weber, 2011). It has been proposed that lactate concentration may remain elevated for some time after aerobic exercise, thus have the potential to mediate human memory and cognitive processes (Kalman et al., 2005; Skriver et al., 2014; van Hall, 2010). Indeed, Skriver et al. reported that a higher concentration of lactate after physical activity was associated with greater delayed retention of a visuomotor tracking task. In the present study, lactate was assessed at the beginning and end of the acute exercise bout (EXE+INT condition) to allow assessment of any potential association between this biomarker and savings in procedural skill learning resulting from exposure to the acute bout of exercise.

CHAPTER II

METHODS

Participants

A total of 46 undergraduate students between 18 and 22 years were recruited as participants for the experiment. Participants were randomly assigned to one of three experimental conditions (CON, INT, and EXE+INT condition, see Table 1 and 2). The study was approved by the ethics committee at Texas A&M University, and was performed in accordance with the ethical standards described in the Declaration of Helsinki. Informed consent was obtained before any involvement of individuals in this study.

Tasks

Graded Exercise Test

At least 48 hours before participation in the experiment, a graded exercise protocol was administered to a subset of participants in the CON (n=5) and INT (n=5) as well as all individuals assigned to the EXE+INT conditions (n=12). The graded test was conducted on a MONARK cycle ergometer (Ergomedic 828E, Monark, Sweden), starting with 3 minutes warm-up at a workload of 0 W. After the warm-up, the resistance was gradually increased by 35 W every 3-min until exhaustion. Subjects were instructed to maintain a pedaling rate of 75 rotations per minute (rpm) and to remain seated throughout the test. Exhaustion was defined as the point when individuals could not maintain the cycling rate of 75 rpm for 1-min or when they voluntarily terminated the test because of fatigue. After the graded-exercise protocol, subjects were directed to cycle for an additional 3-min at a workload of 0 W during a cool-down period. Throughout the graded exercise testing, oxygen consumption (VO_2), production of carbon dioxide (VCO_2), and respiratory exchange ratio (RER) were recorded every min by a gas analyzing tool (Ultima; Medical Graphics, Minneapolis, MN). Borg's Rating of Perceived Exertion (RPE), ranging from 6 to 20, was recorded and used to monitor each individual's subjective assessment of perceived workload.

Acute Bout of Exercise

Participants in the exercise group (EXE+INT condition) performed an acute bout of aerobic exercise between practice of the target and interference DSP tasks. Results from the graded exercise test were used to determine the workload experienced by each participant for this bout of exercise. Specifically, the protocol involved 3-min of warm-up at 60% HR_{max} that was followed by 20-min of exercise at the predicted resistance of 80% HR_{max}. Heart rate, recorded by a POLAR HR monitor (E600), was utilized to regulate the intensity of the exercise. Oxygen consumption (VO_2), production of carbon dioxide (VCO_2), and respiratory exchange ratio (RER) were recorded to ensure that the exercise was of sufficient intensity. During the entire exercise protocol, participants were required to maintain a cadence of 75 rpm. After the completion of the acute exercise bout, all individuals cycled at 0 W for an additional 3-min during a cool-down period. In addition to HR, RPE reports were required to facilitate the assessment of each individual's workload during the acute exercise bout. Percent HR_{max} was maintained within ± 5 beats per minute by adjusting workload during exercise. It was anticipated that this protocol would approximate 70% VO_{2max} and a RPE of 14-15. Both prior to and after the acute exercise, lactate measures were taken by finger prick using a lactate analyzer (Lactate Scout+, EKF Diagnostics). It was expected that lactate production would increase as a result of the workload experienced by each participant

Motor Sequence Tasks

All participants (CON: n=17, INT: n=17, EXE+INT: n=12) used their non-dominant hand to perform a target sequence that involved an eight-key discrete sequence production (DSP) task, 4-1-3-2-3-1-4-2 on a standard PC keyboard using the V, B, N, M keys. For this task, the “1” represented the leftmost key (V key) and “4” was the rightmost key (i.e., M key). Four white square boxes that acted as placeholders were displayed on a computer display with a black background. The leftmost box was associated with “1” and the leftmost key (i.e., “V”), and the rightmost box was related to “4” and the rightmost key (i.e., “M”). When a square turned green, participants were instructed to press the spatially compatible key with the finger resting on the key [little (“V”), ring (“B”), middle (“N”), and index (“M”) fingers] associated with the location of the square that changed color. When the correct key was pressed, the color in the placeholder changed back to white at which point the next square changed color (i.e., to green) at the next spatial location (i.e., 1-4) specific to the DSP task being performed. Between key-press four and the presentation of the visual signal for key-press five, there was a random temporal pause of 200-750 ms (i.e., the response-to-stimulus interval or RSI). This process has been used previously to encourage participants to organize the execution of the DSP task as two separate motor chunks (Abrahamse, Jimenez, Verwey,

& Clegg, 2010; Verwey & Dronkert, 1996).

All individuals also performed the target DSP task during a delayed test administered 6-hrs after completion of the original training with this task (See Figure 1). During the test, the temporal pause between key-press 4 and the visual signal for key press 5 was removed. Some individuals also experienced an extra session of practice with an alternative DSP task that also required eight-key presses, namely, 2-3-1-4-1-3-2-4. The additional practice with this new DSP task was performed in the same manner as those with the target DSP task.

Procedures

Prior to participation in the experiment, all participants completed an informed consent, the International Physical Activity Questionnaire (Craig et al., 2003) and the Edinburgh Handiness Inventory (Oldfield, 1971). Some participants performed a graded maximal exercise test at least 48-hr prior to any involvement with the subsequent phases of the experiment. Figure 1 depicts the general sequence of events that are followed by each experimental condition. On first arrival at the laboratory, individuals were assigned to one of three experimental conditions (i.e., CON, INT, and EXE+INT). Individuals in all conditions practiced the DSP task, 4-1-3-2-3-1-4-2, as the target sequence. A practice trial consisted of correctly executing the string of eight key-presses as accurately and quickly as possible in response to a set of visual signals presented on a computer monitor. All individuals performed 200 trials of practice of the target DSP task. The 200 practice trials were performed in 10 blocks of 20 trials with each block separated by a 1-min interval. A 5-sec delay occurred between the completion of one trial and the beginning of the next trial in each block of 20 trials.

Some individuals (i.e., INT & EXE+INT condition) experienced an additional set of 200 trials of practice of a new DSP task 45-min after practice with the target DSP task. Presentation of the extra set of 200 practice trials followed the same protocol as described for the target DSP task. Individuals assigned to the CON condition did not receive any additional practice beyond that with the target DSP task. An acute bout of exercise was experienced between practice with target and new DSP tasks by the participants in the EXE+INT condition which was designed to create a workload of approximately 80% HR_{max} determined from each participant's individual performance during the graded exercise test. During the exercise bout, lactate was assessed from blood drawn using a finger prick prior to and after the exercise.

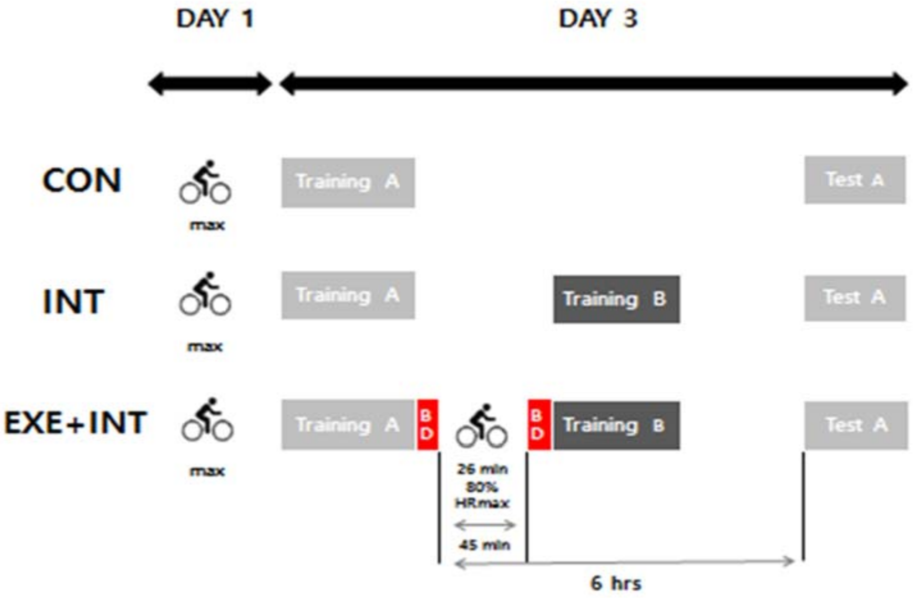

Figure 1. Overview of the experiment including three experimental groups (CON, INT, and EXE+INT condition). Target DSP task (A) was practiced by all participants, whereas a novel DSP task (B) was only practiced by participants assigned to the INT and EXE+INT conditions. An acute exercise bout was performed by the EXE+INT condition, and blood samples were drawn (BD) before and after the acute exercise to assess blood lactate level.

Six hours after completion of practice with the target DSP task, all individuals performed an additional 10 trials with the target sequence. During these trials, the temporal pause presented during DSP practice was removed. To evaluate general performance during practice and test trials, *response time* (RT) which was the mean time to perform key presses during the execution of the DSP task was used as the primary dependent variable of interest.

CHAPTER III

RESULTS

Participants' Demographics

Table 1 displays demographics for all participants assigned to CON, INT, and EXE+INT conditions. The number of female (Pearson *p* = 0.1774) and the number of left handed participants were similar across conditions (Pearson *p* = 0.9475,). Age for each individual in Table 1 were subjected to a one-way between-subjects (Condition: CON, INT, EXE+INT) analysis of variance (ANOVA) which revealed no significant main effect [F(2,43) = 0.4250, *p* = 0.65; CON = 19.5 year, INT = 19.7 year, EXE+INT = 19.3 year].

Table 1. Demographics (SD) of all participants

	N	Age (yrs)	# Male	# Female	# Right handed	# Left handed
CON	17	19.52 (1.23)	10	7	15	2
INT	17	19.76 (1.30)	5	12	15	2
EXE+INT	12	19.33 (1.23)	4	8	11	1
Total	46	19.56 (1.24)	19	27	41	5

Physiologic Responses of Individuals Assigned to the CON, INT, and EXE+INT Conditions

Graded Exercise Test

A subset of five individuals was used from CON and INT conditions in addition to the 12 participants from EXE+INT condition to evaluate HR_{max} and VO_{2max} prior to participation in the experiment. Each individual's physiological data, reported in Table 2, were submitted to separate one-way between-subject (Condition: CON, INT, EXE +INT) ANOVAs which indicated no significant main effect of condition for Age [F(2,19) = 0.1825, *p* = 0.8346; CON = 19.4 year, INT = 19.0 year, EXE+INT = 19.33 year], Resting HR [F(2,19) = 0.5799, *p* = 05696; CON = 82.4 bpm, INT = 80.8 bpm, EXE+INT = 77.5 bpm], maximum HR [F(2,19) = 0.2189, *p* = 0.8054; CON = 189.4 bpm, INT = 188.0 bpm, EXE+INT = 188.83 bpm], VO_{2max} [F(2,19) = 0.3141, *p* = 0.7341; CON = 37.32 ml/min/kg, INT = 39.4 ml/min/kg, EXE+INT = 36.6 ml/min/kg], Mean RER [F(2,19) = 0.1639, *p* = 0.8500; CON = 1.05, INT = 1.04, EXE+INT = 1.03], final RPE [F(2,19) = 0.0020, *p* = 0.9980; CON = 19.4, INT = 19.4, EXE+INT = 19.41], and IPAQ score [F(2,19) = 0.1439, *p* = 0.8669; CON = 8182.8, INT = 6270.3, EXE+INT = 7061.6]. These data suggest that mean demographic and physiological responses during the graded exercise test were similar across individuals assigned to the CON, INT, and EXE+INT conditions.

Table 2. Means (SD) of physiological measures for the graded exercise test to each condition

Graded Exercise Test

Condition	Age (yrs)	Resting HR (bpm)	HR$_{max}$ (bpm)	VO$_{2max}$ (ml/min/kg)	Mean RER	Final RPE	IPAQ Score
CON (n=5)	19.40 (1.14)	82.40 (9.60)	189.40 (3.97)	37.32 (4.47)	1.05 (0.01)	19.40 (0.54)	8182.80 (6392.11)
INT (n=5)	19.00 (1.00)	80.80 (4.32)	188.00 (2.34)	39.40 (9.20)	1.04 (0.01)	19.40 (0.54)	6270.30 (5722.15)
EXE+INT (n=12)	19.33 (1.23)	77.50 (10.28)	188.83 (3.45)	36.64 (5.99)	1.03 (0.01)	19.41 (0.66)	7061.63 (5387.04)

Acute Exercise Test

Condition	Target HR (bpm)	Actual HR (bpm)	Target VO$_{2max.}$ (ml/min/kg)	Actual VO$_{2max.}$ (ml/min/kg)	Pre-lactate (mmol/L)	Post-lactate (mmol/L)	Final RPE
EXE+INT (n=12)	151. 0 (2.76)	141.3 (8.04)	25.64 (4.19)	22.91 (3.39)	2.15 (0.66)	4.55 (1.26)	17.16 (0.93)

Table 3. Demographics for each subject and their physiological measures for the graded exercise test and acute bout of exercise assigned to each condition

Graded exercise test											*Acute exercise test*						
Sub #	Gender	Hand	Age	Exercise duration	Rest HR	HR_{max}	VO_{2max}	Mean RER	Final RPE	IPAQ Score	Target HR	Actual HR	Target VO_2	Actual VO_{2max}	Pre-lactate	Post-lactate	Final RPE
CON																	
13	F	R	20	21	72	192	36.3	1.10	20	1935							
14	M	R	19	23	82	184	39.6	1.04	19	17667							
15	F	R	19	19	87	194	35.6	1.05	19	2868							
16	M	R	18	24	75	190	43.5	1.05	19	7800							
17	M	L	21	22	96	187	31.6	0.99	20	10644							
INT																	
30	M	R	19	24	82	192	37.1	1.08	19	3041.5							
31	M	R	20	26	75	188	55.4	0.92	19	13092							
32	F	L	18	17	78	187	36.7	1.11	19	2031							
33	F	R	20	17	86	186	31.7	1.01	20	1310							
34	F	R	18	18	83	187	36.1	1.09	20	11877							
EXE+INT																	
35	M	R	20	26	57	191	40.8	0.95	19	5578.5	152	140	28.5	27.2	1.5	5.7	18
36	M	L	19	22	90	193	34.6	1.16	20	865	154	145	24.2	24.2	2.4	7.1	17
37	F	R	19	20	87	194	24.8	1.03	18	3448	155	152	17.3	18.1	2.9	5	16
38	M	R	18	24	85	191	35.2	1.01	19	10659	152	135	24.6	22.1	2.7	5.6	17
39	F	R	18	18	63	188	31.9	1.03	20	13740	150	142	22.3	19.4	2.4	4	18
40	F	R	20	23	80	184	39.3	1.04	20	2740	147	140	27.5	24.1	2	3.1	17
41	F	R	21	21	85	192	35.6	1.02	20	3132	153	147	24.9	19.9	3.4	3.4	16
42	F	R	19	23	85	185	48	0.92	19	4176	148	138	33.6	28.4	2.4	5.7	19
43	F	R	19	23	75	185	39.2	1.10	20	19449	148	132	27.4	25.4	1.5	3.6	17
44	F	R	18	19	73	189	32.7	1.06	19	8343	151	144	22.8	21.2	1.7	4.4	18
45	M	R	19	25	69	185	43.3	1.05	20	4143	148	123	30.3	25.4	1.1	4	16
46	F	R	22	19	81	189	34.3	0.95	19	8466	151	151	24.0	19.2	1.8	3.1	17

Acute Bout of Exercise

Physiological data from the participants in the EXE+INT condition from the acute exercise bout are reported in Table 2 and were subjected to a 2 (Score: Target, Actual) repeated measures ANOVA which revealed a significant main effect of Score for HR [F(1,22) = 15.76, $p < 0.01$; Target HR = 151.0 bpm, Actual HR = 141.3 bpm], but not for VO_{2max} [F(1,22) = 3.07, $p = 0.09$; Target VO_{2max} = 25.64 ml/min/kg, Actual VO_{2max} = 22.91 ml/min/kg]. These data provide some evidence that the experimental protocol for the acute bout of exercise accomplished the intended workload.

Mean lactate levels for each individual in the EXE+INT condition were also subjected to a 2 (Time: pre-exercise, post-exercise) repeated measures ANOVA which revealed a significant main effect of Time, [F(1,22) = 34.14, $p < 0.01$; Pre-exercise = 2.15 mmol/L, Post-exercise = 4.55 mmol/L]. As expected, the acute bout of exercise resulted in an increase in lactate production.

Select physiological data reported in Table 2 was submitted to a 2 (Bout: Graded, Acute) repeated measures ANOVA which showed a significant main effect of Bout for HR_{max} [F(1,22) = 353.53, $p < 0.01$; Graded test = 188.8 bpm, Acute test = 141.3 bpm], VO_{2max} [F(1,22) = 47.62, $p < 0.01$; Graded test = 36.64 ml/min/kg, Acute test = 22.91 ml/min/kg], and final RPE [F(1,22) = 45.82, $p < 0.01$; Graded test = 19.41, Acute test = 17.16] (See Table 3). As anticipated, these data indicate that physiological responses to the workload experienced by the individuals in the EXE+INT condition unfolded as expected. That is, an acute bout of exercise was of a lower intensity than observed during the graded exercise test.

Online Effects for the Target DSP

To assess online performance improvement for the target DSP task during the initial practice phase, mean response time (RT) was calculated for each individual for each block in each condition (i.e., CON, INT, and EXE+INT, See Figure 2 - leftmost graphs). These data were subjected to a 3 (Condition: CON, INT, EXE+INT) x 2 (Block: 1, 10) ANOVA with repeated measures of the last factor. This analysis revealed a significant main effect of Block, F(1,43) = 363.39, $p < 0.01$. The analysis revealed no significant main effect of Condition, F(2, 43) = 0.63, $p = 0.5392$ or Condition x Block interaction, F(2, 43) = 0.20, $p = 0.81$.

To examine the role of each of the processes in the theoretical framework of Abrahamse et al. (2013) during DSP task performance, mean initiation time (IT), concatenation time (CT), and execution time (ET) were also calculated for Block 1 and Block 10 for the target DSP task (see Figure 3). These data were submitted to separate 3 (Condition: CON, INT, EXE+INT) x 2 (Block: 1, 10) ANOVA with repeated measures of the last factor. The analysis of mean IT revealed a significant main effect of Block, F(1,43) = 8.26, $p < 0.01$. The analysis showed no significant main effect of Condition, F(2, 43) = 0.99, $p = 0.3798$ or Condition x Block interaction, F(2, 43) = 1.18, $p = 0.3161$. For the mean CT, this analysis revealed a significant main effect of Block, F(1,43) = 61.85, $p < 0.01$. The analysis displayed no significant main effect of Condition, F(2, 43) = 0.30, $p = 0.74$ or Condition x Block interaction, F(2, 43) = 0.95, $p = 0.3947$. For mean ET, the analysis revealed a significant main effect of Block, F(1,43) = 361.92, $p < 0.01$. The analysis showed no significant main effect of Condition, F(2, 43) = 0.50, $p = 0.6087$

or Condition x Block interaction, F(2, 43) = 0.28, *p* = 0.7574.

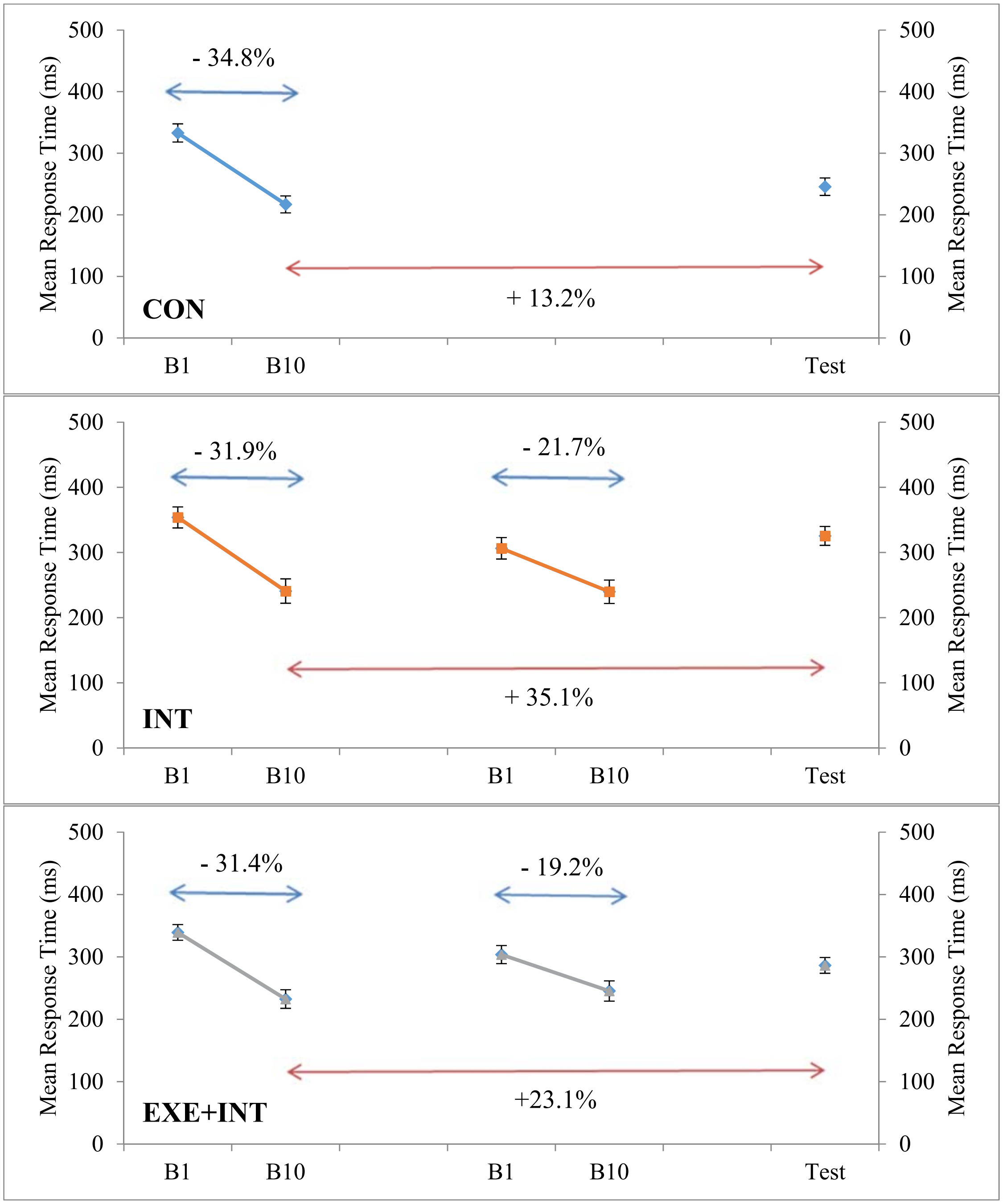

Figure 2. Mean response time for the CON, INT, and EXE+INT conditions during practice and test with the target DSP task (*leftmost & rightmost symbols*) and the alternative DSP task (*middle symbol*). Note only the INT and EXE+INT condition conducted practice with the alternative DSP task.

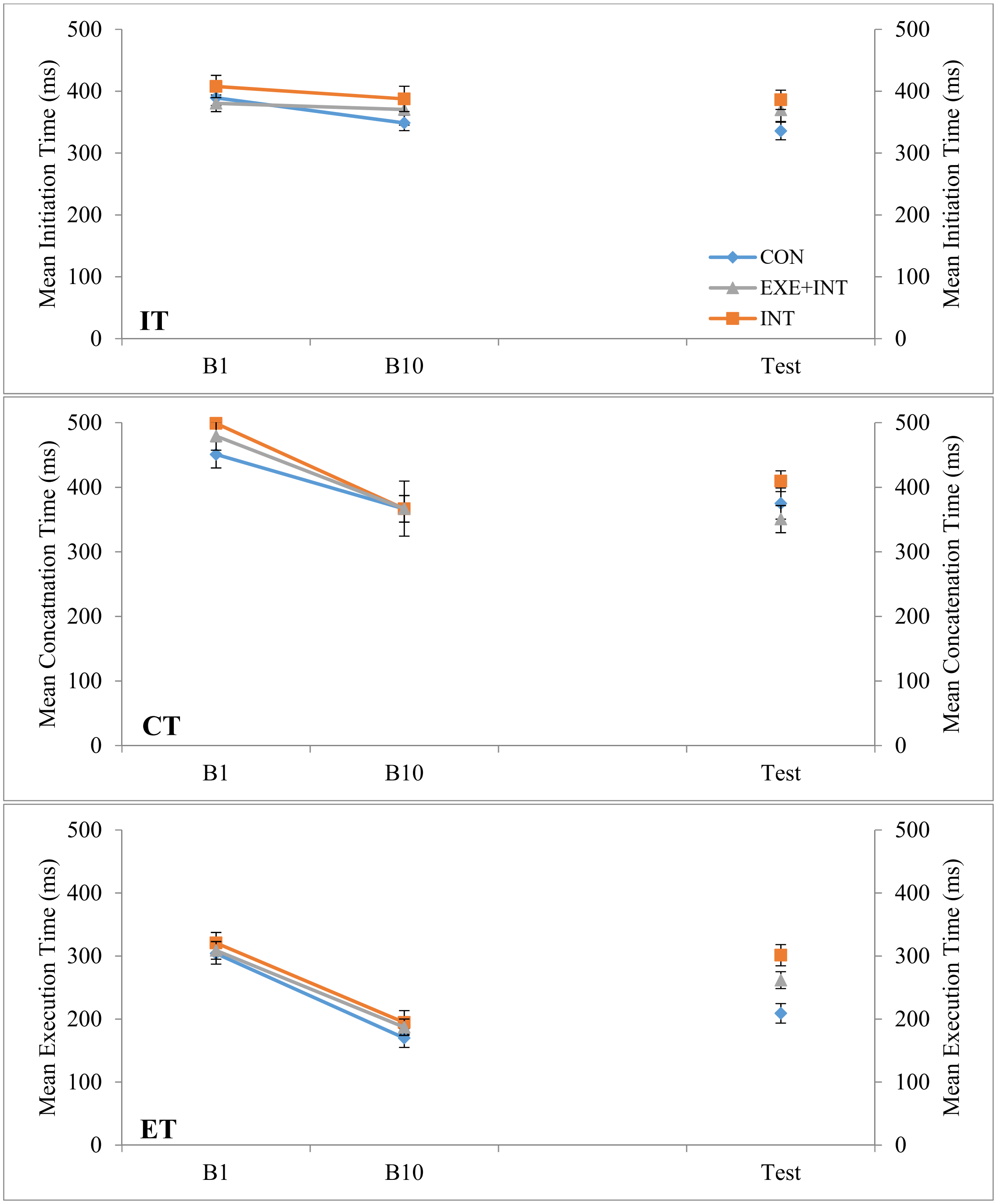

Figure 3. Mean initiation time (IT), concatenation time (CT), and execution time (ET) for the CON, INT, and EXE+INT conditions during practice and test with the target DSP task. Note that graphs for practice with an alternative DSP task are not plotted on this figure.

Comparison of Online Performance of the Target and Interfering DSP Tasks

For individuals assigned to the INT and EXE+INT conditions, additional practice with an alternative DSP task was performed. Mean RT was calculated for each individual for each block with the alternative DSP task in the same manner as used when assessing target sequence learning (See Figure 2 - middle symbols). These data were combined with the equivalent blocks from practice of the target DSP task and submitted to separate 2 (Condition: INT, EXE+INT) x 2 (Sequence: Target, Alternative) x 2 (Block: 1, 10) ANOVAs with repeated measures of the last two factors. These analyses revealed a significant main effect of Block, F(1,110) = 54.48, $p < 0.01$. Interpretation of this main effect was superseded by a significant Sequence x Block interaction, F(1,110) = 4.02, $p < 0.05$ (See Figure 2). Simple main effects analysis of this interaction indicated that mean RT was significantly greater for the target DSP task compared to the alternative DSP task for Block 1, F(1,56) = 11.14, $p < 0.01$. However, the mean RT did not differ significantly for the target and alternative DSP tasks for Block 10, F(1,56) = 0.0065, $p = 0.93$. Mean RT differed significantly for Block 1 and Block 10 for the target DSP task, F(1,56) = 44.06, $p < 0.01$, and the alternative DSP task, F(1,56) = 14.44, $p < 0.01$. Taken together, these data suggest that there was a positive transfer from the initial training to training with the alternative DSP task. Moreover, exercise did not impact the extent of positive transfer.

Offline Effects for the Target DSP Task

In order to address the offline effects in general performance, the difference between mean RT ($RT_{diff.}$) for the target task for the last block of acquisition and that observed during the test block was calculated for each individual for all conditions (Reis et al., 2009). These data was subjected to a between-subject one-way 3 (Condition: CON, INT, EXE+INT) ANOVA. The analysis of the mean $RT_{diff.}$ revealed a significant main effect of Condition, F(2,43) = 7.36, $p < 0.01$. Post-hoc analysis indicated that the mean $RT_{diff.}$ for the CON (M = 29 ms) was significantly different from the mean $RT_{diff.}$ for the INT (M = 85 ms) but not the EXE+INT condition (M = 54 ms). The mean $RT_{diff..}$ for EXE+INT condition was marginally significant from that observed for the INT condition, ($p = 0.06$).

To examine the locus of the reported exercise-mediated benefit in mean $RT_{diff..}$, similar analyses were conducted for mean $IT_{diff.}$, mean $CT_{diff.}$, and mean $ET_{diff.}$. The analyses of mean $IT_{diff.}$ revealed no significant main effect of Condition, F(2,43) = 2.21, $p = 0.80$. Similarly, for mean CT_{diff}, there was no significant main effect of Condition, F(2,43) = 0.67, $p = 0.51$. In contrast, the analysis of mean $ET_{diff.}$ revealed a significant main effect of Condition F(2,43) = 8.44, $p < 0.01$. Post-hoc analysis indicated that the mean $ET_{diff.}$ for the CON (M = 39 ms) was significantly different from the mean $ET_{diff.}$ for the INT (M = 107 ms) but not the EXE+INT (M = 75 ms). The mean $ET_{diff.}$ for EXE+INT condition was not significantly different from that observed for the INT condition, ($p = 0.08$).

The Role of Lactate for Memory for the Target DSP Task

Recall that capillary blood samples were drawn from a fingertip before and after the acute exercise test allowing blood lactate to be assessed. Recent studies has reported that higher concentration of lactate immediately after exercise are associated with better retention of a newly acquired motor skill (Skriver et al., 2014). In order to evaluate the impact of lactate production on facilitating motor memory, lactate levels for each individual in the EXE+INT condition before and after an acute bout of exercise were subjected to a repeated measures 2 (Time: pre, post) ANOVA. As expected, a main effect of Time was revealed, F(1,22) = 34.14, $p < 0.01$. Post hoc analyses indicated that mean blood lactate level after exercise (*M* = 4.55 mmol/L, *SEM* = 0.36) was significantly greater than that at rest (*M* = 2.15 mmol/L, *SEM* = 0.19).

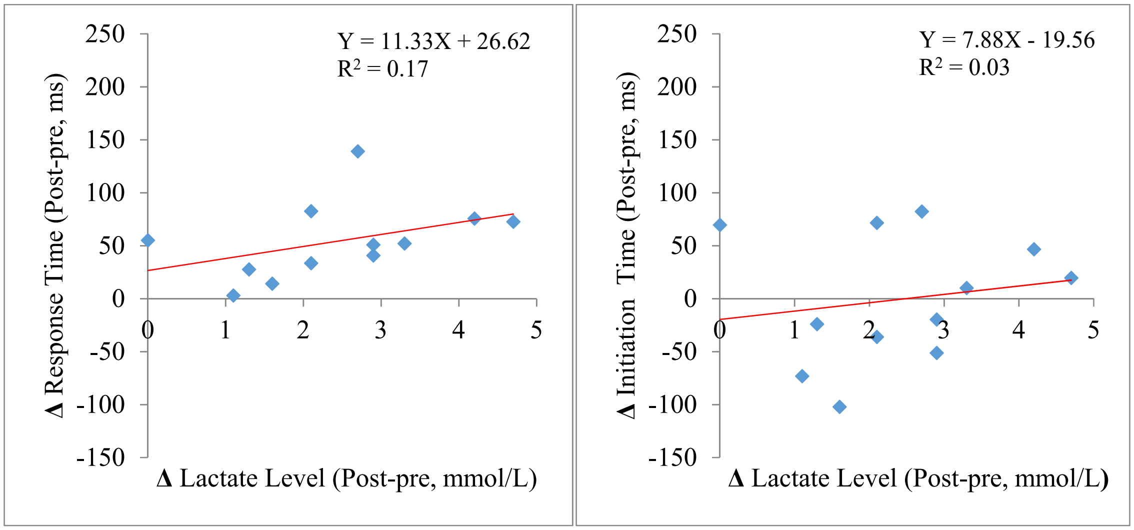

Figure 4. Correlations between Δ lactate level (mmol/L) and Δ performance (TT, IT, CT, and ET, ms) from block 10 to the test block.

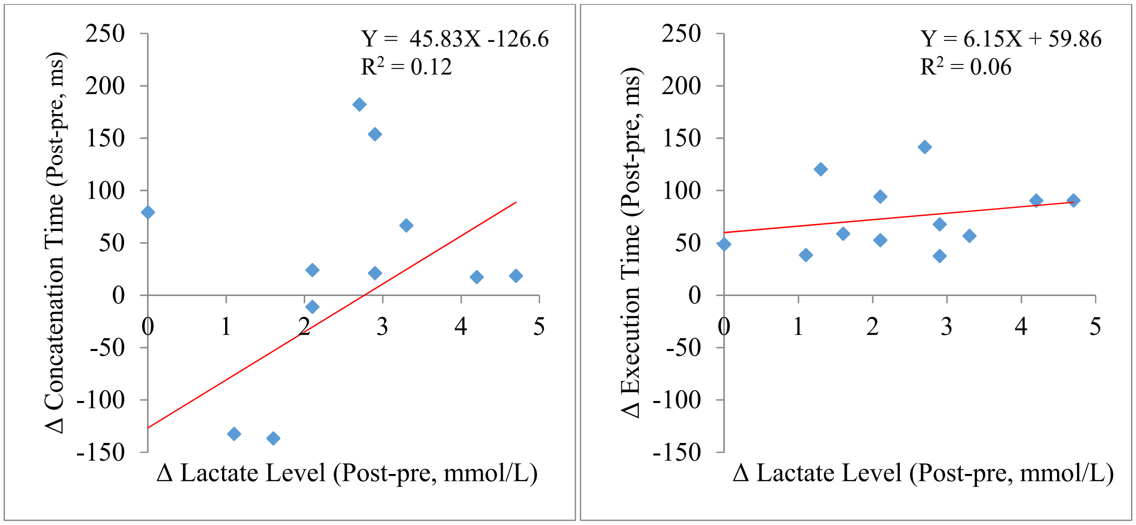

Figure 4. Continued.

To assess the association between the change in lactate level and memory improvement, the difference in lactate concentration from post to pre-exercise was correlated with the change in mean RT, IT, CT, and ET from Block 10 to test. In this case, a positive relationship implies less forgetting of the target DSP task as a result of a greater increase in lactate production during exercise. In order to address this issue, separate Pearson-product correlations were performed with changes in lactate level (Post-Pre) and the change in mean RT, IT, CT and ET from Block 10 to test (See Figure 4). These analyses revealed no significant relationship between the changes in lactate level and the change in mean RT ($R^2 = 0.17$, $p = 0.17$), mean IT ($R^2 = 0.03$, $p = 0.58$), mean CT ($R^2 = 0.12$, $p = 0.26$), and mean ET ($R^2 = 0.06$, $p = 0.43$).

We also explored the possibility that it is the absolute level of lactate at the time of consolidation (i.e., post-practice with target DSP task) that might be associated with the change in mean RT, IT, CT or ET. Separate Pearson-product correlations were conducted between absolute lactate levels at the end of exercise and the change is mean RT, IT, CT or ET (See Figure 5). These analyses failed to reveal significant correlations for mean RT ($R^2 = 0.17$, $p = 0.17$), mean IT ($R^2 = 0.08$, $p = 0.35$), mean CT ($R^2 = 0.23$, $p = 0.11$), and mean ET ($R^2 = 0.01$, $p = 0.74$).

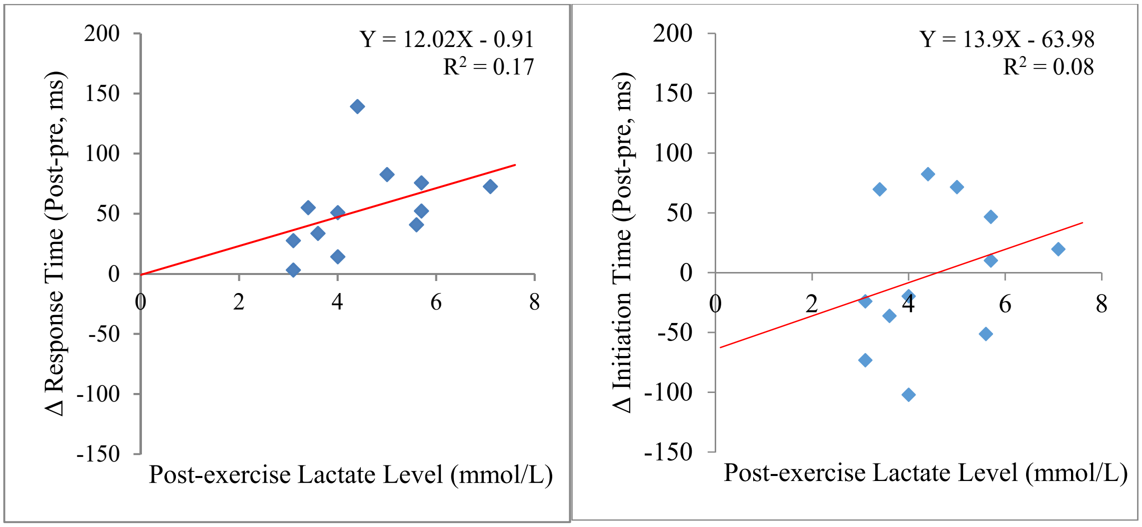

Figure 5. Correlations between post-exercise lactate level (mmol/L) and Δ response time (TT, IT, CT, and ET, ms) from block 10 to the test block.

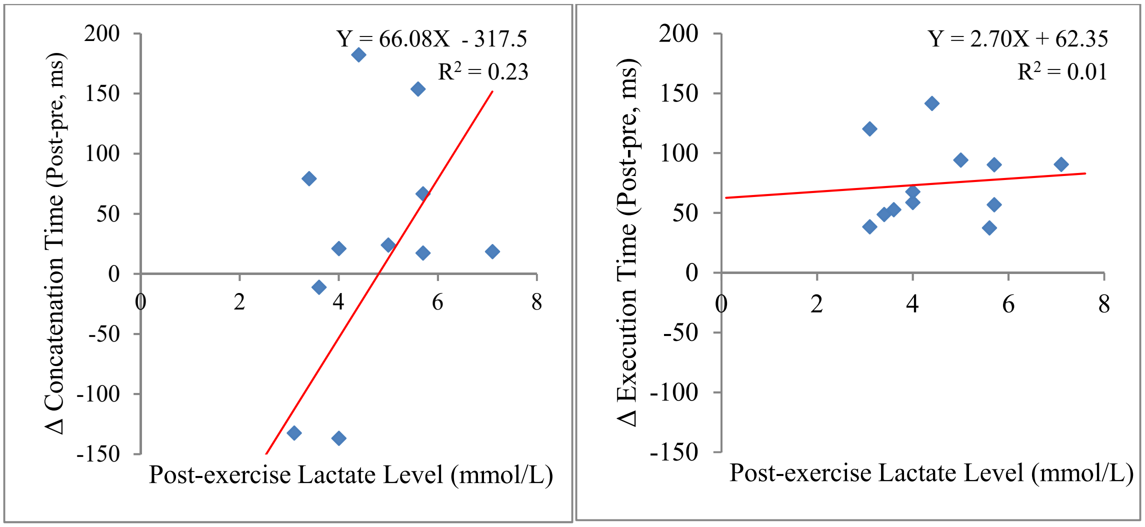

Figure 5. Continued.

CHAPTER IV

DISCUSSION

The present study was designed with a number of objectives in mind. First, and most importantly, it eliminated the inclusion of sleep between training and test of a discrete sequence production (DSP) task to assess the independent impact of an acute bout of exercise for procedural learning (see Figure 1). This was in contrast to Rhee et al. (2016), as well as others (e.g., Roig et al., 2012), that have reported exercise-mediated learning benefits but afforded participants the opportunity to sleep prior to test. Secondly, these exercise-mediated influence on the memory for a new motor skill was most likely localized to just a single of planning processes that was proposed as part of a contemporary theoretical account for the production of sequential actions (see Abrahamse, et al., 2013). Finally, a proposed relationship between the lactate concentration following exercise and procedural skill memory was also addressed. Each of these issues is discussed separately and in more detail in the following sections.

An Independent Role for Exercise in Protecting Newly Acquired Procedural Skills

The most critical feature of the present work was to isolate the unique role of an acute bout of physical activity as a means to facilitate offline consolidation processes that are central to successful procedural learning. There is ample evidence for the central role of post-practice consolidation for procedural learning. Consolidation has been characterized as a process by which a labile memory for a skill is made more resilient such that it is less susceptible to interference (Cantarero, Tang, O'Malley, Salas, &

Celnik, 2013; Krakauer & Shadmehr, 2006; Robertson, Pascual-Leone, & Miall, 2004) as well as provide the foundation for procedural skill enhancement through further enrichment via sleep (Diekelmann, Wilhelm, Wagner, & Born, 2013; Korman et al., 2007; Walker, Brakefield, Seidman, et al., 2003).

The behavioral paradigm adopted in the present experiment, in which additional practice with a novel skill is afforded in close temporal proximity to practice with the target motor skill, has been used extensively to delineate the important role played by post-practice consolidation. For example, Brashers-Krug, Shadmehr, and Bizzi (1996) had participants practice a directed-pointing task that involved rapid positioning of a force-producing manipulandum in a unique force environment. For some individuals, the pattern of forces apparent when moving the manipulandum during a second bout of training was opposed to the forces experienced throughout original training. Performance of the pointing skill in the initial force environment was reassessed 24-hr later. For the present discussion, it is important to note that the second bout of practice, in the presence of the novel force environment, occurred after different temporal delays for different subsets of participants. Subjects trained with short time intervals between practice bouts exhibited the most severe forgetting manifest as poor performance of the pointing skill in the initial force environment when tested next day. However, as the time between training sessions was increased, the impact of practice in the second force environment was reduced. Eventually, with the delay of greater than 4-hr between practice sessions, the second set of trials exerted little to no influence on the 24-hr delayed test performance of the pointing skill. The data of Brashers-Krug et al. (1996)

highlight the importance of memory consolidation processes that occur during brief time windows after procedural skill acquisition is completed (Brashers-Krug et al., 1996; Goedert & Willingham, 2002; Shadmehr & Holcomb, 1997; Walker, Brakefield, Hobson, et al., 2003).

Rhee et al. (2015) considered the possibility that the susceptibility of a newly acquired procedural skill, a DSP task, might be reduced if a brief bout of exercise was experienced after practice of the target skill but prior to experiencing practice with the novel DSP that was assumed would create interference. The theoretical rationale for this proposal was the claim that an acute bout of physical activity can support the upregulation of the consolidation process that begins immediately after a bout of practice. This claim emanates from work by Roig et al. (2012) who reported that the delayed retention of visuomotor tracking skill was enhanced when practice was followed by 15-min of high intensity interval exercise compared to a non-exercise control group. Rhee et al. revealed that a short, moderate-intensity bout of cycling provided some protection to new procedural learning. That is, the extent of retrograde interference for the target task from the practice with a novel motor sequence skill was significantly less when practice with the target sequence was immediately followed by physical activity.

Despite this outcome, for both Rhee et al. and others (Mang, Snow, Campbell, Ross, & Boyd, 2014; Roig et al., 2012; Skriver et al., 2014), the assertion that exercise has an independent or unique contribution to the memory for a procedural skill is marred by the inclusion of a period of sleep during the retention interval in these initial studies. This is because sleep has been reported to exert a powerful influence on consolidation and may well be necessary to allow the reported exercise-mediated effects to emerge (Walker et al., 2003).

This problem was circumvented in the present work by including a retention test after only 6-hrs thus removing sleep's contribution from an individual's test performance. In this case, when no interfering practice was experienced during the 6-hr interval it was anticipated that individuals would exhibit stabilization or minimal forgetting of the newly acquired DSP task at the time of test (Walker, Brakefield, Seidman, et al., 2003). In keeping with this prediction, the individuals in the CON condition displayed only a small loss in performance (~13%) for the target DSP task from the last block of acquisition to the time of test (see Figure 2). In contrast, participants in the INT condition suffered a much greater loss (~35%) across the same time frame presumably as a result of being exposed to the additional training with the novel DSP task. These data then are consistent with those noted earlier (Brashers-Krug et al., 1996; Rhee et al., 2015). The novel finding in the present study was the positive impact of performing a brief bout of aerobic exercise after initial training had on test performance. Specifically, the extent of forgetting for the EXE+INT condition (~23%), while not as low as that reported for the CON condition, but was significantly less than that observed for the INT condition.

Given that we eliminated any influence of sleep on post-practice processing, we are confident that the reduction in forgetting of the DSP task reported herein is a direct consequence of the acute bout of exercise to which the participants were privy in the EXE+INT condition. Congruent with Roig et al. (2013) and others, our supposition is that exercise expedites the employment of consolidation leading to more rapid stabilization of the initially labile memory for the target DSP task. This means that the newly formed memory establishes greater resiliency prior to being exposed to the new learning that otherwise would disrupt this process and expose the target DSP task memory to greater forgetting.

The exact manner by which consolidation governs this protective feature for the newly acquired motor skill at this point remains unexplained. However, there are a number of interesting proposals that demand some attention going forward. A current account focuses on the efficacy of exercise for changing the excitability of the primary motor cortex (M1) (Mang et al., 2014; Ostadan et al., 2016; Singh, Neva, & Staines, 2014). Activation of this neural site is particularly relevant to the present issue because M1 is viewed by many as a critical component of any neural network assumed to capture motor memory (Dayan & Cohen, 2011; Penhune & Steele, 2012). Moreover, recent experimental evidence has demonstrated that a larger elevation in M1 excitability shortly after practice is associated with increased offline gain of an implicitly learned motor sequence (Ostadan et al., 2016; Tunovic, Press, & Robertson, 2014). It is quite possible then that the positive impact of exercise in the present work was related to a modification of cortical excitability at M1 and the extent of excitation following exercise is a neural signature that can predict the extent to which the target DSP task will be protected from later practice that occurs in close temporal proximity (Cantarero, Lloyd, & Celnik, 2013).

It is critical to note that the present finding does not rule out the possibility that introducing sleep would not further complement the unique contribution of exercise demonstrated herein. Indeed, we have struggled to understand why, in at least two previous studies (Roig et al., 2012; Skriver, et al., 2014), that the inclusion of exercise following practice appears to have its most significant impact on procedural skill performance over sizeable time intervals between practice and test (i.e., 7-days). Indeed, it is after this longer retention period that skill enhancement, rather than just increased memory stabilization, is reported. These data do appear to suggest that there is an important interplay between exercise and sleep with respect to their influence on post-practice memory processes. While verifying the unique contribution from exercise to procedural skill acquisition in the current study is important, going forward, it is necessary to consider the potential interaction between sleep and exercise for optimizing the stabilization, enhancement, and/or retention of procedural knowledge.

An Acute Bout of Exercise Has a Limited rather than a Broad-based Impact of Delayed Sequence Production Performance

To isolate reasons as to how an acute bout of exercise provides protection to a newly acquired procedural skill, the present study utilized an 8-element DSP task that would be executed as two motor chunks (Abrahamse et al., 2013; Bottary, Sonni, Wright, & Spencer, 2016; Verwey & Eikelboom, 2003; Wright, Rhee, & Vaculin, 2010). The use of this type of DSP task allowed the assessment of three key planning processes that, according to recent theorizing regarding the production of sequential behaviors (Abrahamse et al., 2013), are crucial to improved execution of DSP tasks such as those performed in the current experiment. Specifically, Abrahamse et al. (2013) claim that an *initiation* process, indexed by the time to complete the first key-press, governs the selection and preparation of the sequential action including readying the initial motor chunk. Abrahamse et al. noted that a relatively slow key-press, typically observed in the middle of a motor sequence, captures the cost of *concatenating* motor chunks that comprise the motor sequence. Finally, a separate *execution* process indexes the time to implement the most primitive component (i.e., key-press) contained in a motor chunk.

One possibility was that given memory consolidation is pivotal for retrieval-related processes, we initially assumed that exposure to acute exercise would have a positive impact on concatenation and/or initiation processes rather than execution process (Abrahamse et al., 2013; Kuriyama et al., 2004; Wright et al., 2010). Alternatively, if exercise acts in a similar manner to sleep, the expectation was that only concatenation would be impacted because it has been revealed that improvement of the concatenation process is sleep-dependent (Bottary et al., 2016; Kuriyama et al., 2004). For example, Kuriyama et al. demonstrated that the transitions that were the slowest and most difficult at the conclusion of the training period demonstrated the largest benefit from sleep. Slower key transitions during motor sequence production have been interpreted as demarcations of the beginning of a motor chunk and reflect delays associated with the concatenation process (Abrahamse et al., 2013).

Despite this speculation, data from the present experiment was clear in revealing no exercise-dependent influence on the initiation and concatenation processes. In contrast, the data was congruent with the suggestions that the exercise-dependent memory benefits resulted from superior implementation of the execution process at the time of test. This finding is important for a couple of reasons. First, these data suggest that while exercise and sleep both positively influence consolidation, the manner in which consolidation fosters improved memory, is unique to each manipulation. If indeed sleep and exercise facilitate procedural skill memory in distinct ways, functionally, it would be prudent to examine how one can optimize the integration of exercise and sleep to ensure superior motor performance. These data also have theoretical ramifications because they provide further support for the independence of the concatenation and execution processes central to Abrahamse et al.'s (2013) three-process account for the production of sequential behaviors similar to the DSP task (Verwey & Dronkert, 1996; Verwey & Eikelboom, 2003).

Lactate Concentration Does Not Mediate the Protective Benefits of an Acute Bout of Exercise for Newly Acquired Procedural Skills

Given the emergence of studies demonstrating the impact of an acute bout of exercise has on learning and memory, there is considerable interest in evaluating if changes in the concentration of particular biomarkers (e.g., brain derived neurotrophic factor, insulin-like growth factor 1, epinephrine, norepinephrine, dopamine, and lactate) are related to changes in behavior (i.e., memory performance). One biomarker that has been the target of interest in early studies designed to address this issue is brain-derived neurotrophic factor (BDNF). BDNF is known to play a central role in numerous structural adaptations that are associated with the development of long-term memories (Skriver et al., 2014; Vivar, Potter, & van Praag, 2013). BDNF is temporarily increased following moderate to vigorous exercise and can remain elevated for some time.

However, despite the fact that BDNF can cross the blood-brain barrier, there is still considerable debate as to the impact of increased peripheral BDNF production following exercise for memory performance in humans (Skriver et al., 2014; Winter et al., 2007). To date, the data supporting the role of elevated BDNF for enhancing long-term memory is far from convincing (Knaepen et al., 2010).

While Skriver et al., (2014) found limited support for a relationship between higher concentration of BDNF following acute exercise at 1-hr and 7-day intervals, the best predictor of delayed performance of a visuomotor tracking task (see Roig, et al., 2012) was the peripheral concentration of lactate the end of practice. They argued that this benefit may have emerged because of the brain's preferred use of lactate as a source of energy which then facilitated cognitive processing (Rasmussen, Wyss, & Lundby, 2011; van Hall et al., 2009). In the present study, blood lactate was assessed both prior to and after the acute exercise bout. As expected, the concentration increased significantly (>100%) between these two time points. Despite this, the relationships between (a) the concentration of lactate post exercise and (b) the magnitude of change in lactate as a result of the acute exercise bout were not associated with any measure of the change in performance of the DSP task from the end of training to the test block (i.e., RT, IT, CT, or ET). Thus, peripheral lactate concentration appeared to exert little influence on the behavioral outcomes reported in the present work or more critically to any protective role of acute exercise for memory development.

There are however a number of differences in the work of Skriver et al. (2014) and the present study that may account for the observed discrepancy in outcomes. Four issues in particular are particularly noteworthy. The most glaring difference between these studies is the magnitude of the exercise-induced change in peripheral lactate concentration. Skriver et al. used an exercise protocol that was designed to induce a very high work intensity which is consistent with the reported 16-fold increase in lactate concentration immediately after the exercise was completed. In contrast, the present study adopted an exercise protocol that was congruent with that used by Rhee et al. (2015) which involved a relatively short bout of moderate intensity exercise resulting in only a twofold increase in lactate concentration at the end of exercise. It is quite possible that a threshold level of lactate must be surpassed in order to exert any mediating influence on subsequent memory processes and that threshold was not reached in the present work.

Secondly, the acute exercise in Skriver et al. was located prior to practice of the target motor skill as opposed to after as was the case in the present work. One could certainly envision how the different temporal location of exercise might change the resultant impact of lactate availability at key moments relative to memory development. Skriver et al. reported a relationship between lactate concentration for both acquisition rate and retention of the visuomotor skill. However, an elevated level of lactate induced just prior to practice failed to result in the exercise condition outperforming a no-exercise control condition during acquisition. Rather increased lactate production from exercise only enhanced performance of the visuomotor task during the delayed retention tests, a period when the lactate concentration presumably would have returned to resting levels. In the present experiment, lactate levels were increased when extensive task-related processing should be occurring (i.e., post-practice consolidation). Yet we were unable to observe any relationship between this and subsequent test performance. Clearly a more careful assessment of when and how much change occurs in lactate production relative to when training and test of the target motor behavior is assessed is critical to further understand the extant findings.

Thirdly, Skriver et al. used more extensive time delays to test the resilience of the memory for the visuomotor task than adopted in the present experiment. The association between lactate concentration immediately after exercise cessation and retention remained significant through 7-days. Obviously a noted goal of the present work was to eliminate the contribution of sleep to the behavioral outcomes that emerged thus precluding the use of lengthier retention intervals similar to those used by Skriver et al. Given that the retention intervals included overnight sleep, it's possible that the reported relationships between lactate levels and test performance may not be solely a function of exposure to exercise. Only one retention interval adopted by Skriver et al. (i.e., 1-hr) was devoid of sleep yet displayed the noted benefit for test performance from greater lactate availability. In the present experiment, after a 6-hr test interval, this relationship had dissipated. It is plausible that any facilitory influence of elevated lactate for memory performance is short-lived (i.e., less than 6-hr) and that the effects reported for the 1-and 7-delay test in Skriver et al. are associated with the presence of sleep during the retention interval. Clearly these issues warrant additional experimentation in the future.

Finally, one cannot ignore the different motor skills - visuomotor and DSP tasks - used in the two studies. It has been argued that different types of motor skills may be acquired in fundamentally different manners (Dayan & Cohen, 2011; Doyon et al., 2009; Penhune & Steele, 2012). Indeed, we noted in the introduction that at least part of the impetus for the work of Rhee et al. (2015) and the present study was to address the role of an acute bout of exercise for the retention for a motor sequence task because of its greater reliance on memory compared to tracking tasks. It is possible then that an elevation in peripheral lactate concentrations from exercise has no relationship to tasks that rely extensively on memory-related processes (i.e., consolidation). Rather this biomarker is more crucial in cases where perception-action coupling, critical for tracking tasks, is demanded. This is an interesting notion given the consolidation process (i.e., key motor memory processing) is most frequently assumed to be associated with neural activity at M1 whereas perceptual-motor integration has been linked to posterior parietal involvement suggesting that the influence of shifts in lactate production via exercise might have quite diverse consequences depending on the neural site central to the skill being learned.

CHAPTER V

CONCLUSIONS AND FUTURE DIRECTIONS

Conclusions

Clearly there is much to be done with respect to understanding how an acute bout of exercise protects a newly acquired procedural skill from subsequent interference. Nonetheless, the present study revealed the novel finding that a brief bout of moderate intensity exercise was sufficient to reduce the susceptibility of a newly acquired procedural skill to forgetting. Given the temporal location of the exercise, between practice with the target and alternative DSP task, the logical explanation is that the exercise positively impacts the engagement of consolidation immediately after practice with the target task (Roig et al., 2012; Mang et al., 2016). Consolidation has been described as a critical post-practice and has been associated with long-term potentiation which has been identified as the primary mechanism involving synaptic plasticity leading to long-term memory (Cantarero, et al., 2013).

A vital feature of the present study was the removal of sleep from the experimental design in order to verify that exercise per se contributes in an independent manner to later retention improvements. In doing so, the present study revealed that the exercise-mediated benefit was most likely a result of a more stable implementation of the execution process. This process has been identified as a key motor planning operation in a contemporary theoretical account for the implementation of a sequential behavior and responsible for producing the most primitive motor element in a motor chunk. Finally, data from the present work failed to support recent claims that part of the effectiveness of exercise for aiding motor skill performance is at the metabolic level. Specifically, Skriver et al. (2014) have proposed that, at least in part, the observed improvement in delayed skill retention following an acute bout of exercise is a result of the increased peripheral lactate concentrations that accompanies the physical workload experienced by the participant. No significant relationships between lactate production and delayed test performance emerged in the present study questioning the importance of lactate levels for improved procedural skill memory.

Future Directions

Detailing the boundary conditions for the efficacy of acute exercise for improved procedural skill is in its infancy. Starting from a more broad perspective, there are many functional issues that would be of interest to those interested in using exercise to facilitate motor activities in instructional and/or rehabilitation settings. An obvious target would be to delineate features of the exercise regime that provides the greater return in perceptual-motor acquisition and retention. For example, almost all of the work to date has focused on exercise that is cardiovascular in nature and is performed by an effector that is remote to that performing the skill (e.g., cycling while performing hand movements) (Roig et al., 2013; Taubert, Villringer, & Lehmann, 2015). Clearly there are other exercise modalities (rowing, running, etc. as well as resistive exercise) and numerous permutations (e.g., intensity, frequency, duration) that might be used to manipulate exercise volume. As discussed earlier, in relation to the importance of elevate peripheral lactate concentration following exercise, the issue of exercise intensity is certainly one that needs some attention in the near future as there has been examples of motor performance benefits from both moderate (Rhee et al., 2015; Statton et al., 2015) to vigorous protocols (Mang et al., 2014; Skriver, et al., 2013) despite the likelihood that these protocols have quite different consequences for lactate production as well as other potentially influential biomarkers (e.g., BDNF).

Fitness level of the participants is another component that will have to be considered in the next phase of experimentation that attempts to extent our understanding of the effectiveness of exercise for procedural learning. We speculated earlier, on the basis of work by Tunovic et al. (2014) and more recently Ostadan et al., (2016), that acute exercise may operate to amplify cortical excitability (particularly at M1) for a significant time period following the removal of the source of stimulation. Moreover, it has been demonstrated that greater excitation at M1 is associated with improvements in motor acquisition and retention (Reis et al., 2009; Singh, Neva, & Staines, 2016). Individuals with greater cardiovascular fitness have also been reported to exhibit a greater relative increase in M1 excitability in response to an exercise stimulus (Cirillo, Lavender, Ridding, & Semmler, 2009). Thus, it is possible, that individuals classified as high fit are more likely to display greater learning and memory benefits if indeed these outcomes are mediated by changes in M1 excitability. Unfortunately, we only had twelve individuals exposed to acute exercise in the present study and the range of fitness was quite small ($VO_{2\ max}$ ranged from 24.8 to 48 ml/min/kg). Nonetheless, a comparison of the memory loss for the three most fit individuals in this sample (Mean $VO_{2\ max}$ = 44.0 ml/min/kg) and the three least fit (Mean $VO_{2\ max}$ = 29.8 ml/min/kg) was conducted. While the outcome was not significant (F = 0.26, $p = 0.63$), the loss in performance from the end of training with the target DSP task to the test block was less for the individuals characterized as more fit.

Finally, there are numerous possibilities to further investigate system-level neuroscience questions related to the importance of changes in key neural sites from exposure to exercise that have previously been identified as central to procedural learning (Doyon et al., 2009; Hardwick, Rottschy, Miall, & Eickhoff, 2013). Clearly M1 has been the focus of this type of investigation to date (Mang, et al., 2014; Ostadan et al., 2016). However, in the near future it is very likely that the influence of exercise on sites remote from M1 (e.g., preSMA or SMA), and critical for skill learning, will be targeted. With the advent of a large array of non-invasive brain simulation tools, these questions can now be addressed while simultaneously demonstrating the expected behavioral outcomes that were the focus of this work and others who have initiated the examination of the role of acute exercise for procedural skill learning and memory.

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