

Lack of Effects of Acute Exercise Intensity on Mnemonic Discrimination

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Abstract

The hippocampus is thought to support episodic memory by pattern separation, thereby supporting the ability to discriminate high similarity items. Past research evaluating whether acute exercise can improve mnemonic discrimination of high similarity items is mixed. The present experiment attempts to extend these prior mixed findings by evaluating the effects of multiple exercise intensities on hippocampal-dependent, mnemonic discrimination and memory performance. Fifty-seven young adults completed a three-condition (control, moderate-intensity, and vigorous-intensity), within-subjects crossover pretest-posttest comparison. We observed no effects of acute exercise on recognition memory or mnemonic discrimination. We discuss the implications of these null findings with the broader literature by discussing the complexity of this potential exercise-mnemonic discrimination relationship, including the unique role of exercise intensity, differences in the level of processing (e.g., conceptual v perceptual) and unique brain regions involved in mnemonic discrimination.

Keywords: aerobic exercise; cognition; physical activity; recognition memory

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Interest in the effects of acute exercise on cognition has rapidly increased over the last several decades (Brisswalter, Collardeau, & Rene, 2002; Chang, Labban, Gapin, & Etnier, 2012; Gomez-Pinilla & Hillman, 2013; Lambourne & Tomporowski, 2010; Tomporowski, 2003; Tomporowski, Ellis, & Stephens, 1987). This accumulating body of work demonstrates that moderate-intensity acute exercise may improve prefrontal cortex-dependent higher-order cognition (Chang, Labban, Gapin, & Etnier, 2012), whereas high-intensity acute exercise may improve lower-order cognition, such as simple and choice reaction time tasks (McMorris, 2016). Research within this area has also started to exclusively focus on memory function (Roig, Nordbrandt, Geertsen, & Nielsen, 2013). This body of research demonstrates that, among young adults, acute exercise, particularly high-intensity exercise, may improve memory function (Loprinzi et al., 2019), but see other work for conflicting findings regarding intensity-specific effects of acute exercise on memory (Marchant, Hampson, Finnigan, Marrin, & Thorley, 2020). Findings, however, are not consistent across the literature, as some work suggests that high-intensity acute exercise improves prefrontal cortex-dependent cognition but not hippocampal-dependent memory (Basso, Shang, Elman, Karmouta, & Suzuki, 2015). Here we investigate the potential effects of acute exercise on hippocampal-dependent episodic memory function (Eichenbaum, Yonelinas, & Ranganath, 2007).

In a comprehensive review, El-Sayes et al. (2019) discussed potential mechanisms through which acute (and chronic) exercise may improve memory via neural plasticity. Acute exercise may induce molecular changes, including an increase in vascular endothelial growth factor and brain-derived neurotrophic factor. Assuming enough time has elapsed between the bout of exercise and the memory task, these changes may lead to functional responses (e.g., increased blood flow, glucose and oxygen metabolism, neurotransmitter release, neural/receptor

activity), ultimately leading to behavioral improvements (e.g., improved cognition). These effects, but specific to hippocampal-dependent long-term potentiation and episodic memory, have been discussed in detail elsewhere (Moore & Loprinzi, 2021). For example, ample research demonstrates that chronic exercise-induced neurogenesis contributes to enhanced memory performance (Voss et al., 2019). At shorter timescales, these mechanisms are unlikely accounts of behavioral effects. When there is a relatively short timescale (e.g., within minutes) between exercise and the memory task, it has been hypothesized that acute exercise may influence memory via increased neural activity in the hippocampus (Loprinzi, Ponce, & Frith, 2018). For example, in an immobilized dog model, prior work evaluating the Afferentation Theory of Cerebral Arousal demonstrates that pharmaceutical (succinylcholine¹) activation of the muscle spindles increases cerebral activation within minutes (Lanier, Iaizzo, & Milde, 1989, 1990; Lanier, Milde, & Michenfelder, 1986). It is likely that similar effects would be observed with acute exercise in humans, as muscular contraction of the extrafusal fibers would – similar to direct activation by select drugs – activate the muscle spindles to produce increases in muscle afferent activity.

Although acute exercise can modulate these aforementioned mechanisms (El-Sayes, Harasym, Turco, Locke, & Nelson, 2019) and improve episodic memory performance (Loprinzi et al., 2019; Roig, Nordbrandt, Geertsen, & Nielsen, 2013), at this point, an interesting, underexplored possibility is that acute exercise might improve episodic memory by facilitating the discrimination of high similarity items (Cowell, Barense, & Sadiq, 2019; Cowell, Bussey, & Saksida, 2010; Forwood, Cowell, Bussey, & Saksida, 2012). Similar, or overlapping stimuli,

¹ Intravenous administration of the depolarizing neuromuscular relaxant, succinylcholine, is thought to act on receptors of the muscle spindle. Once activated, the muscle afferents are transmitted by the peripheral nerves to the dorsal spinal cord, ultimately reaching the brain to induce cerebral activation.

present a major challenge to memory. A recent review (Li, Liu, Li, & Zhou, 2020) demonstrated that chronic exercise is effective in discriminating high similarity items, possibly via increasing neurogenesis and neurotransmitter-induced synaptic plasticity. However, the effect of acute exercise, too fast for such mechanisms, on such visual discrimination is less consistent (Crawford & Loprinzi, 2019).

The majority of studies evaluating the effects of acute exercise on visual discrimination of items or episodes have used paradigms, such as the Rey-Auditory Verbal Learning Test (RAVLT) (Haynes IV & Loprinzi, 2019) and the AB/AC learning task (Crawford & Loprinzi, 2019; Crawford, Caplan, & Loprinzi, 2021), which may be less sensitive to exercise-related modulation of the discrimination of high similarity items (Crawford, Li, Zou, Wei, & Loprinzi, 2020). The RAVLT involves learning one list of words, followed by learning a second list of words. Recall of the second list may be impaired due to memory of the first list. However, the RAVLT procedure does not typically include a non-interference condition. The standard AB/AC task, unlike the RAVLT, is built upon a paired-associate learning procedure which appears to be hippocampal-dependent (Caplan, Hennies, & Sommer, 2022; Caplan & Madan, 2016), including, for example, learning one set of paired words (AB), followed by learning a second set of paired words that have overlapping cue words (AC) (e.g, AB = Dog-Happy; AC = Dog-Tree). The inclusion of control word pairs (DE, FG) can allow for both proactive (AC-FG) and retroactive interference (AB-DE) to be measured simultaneously. However, this task does not always consistently induce both proactive and retroactive memory interference (Crawford, Caplan, & Loprinzi, 2021), as the direct competition between AB and AC in the AB/AC paradigm is largely resolved by participants by the time memory is measured (Burton, Lek, & Caplan, 2017; Caplan, Hennies, & Sommer, 2022; Caplan, Rehani, & Andrews, 2014). These findings weaken the

evidence that exercise influences all functions of the hippocampus and medial temporal regions similarly.

Stark et al. (2013) developed a mnemonic similarity/discrimination task that involves studying a series of items (images), and then at test, repeating old items and including new items that are similar (similar lure) and different (foil) from the old items (example stimuli shown in Figure 1). They demonstrated an age-associated decline in the discrimination of high similarity items and also showed worse discrimination among those with mild cognitive impairment when compared to age-matched controls. Utilization of such a memory task will improve our ability to determine the extent to which acute exercise may influence hippocampal-dependent memory.

More specifically, this mnemonic similarity task activates key memory-related brain structures (e.g., hippocampus) involved in discrimination of high similarity items via pattern separation² (Cowell, Barense, & Sadil, 2019; Cowell, Bussey, & Saksida, 2010; Forwood, Cowell, Bussey, & Saksida, 2012);³ areas of the brain that are also highly sensitive to exercise engagement. Specifically, using this task, the correct discrimination of similar lures (i.e., new items at test that were not presented at study but are similar to a studied item) engages the CA3/dentate gyrus (Kirwan & Stark, 2007; Yassa et al., 2011; Yassa, Mattfeld, Stark, & Stark, 2011), is associated with the volume of the hippocampus (Stark & Stark, 2017), is sensitive to pharmacological manipulation of the hippocampus in amnesic mild cognitive impairment patients (Bakker et al., 2012), declines with age (Toner, Pirogovsky, Kirwan, & Gilbert, 2009), is a sensitive marker for detection of early memory impairment (Pishdadian, Hoang, Baker, Moscovitch, & Rosenbaum, 2020; Stark, Yassa, Lacy, & Stark, 2013), is robust to task variations

² Pattern separation defined here as the ability to discriminate similar (or overlapping) representations.

³ We retain the use of this label, but remain agnostic as to this being the mechanism of visual discrimination of high similarity items.

and practice effects (Stark, Stevenson, Wu, Rutledge, & Stark, 2015), and is sensitive to changes in aerobic fitness (Dery et al., 2013; Heisz et al., 2017; Nauer, Dunne, Stern, Storer, & Schon, 2020; Nauer, Schon, & Stern, 2020) and a 10-minute bout of acute moderate-intensity exercise (Suwabe et al., 2017). Regarding the latter, acute exercise may help facilitate mnemonic discrimination via anti-inflammatory processes (e.g., altering intermediate counts of monocytes) (Pena, Callow, Evans, Prior, & Smith, 2022).

The present experiment aims to evaluate the effects of acute exercise on mnemonic discrimination. Several studies have evaluated this topic, which are outlined below. Suwabe et al. (2017) had participants either rest or engage in a 10-min bout of moderate-intensity exercise, followed by an encoding phase of a mnemonic similarity task (MST), and then rested for 45-min before completing the retrieval MST. Their findings demonstrated that exercise helped participants discriminate between highly similar items, implying that exercise facilitated mnemonic discrimination. In a follow-up experiment, they demonstrated that 10 minutes of acute light-intensity exercise was effective in increasing pattern separation in the hippocampus (for both high and moderate similarity lures), increased functional connectivity between the hippocampus and various cortical areas, and also improved mnemonic discrimination when the encoding and retrieval tasks were employed within 5 minutes after acute light-intensity exercise (Suwabe et al., 2018). This exercise-related functional connectivity was associated with improved memory performance.

Some beneficial effects have also been observed in older adults. Callow et al. (2023) had older adults complete a baseline MST, then either exercise (moderate-intensity) or rest for 30 minutes, and then completed another MST. In their initial analysis, they did not demonstrate a main effect for condition, but did show a condition by time interaction, with no pre-post changes

in mnemonic discrimination from exercise but a significant decline in mnemonic discrimination with rest. Thus, acute exercise did not influence mnemonic discrimination, but rather, a decline in mnemonic discrimination occurred with a period of rest. When focusing on the post-data only (not pre-post changes), they observed higher mnemonic discrimination after exercise compared to after rest. Using a similar design in older adults, Pena et al. (2022) showed that, with their post-data, there was a higher mnemonic discrimination after moderate-to-vigorous exercise compared to after rest.

Using a between-subject, posttest design, Acevedo-Triana et al. (2021) had young adult participants either engage in 10 minutes or 20 minutes of moderate-intensity exercise, or a rest condition. Following this, they completed the MST, with retrieval occurring 45 minutes, 24 hours, 48 hours, and 160 hours later. Their results showed that acute exercise was only associated with mnemonic discrimination for low similarity lures and this effect occurred after 45 minutes of encoding but disappeared after 24-hours. Finally, in a relatively young sample ($M_{\text{age}} = 31$ years), Bernstein and McNally (2019) observed no effects of 30 minutes of moderate-intensity acute exercise on mnemonic discrimination when employing a crossover pretest posttest design with no break between encoding and retrieval.

Collectively, these aforementioned studies evaluating the effects of acute exercise on mnemonic discrimination are mixed. Some have observed a beneficial effect of acute exercise on mnemonic discrimination, but only with their posttest data or for either low/moderate/high similarity lures, while others observed no effects. These mixed findings underscore the importance of additional work on this topic. From these results, which included short (e.g., < 5 minutes) and longer retention intervals (e.g., 45+ minutes), there is some evidence that acute exercise can influence mnemonic discrimination potentially via encoding and perhaps

consolidation or offline transformation processes, but not retrieval (at least not directly). Thus, we see two possible mechanisms that could explain these sets of results. First, acute exercise might have facilitated encoding processes. Second, acute exercise might have facilitated (long-lasting) long-term potentiation (LTP), and a longer delay (e.g., 45-minute) may be necessary; generally, at least 30-min is necessary for synaptic plasticity mechanisms to be attributed to LTP as opposed to short-term potentiation (Schulz & Fitzgibbons, 1997). To decide between these mechanisms (which might also both coexist given the prior results showing an effect with both shorter and longer retention intervals), we eliminated the longer retention interval. Specifically, the present experiment implements a within-subjects crossover pretest-posttest comparison involving no retention interval, including the encoding and test phases occurring both before and after each experimental condition (control, moderate-intensity, vigorous-intensity). Thus, if the effect of acute exercise is found in the present study (supporting the findings of Suwabe et al., 2018, and also partially supported by Callow et al. 2023, and Pena et al., 2022), this would suggest either that exercise modulates similarity discrimination quite generally or by influencing short-term as well as long-term plasticity. If the effect of exercise on similarity discrimination is not found in the present study (supporting the findings of Bernstein and McNally, 2019, and also partially supported by the findings of Callow et al., 2023), the mechanism may more influenced by the late phase of LTP. Unlike the prior studies, we also sought to evaluate if there was an intensity-specific effect by employing multiple exercise intensities.

Similar to Callow et al. (2023), Pena et al. (2022), and Bernstein and McNally (2019), but in contrast to that of Suwabe et al. (2017, 2018) and Acevedo-Triana et al. (2021), the present experiment employed a within-subject pretest posttest design. This was done to allow for a time-efficient pretest-posttest design, which is a stronger causal design than a posttest-only design

(Pontifex et al., 2019). Further, implementing the study and test phases close together would allow exercise to impact processes related to both encoding and retrieval, ultimately increasing the likelihood of observing an exercise effect on memory. However, we recognize that reducing the length between the pretest and posttest may influence potential time-dependent hippocampal dependencies, research demonstrates that – in a design similar to that employed in the present study (no break between study and test) – neural activity within the hippocampus was associated with behavioral pattern separation performance (Kirwan & Stark, 2007). Relatedly, in accordance with Representational Hierarchical Theory (Cowell, Barense, & Sadiq, 2019; Forwood, Cowell, Bussey, & Saksida, 2012), regions within the medial temporal lobe are responsible for discrimination of high similarity items, irrespective of the time scale. For example, this model suggests a hierarchical organization of information within the MTL. Representations of simple visual features (e.g., color, shape) may be contained in the posterior region, whereas such features are conjoined (e.g., color, shape, and size of an object are perceptually combined to create the representation of the whole object) in the anterior brain region; these conjunctive representations may be critical when the simple features are insufficient in aiding in the discrimination of related objects.

Couched within the above, the present experiment employs a pretest-posttest within-subject design to evaluate the potential intensity-specific effects of acute exercise on putative hippocampal-dependent memory and mnemonic discrimination. Although past work has suggested an intensity-dependent effect of acute exercise on memory (Loprinzi, 2018), with high-intensity acute exercise having a greater effect on enhancing episodic memory (Loprinzi et al., 2019), additional research is needed to determine the optimal exercise intensity to induce mnemonic discrimination. We anticipate that higher-intensity acute exercise, when compared to

moderate-intensity exercise and a seated rest condition, will be optimal in behavioral performance on the mnemonic similarity task. We hypothesize this intensity-dependent effect because (1) past work shows that high-intensity acute exercise benefits episodic memory more than moderate-intensity acute exercise and (2) both the amplitude and frequency of exercise-induced neural activity in the hippocampus are closely related with the speed of locomotion (Ahmed & Mehta, 2012).

Methods

Participant Recruitment. Participant recruitment occurred via a convenience, non-random sampling approach; participants were recruited from undergraduate and graduate courses at the University of Mississippi. Fifty-seven participants (35 female) comprised the sample; this was based on recruiting a sample size comparable to – or higher than – other related work on this topic; e.g., N of 21 by Suwabe et al (2017). Further, Bayes factors are reported to evaluate whether any observed null effects are underpowered versus evidence in favor of the null, as well as to evaluate the robustness of non-null effects (Kass & Raftery, 1995).

Eligibility Criteria. Due to potential confounding effects on memory, participants were excluded if they (1) self-reported as a daily smoker; (2) self-reported being pregnant; (3) exercised within five hours of testing; (4) consumed caffeine within six hours of testing; (5) took medications used to regulate emotion (e.g., SSRI's); (6) had a concussion or head trauma within the past 30 days; (7) took marijuana or other mind-altering drugs within the past two days; (8) were considered a daily alcohol user (> 30 drinks/month for women; > 60 drinks/month for men) or consumed alcohol in the past 12 hours, (9) were diagnosed with COVID-19 within two weeks of testing, (10) outside the age range of 18-35 years, (11) had a current diagnosis of a psychological disorder, (12) been diagnosed with a learning disorder, or (13) answered “yes” to

any of the seven questions on the Physical Activity Readiness Questionnaire (PAR-Q), suggesting that medical clearance is needed before exercise participation.

Study Design and Procedures. The present experiment included a three-condition (Control, Moderate-intensity, Vigorous-intensity), within-subjects crossover pretest posttest comparison. With multiple within-subject conditions, there is a possibility that the order in which the conditions occurred (even with randomization and counterbalancing) could confound the results. We did not, however, observe an order*condition*time interaction with mnemonic discrimination as the dependent variable ($F(4, 108) = 1.42, p = 0.234$), ultimately reducing this potential concern.

Allocation concealment occurred by both the researcher and participant not knowing which condition the participant would complete until arriving in the lab.

The first visit included a maximal treadmill-based exercise protocol. During this first visit, participants were familiarized to the memory task (i.e., 4 encoding items and 8 retrieval items, different from the experimental task sets, to ensure they understood the task instructions and procedures) and completed a maximal exercise test to determine their maximal heart rate, which was used to set the exercise intensity for the Moderate-intensity and Vigorous-intensity conditions.

Visits 2-4 (Control (A), Moderate-Intensity (B), Vigorous-Intensity (C)) occurred in a counterbalanced order, including 6 possible counterbalanced orders (ABC, ACB, BAC, BCA, CAB, CBA), with at least 9 participants in each of the 6 counterbalanced orders; the selection of which counterbalanced order was randomized (via computer algorithm) across participants (e.g., Participant 1 = BCA; Participant 2 = CAB, etc.).

Each of the three conditions (Control, Moderate-intensity, Vigorous-intensity) involved the completion of two unique memory tasks (pretest and posttest), totaling 6 memory tests (pretest and posttest for the three conditions). Each of the 6 memory tests included a unique set of matched stimuli. The use of the two unique memory tests for each session were randomly selected. Further, the order of the stimuli (at both study and test phases), within each memory set, were randomized for each participant.

The three conditions (Control, Moderate-intensity, Vigorous-intensity), occurring around the same time of day, occurred 24-72 hours apart. This wash-out period (24-72 hours) was chosen for several reasons; this should be of sufficient duration to allow for recovery from exercise, should be short enough so all three visits could be completed in a reasonable time frame, and not too far apart where re-familiarization training may be needed.

Participants complete 25-minutes of the randomly selected condition; this was either 25-minutes of the Control condition, 20-minutes of Moderate-intensity exercise followed by five minutes of rest, or 20-minutes of Vigorous-intensity exercise followed by five minutes of rest. Immediately before (pretest) and immediately after (posttest) this 25-minute period, participants completed a mnemonic similarity task.

Maximal Exercise Visit (1st session). The first laboratory visit included a maximal treadmill-based assessment. The specific assessment included an individualized protocol (Mier & Gibson, 2004). Participants warmed-up for 3 minutes by walking at 3.5 miles per hour. Following this, they engaged in a constant speed throughout the test while the grade increased by 2% every 2 minutes. After the warm-up period, the speed was set, and remained, at 5.5 mph, for the entire exercise protocol. The test terminated when participants reached exhaustion or after 20

minutes, whichever came first. During the maximal treadmill test, heart rate (HR) was monitored throughout the test (H10 Polar Monitor).

Control, Moderate-intensity Exercise, Vigorous-intensity Exercise. The Control condition involved a time-matched (25-min) cognitive engagement task (The Office bloopers). There is experimental evidence suggesting that this type of control task (video viewing) does not prime or enhance memory function (Blough & Loprinzi, 2019). The video was watched without sound to induce a low stimulus condition. To maintain the same context and posture, this Control condition involved the participant watching the video while standing on the treadmill; a monitor was placed in front of the treadmill for the participant to view the video.

The two exercise conditions involved treadmill exercise for 20 minutes; all participants were instructed that they would exercise for 20 minutes and none stopped prematurely. Following this 20-minute bout of exercise was 5 minutes of rest (standing on the treadmill); this 5-minute rest period is the same duration used by Suwabe et al. (2017). During the 20-minute exercise and 5-minute rest periods, participants had a video (sound off; The Office bloopers) placed in front of the treadmill to match the context of the Control condition.

Using the participant's maximal heart rate achieved during their maximal exercise bout (visit 1), participants exercised at 50% of their HR reserve for the Moderate-intensity condition and 80% of their HR reserve for the Vigorous-intensity condition (Garber et al., 2011). Heart rate reserve was calculated as $[(HR_{\max} - HR_{\text{rest}}) * \% \text{ target intensity}] + HR_{\text{rest}}$. The resting heart rate measurement (before exercise) occurred after resting quietly for five minutes. The treadmill speed/incline was manipulated to achieve the desired heart rate. At baseline, throughout the acute exercise bout (every 5 minutes), and at 5-minutes post-exercise, heart rate was assessed.

Due to concerns with COVID-19, during the entire experimental session (exercise and cognitive testing), participants wore a facemask that they brought with them (usually a cloth facemask). We anticipate that this had minimal effects on the data. For example, even during or after walking exercise, wearing a mask does not appear to influence mood or cognitive performance (Caretto, 1999). Similar findings have been shown for light-intensity cycling (Morris, Piil, Christiansen, Flouris, & Nybo, 2020). Further, even during high-intensity exercise, wearing a facemask does not appear to induce meaningful effects on the work of breathing, blood gases, and other physiological parameters (Hopkins et al., 2020).

Mnemonic Similarity Task. The mnemonic similarity task involved the same stimuli and procedures as discussed elsewhere (Stark, Yassa, Lacy, & Stark, 2013); using the developed task by Craig Stark, we used version 0.96, including sets 1-6 within the software.

Participants viewed (on a computer screen) 128 color photographs of everyday objects. Each object appeared on the screen for 2 seconds (0.5-sec ISI) and involved an orienting judgement (whether the object is an indoor or outdoor object); these parameters (i.e., stimulus duration, ISI, and orienting judgement) are consistent with work that has demonstrated an exercise-induced effect on this memory task (Suwabe et al., 2017). Immediately following each study phase, participants commenced the test phase, including viewing 192 items, one at a time. This included 64 repeated/old items, 64 similar lure items and 64 foil items. For each item, participants indicated if the item was “Old”, “Similar”, or “New” via button presses. One-third of the images in the test were exact repetitions of the images viewed in the study phase (target); one-third were new images not previously seen (foil); and one-third were images that are similar to those seen during the study phase, but not identical (similar lures). See Figure 1 for an illustration of these response options and item types.

Primary memory outcomes include: (1) Item Recognition [$p(\text{Old} | \text{Target}) - p(\text{Old} | \text{Foil})$] and (2) Mnemonic Discrimination [$p(\text{Similar} | \text{Lure}) - p(\text{Similar} | \text{Foil})$]. This mnemonic discrimination score is interpreted as the difference between the rate of “similar” responses given to the similar lure items minus “similar” responses given to the foils (in order to correct for response bias). This mnemonic discrimination index is associated with age-related changes in input to and within hippocampal subfields (dentate gyrus and CA3), as well as hippocampal-dependent memory performance (Yassa, Mattfeld, Stark, & Stark, 2011). Consequently, this test and its associated mnemonic discrimination score is appropriate for evaluating putative hippocampal pattern separation.

Other reported outcomes (see supplementary file) include the individual probabilities of responding “Old”, “Similar”, and “New” to target, similar lure, and foil items.

Analyses. For item recognition and mnemonic discrimination, a 3 (*Condition*: Control, Moderate-Intensity, Vigorous-Intensity) \times 2 (*Time*: Pre, Post) rmANOVA (repeated measures analysis of variance) was employed. When sphericity was violated, Huynh-Feldt sphericity correction was employed. Holm-corrected post-hoc tests were employed to evaluate significant main and interaction effects. Statistical significance was set at an alpha of 0.05. Notably, based on a sensitivity power analysis,⁴ with inputs an α of 0.05, power of 0.80, 57 participants, 3 conditions, 2 measurements per condition,⁵ and an assumed repeated measures correlation of 0.50, we were powered to detect a small-to-medium effect (effect size f of 0.138; small effect = 0.10 and medium effect = 0.25; to convert F to $\eta_p^2 = F^2 / (1 + F^2)$). Frequentist analyses were supplemented with Bayesian analyses, with these analyses computed in JASP (v .16). The

⁴ In G*Power, Test Family is “F tests”, Statistical Test is “ANOVA: Repeated measures, within factors”, and Type of Power Analysis is “Sensitivity: Compute required effect size – given α , power, and sample size.”

⁵ In the sensitivity power analysis in G*Power, this is entered as 1 for “Number of Groups” and 6 for “Number of Measurements.”

inclusion Bayes factor (BF) is reported,⁶ with BFs between 1 and 3 being anecdotal and > 3 indicating moderate evidence in favor of the alternative (v null) hypothesis, whereas BFs between 1 and 0.33 being anecdotal and $< .33$ indicating moderate evidence in favor of the null (v alternative) hypothesis (Kass & Raftery, 1995). These analyses were computed in JASP using its point-and-click menu system, but the means and analyses can be computationally reproduced using the source code for SPSS provided in the supplementary file. Data and materials are available at <https://osf.io/gj8he/>.

Results

Table 1 displays the demographic and behavioral characteristics of the sample. The participants, on average, were 21 (SD = 1.5) years of age (range = 18-27), predominately female (61%), and regularly physical activity (165 min/week of moderate-to-vigorous intensity physical activity).

Table 1. Demographic, behavioral, and performance characteristics of the sample (N = 57).

Variable	Mean	SD	Range
Age, mean years	20.6	1.5	18-27
Gender, % Female	61.4		
Measured body mass index, mean kg/m ²	24.3	5.0	17.2-44.8
Physical activity, mean min/week of MVPA	173.3	120.6	0-450
Duration lasted on maximal treadmill test, mean sec	734.2	266.6	109-1200

MVPA, Moderate-to-vigorous physical activity, assessed from the two item Physical Activity Vital Sign questionnaire (Ball, Joy, Gren, & Shaw, 2016).

Table 2 displays the memory recognition results. As shown below, all of the effects, with the exception of a main effect for time, demonstrated evidence toward the null hypothesis.

⁶ Order: compared to null model; Effects: across matched models.

Item Recognition. There was no main effect for condition, $F(2, 112) = 1.24, p = .293, \eta^2 = .01$, $BF = .19$, time, $F(1, 56) = 2.03, p = .160, \eta^2 = .006, BF = .25$, or condition by time interaction, $F(2, 112) = .57, p = .568, \eta^2 = .002, BF = .08$.

Mnemonic Discrimination. There was no main effect for condition, $F(1.86, 104.14) = .34, p = .699, \eta^2 = .003, BF = .05$, or condition by time interaction, $F(2, 112) = 1.99, p = .142, \eta^2 = .009, BF = .18$, but there was a main effect for time, $F(1, 56) = 8.53, p = .005, \eta^2 = .02, BF = 2.96$.

Regarding the main effect for time, pre scores were higher than post scores, $M_{diff} = .03, t = 2.92, p = .005, BF = 9.05$.

Table 2. Memory recognition results expressed as proportions (SD).

	Control		Moderate		Vigorous	
	Pre	Post	Pre	Post	Pre	Post
Old Target	.84 (.11)	.84 (.13)	.84 (.12)	.83 (.13)	.86 (.11)	.87 (.10)
Similar Target	.11 (.07)	.11 (.09)	.11 (.09)	.11 (.10)	.09 (.08)	.09 (.08)
New Target	.06 (.06)	.05 (.07)	.05 (.07)	.06 (.09)	.05 (.06)	.04 (.06)
Old Similar Lure	.32 (.15)	.31 (.17)	.30 (.14)	.32 (.14)	.33 (.14)	.33 (.15)
Similar Similar Lure	.58 (.18)	.59 (.19)	.60 (.18)	.57 (.18)	.58 (.17)	.58 (.19)
New Similar Lure	.11 (.08)	.10 (.08)	.10 (.08)	.12 (.12)	.09 (.08)	.10 (.09)
Old Foil	.03 (.06)	.04 (.06)	.04 (.07)	.04 (.07)	.05 (.07)	.05 (.08)
Similar Foil	.09 (.12)	.11 (.12)	.08 (.06)	.10 (.08)	.09 (.09)	.10 (.07)
New Foil	.88 (.14)	.84 (.15)	.89 (.11)	.86 (.11)	.87 (.15)	.85 (.12)
Item Recognition	.81 (.14)	.79 (.16)	.81 (.16)	.79 (.17)	.82 (.13)	.82 (.15)
Mnemonic Discrimination	.49 (.25)	.48 (.25)	.52 (.20)	.47 (.19)	.50 (.21)	.48 (.20)

Item Recognition, calculated as (Old | Target) – (Old | Foil)

Mnemonic discrimination, calculated as (Similar | Lure) – (Similar | Foil)

Given that the findings for Suwabe et al. were only significant for moderate/high-similarity lures and significant only for low-similarity lures for Acevedo-Triana et al. (2021), we computed a sensitivity analysis by categorizing the images based on how similar they were to the

target, using the 5 lure bins (most similar to least similar) described elsewhere (Stark, Kirwan, & Stark, 2019); a 3 (condition) \times 2 (time) \times 5 (lure bins) linear mixed model demonstrated no three-way interaction for mnemonic discrimination ($p(\text{similar} \mid \text{lure}) - p(\text{similar} \mid \text{foil})$), $F(8, 1470.25) = 1.14$, $p = .334$, and similarly, no condition by similar lure bin interaction, $F(8, 1470.25) = .34$, $p = .950$.; additional results can be found in the supplementary file. Thus, our findings that acute exercise are not associated with mnemonic discrimination do not appear to be influenced by the similarity level of the similar lures.

Discussion

Accumulating research has demonstrated that acute exercise can improve episodic memory performance (Loprinzi et al., 2019; Roig, Nordbrandt, Geertsen, & Nielsen, 2013). The proposed mechanisms of this effect are thought to include a range of explanations, such as enhanced attention during encoding, altered neurotransmitters (e.g., norepinephrine, dopamine) to augment memory consolidation, executive control processes to facilitate item retrieval (Loprinzi, Roig, Etnier, Tomporowski, & Voss, 2021), as well as longer timescale processes such as long-term potentiation and protein synthesis (Loprinzi, Edwards, & Frith, 2017; Loprinzi, Ponce, & Frith, 2018). Recent theoretical work has suggested that acute exercise may specifically improve memory by improving visual discrimination (Crawford, Li, Zou, Wei, & Loprinzi, 2020). The present study was conducted to evaluate if acute exercise can improve memory by mnemonic discrimination of highly similar items in young adults. If the positive effects of acute exercise on mnemonic discrimination depend on slow processes, we would not expect to observe an effect of acute exercise on mnemonic discrimination with our design. If instead, the effects result from facilitation of cognitive processes or immediate effects on activity or neuromodulation, we would expect to find that acute exercise improves visual discrimination

with our procedure. The main findings of this experiment were twofold: (a) the employed memory task caused participants to confuse studied items with new similar lure items (i.e., responded “old” to new similar lure items), and at a relatively high rate (30-33%); and (b) despite this effect of creating memory confusion between studied and new similar lures, acute exercise, regardless of exercise intensity (i.e., moderate or vigorous), was not effective in enhancing recognition memory or facilitating mnemonic discrimination.

The null results from our experiment are in accordance with the work by Bernstein and McNally (2019) and also in partial support of the work by Callow et al. (2023) who only observed an effect of acute exercise on mnemonic discrimination when restricting their analyses to the post-assessment data. Thus, our findings replicate other findings that fail to observe an effect of acute exercise on mnemonic discrimination.

Our null findings, however, are in contrast to the experiments by Suwabe et al. (2017, 2018) and Acevedo-Triana et al. (2021). These experiments, using a posttest only design, showed that acute exercise was associated with better mnemonic discrimination than a resting condition. However, their findings were still in conflict with each other, as exercise was only associated with mnemonic discrimination for moderate/high similarity lures (Suwabe et al., 2017, 2018) or low similarity lures (Acevedo-Triana et al., 2021). Adding further complexity to these mixed findings, Suwabe et al. observed their effects when employing no retention interval (Suwabe et al., 2018, Experiment 2) and also when incorporating a delayed retention interval (45-minutes) between encoding and retrieval (Suwabe et al., 2017; Suwabe et al., 2018, Experiment 1). In contrast, Acevedo-Triana et al. only incorporated delayed retention intervals and showed an effect of acute exercise on mnemonic discrimination after a 45-min delay, but this effect disappeared with long retention intervals. In the present experiment, we did not

demonstrate an effect of acute exercise on mnemonic discrimination when there was no delay between encoding and retrieval. This finding, which is in contrast to that of Suwabe et al. (2018, Experiment 2), may be attributed to the employed exercise intensity. When both encoding and retrieval occurs shortly after acute exercise (as done in the present experiment and Suwabe et al., 2018), perhaps higher intensities of exercise (moderate-to-vigorous, such as that employed in the present experiment) may be less optimal with challenging cognitive tasks that require a high degree of mnemonic discrimination. Short-duration, light-intensity exercise, as that employed by Suwabe et al. (2018), may be desirable for enhancing alertness and arousal for optimal encoding and mnemonic discrimination. This may also help explain the somewhat discrepant results between Suwabe et al. and Acevedo-Triana et al. Suwabe et al. (2017, 2018) showed an effect of acute exercise only for mnemonic discrimination for moderate/high similarity lures, whereas Acevedo-Triana et al. (2021) showed an effect of acute exercise only for mnemonic discrimination for low similarity lures. Acevedo-Triana et al. employed a higher-intensity of acute exercise (i.e., moderate-intensity) than that of Suwabe et al. (2018), which may have been too intense to discriminate moderate-high similarity lures. Notably, other work (Suwabe et al., 2017) has shown that moderate-intensity acute exercise can improve mnemonic discrimination for moderate/high similarity lures, but this specific work employed a delayed retention interval. Mnemonic discrimination of high similarity lures may be possible at both a short and longer time scale, but for exercise to exert such effects, perhaps low-intensity exercise is needed to ensure optimal allocation of attentional resources at the shorter timescale, and for the longer timescale, nearly any exercise intensity may be sufficient in upregulating select proteins and processes for long-term potentiation to induce such mnemonic discrimination effects. Thus, the varied intensity of acute exercise may help explain the differing results between Suwabe et al. and

Acevedo-Triana et al. when sometimes acute exercise improves mnemonic discrimination for moderate/high similarity lures, whereas other times it improves mnemonic discrimination for low similarity lures. Further, the employed intensity of acute exercise may also explain the differing results between the present study and that of Suwabe et al. (2018) that both employed no retention interval between encoding and retrieval immediately after exercise.

There also may be some other potential methodological explanations for the discrepancy between our null findings and the significant findings of others (e.g., Suwabe et al.). Although we used a similar mnemonic similar task, there were, however, a few notable methodological differences. First, the number of encoding trials was less (128) in the present study compared to that of Suwabe (196). Due to the shorter list length in the present experiment, it is possible that our task was not difficult enough to show sensitivity to exercise. This, however, is an unlikely explanation, as memory performance in the present study was far below ceiling and we observed robust similarity effects (“similar” responses to lures was .56-.60).

Although speculative, we wonder whether some of the previously (e.g., Suwabe et al., 2017, 2018) observed effects of acute exercise on mnemonic similarity task performance may be due to mechanisms distinct from pattern separation. Research demonstrates that conceptual – but not perceptual – distinctiveness within a category better predicts visual long-term memory (Konkle, Brady, Alvarez, & Oliva, 2010). To illustrate, Konkle et al. had participants view thousands of visual objects, varying the number of exemplars from one to 16 for different categories. Then during a 2-alternative forced choice test, participants had to decide whether the new category exemplar or the studied category exemplar was old. Results showed that visual discrimination of highly similar items within a category decreased as the number of studied items from each category increased, suggesting an important role of categorical distinctiveness for

visual long-term memory. In contrast, varying the degree of perceptual distinctiveness by altering the color or shape of the object did not correlate with visual long-term memory interference. Thus, after a prolonged period post-encoding, the visual discrimination of highly similar items may rely less on separating perceptual details of the stimuli and more on conceptual processing. If true, then the findings of others (e.g., Suwabe et al. (2017)) – demonstrating that exercise alters performance on a mnemonic similarity task after a prolonged delay between encoding and retrieval – could be interpreted as exercise improving visual long-term memory not from pattern separation per se, but rather from changes in the strength of memory, and moreover, retaining low-level features even while memories shift to a more abstract level of representation. We acknowledge this is a speculation and encourage future work to consider this possibility. This perspective may align with human empirical work demonstrating that acute exercise improves memory without impacting the ability to attenuate memory interference (Crawford, Caplan, & Loprinzi, 2021; Roig, Nordbrandt, Geertsen, & Nielsen, 2013). Future work, however, will need to be carefully designed to evaluate these nuances. In summary, we speculate here that with a prolonged delay between encoding and retrieval, changes in conceptual processing and precision of memory, rather than pattern separation, could be responsible for select exercise-related improvements in long-term mnemonic discrimination. However, it should be noted that other studies (e.g., Suwabe et al., 2018, Acevedo-Triana et al., 2021; Callow et al., 2023) have shown similar beneficial effects of acute exercise on mnemonic discrimination when retrieval occurred very shortly after encoding. Future work should carefully consider the temporality between encoding and retrieval when evaluating the effects of acute exercise on mnemonic discrimination. Such work would help provide useful insights into the potential mechanisms to explain the effect of acute exercise on

mnemonic discrimination, if such an effect is a reliable phenomenon, which still awaits future investigation.

Another possibility to consider is that such discrimination of high similar items may occur in brain structures (e.g., perirhinal and entorhinal) upstream to the hippocampus (Ferko et al., 2022). If our employed memory task, as well as the effects of acute exercise, are influenced by hippocampal processing and function, it is possible that more sensitive measures of perirhinal and entorhinal visual discrimination would allow for a greater ability to detect the effects of exercise on mnemonic discrimination. This could be explored in future work. Relatedly, Huffman and Stark (2017) found an age-related impairment in a forced-choice version of the MST task specific to choices between a studied item and a similar lure (A-A' forced-choice probes, in their notation). Intriguingly, although it was the worst condition, choices between a studied item and an item similar to a *different* studied item (A-B' in their notation) showed no effect of age. They successfully modelled the effect of age as a reduction in the probability that any given stimulus-feature was encoded. In other words, although they noted reduced hippocampal function in aging, the locus of the age effect did not appear to be hippocampal, but arguably just upstream of the hippocampus (as in Representational Hierarchical Theory; (Cowell, Barense, & Sadiq, 2019; Forwood, Cowell, Bussey, & Saksida, 2012)). Their procedure had no substantial delay between study and test phases. Thus, with a short retention interval, the effects of similar lures may be extra-hippocampal, depending more on earlier sensory-processing regions that may be less affected by acute exercise. After a sufficiently long delay, handling similarity might become substantially hippocampal-dependent and thus the putative influence of acute exercise on hippocampal function might have influenced prior results showing mnemonic discrimination from acute exercise.

Another interesting avenue to explore is to evaluate potential priming effects of multiple bouts of acute exercise. For example, prior work in animals shows that a particular dose of acute exercise – previously shown to be insufficient in upregulating key proteins (e.g., brain-derived neurotrophic factor) thought to play a role in pattern separation (Bekinschtein et al., 2013) – is effective in producing levels of such proteins to improve memory performance when occurring after a prior bout of exercise (Berchtold, Chinn, Chou, Kessler, & Cotman, 2005). Relatedly, other work, in older adults, demonstrates the possibility that *chronic* exercise engagement may be able to facilitate mnemonic discrimination (Heisz et al., 2017). This possibility (chronic exercise) could also be explored in younger adult populations, but a comparison of acute exercise on mnemonic discrimination should be directly compared between young and older adults, as the present study and that of Bernstein and McNally (2019) showed no effects in younger populations (but for opposing results, see Suwabe et al., 2017, 2018), whereas other work in older adults shows an effect of acute exercise on mnemonic discrimination (Callow, Pena, Stark, & Smith, 2023; Pena, Callow, Evans, Prior, & Smith, 2022).

In conclusion, the present experiment did not observe acute exercise modulating mnemonic discrimination, at two levels of exercise intensity and with a full pre-post design. This null finding replicates the findings of some (e.g., Bernstein & McNally, 2019), but not others who have shown that acute exercise can facilitate mnemonic discrimination (e.g., Suwabe et al., 2017, 2018). Regarding the potential beneficial effects of acute exercise on mnemonic discrimination, the timescale between encoding and retrieval may interact with the intensity of acute exercise to influence mnemonic discrimination. Future work may wish to incorporate multiple exercise intensities and multiple retention intervals (including no retention interval and multiple delayed intervals) to evaluate these potential interaction effects. Such work may also

wish to consider evaluating whether these potential interaction effects are attributed to mechanisms within the hippocampus or more upstream structures. Such mechanistic work would also benefit by determining whether the potential effects of acute exercise on mnemonic discrimination occur from processes related to separating perceptual details of similar items, or rather, from mechanisms related to conceptual processing.

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Study Phase



Test Phase



Target Image
“Old”



Lure Image
“Similar”



Foil Image
“New”

Figure 1. Illustrations of stimuli and choices used in the mnemonic similarity task.

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