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Acute physical exercise in humans enhances reconsolidation of emotional memories

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ABSTRACT

Increasing evidence suggests that when a memory is reactivated through retrieval, it becomes temporarily vulnerable to environmental or pharmacological manipulation, which can consequently update or strengthen the memory. Physical exercise has been shown to modulate the maintenance of fear memories in animals following memory reactivation. This study investigated the effect of intense exercise in modulating the reconsolidation of trauma memories. Fifty-four undergraduate students watched a trauma film depicting the aftermath of a highway car crash. Two days later, participants engaged in either (a) 20–25 min of incremental cycling following a memory reactivation induction (Reactivation/Exercise), (b) 20–25 min of mild cycling (Reactivation/No Exercise) following memory reactivation, or (c) 20–25 min of incremental cycling but no memory reactivation (No Reactivation/Exercise). Saliva samples were collected to index salivary amylase and cortisol at baseline and post activity. Participants completed memory questionnaires relating to declarative and intrusive memory recall two days after memory reactivation. Reactivation/Exercise participants recalled more central details of the trauma film relative to other participants. Increased cortisol predicted better total memory recall in the Reactivation/Exercise, but not in the other conditions. These findings suggest that intense exercise during the period of memory reactivation enhances subsequent trauma memory, and provides human evidence consistent with recent findings of exercise-induced fear reconsolidation in animals.

1. Introduction

Memory for emotionally arousing events are typically stronger than non-emotional events, with particularly greater recall of central details of these memories (Adolphs et al., 2005; Shields et al., 2017). This memory bias for emotionally significant information is driven by the release of noradrenaline and cortisol at the time of an emotionally arousing event (Cahill et al., 2003; Roozendaal et al., 2004,2006), where an interaction between these catecholamines is modulated within the basolateral amygdala (McGaugh, 2004). Whilst recall of central information is arguably adaptive in navigating subsequent threatening experiences, overconsolidated memories for emotionally arousing details with accompanying high levels of distress can lead to debilitating psychopathological states, such as posttraumatic stress disorder (PTSD; Pitman, 1989).

Increasing evidence suggests that when a memory is reactivated it returns to a labile, protein-synthesis dependant state (Nader et al., 2000), making it susceptible to modifications in the form of environmental (Schiller et al., 2010) or pharmacological (Kindt et al., 2009) manipulations. Research suggests that a mere reminder is not sufficient in inducing this labile state (Forcato et al., 2009), instead a prediction error involving a mismatch between expected and actual experience must be accompanied in order for the original memory trace to be destabilised (Sevenster et al., 2014). Empirical evidence suggests that a destabilised memory trace can be updated by incorporating new information (Forcato et al., 2007; Hupbach et al., 2007), or modulating its strength (Forcato et al., 2014). Glucocorticoid administration following memory reactivation impairs recall of a contextual fear memory in animals (Cai et al., 2006), with some evidence suggesting that this effect may be selective to strong emotional memories (Abrari et al., 2008). In humans, glucocorticoid administration following memory reactivation enhances conditioned fear (Drexler et al., 2015), and declarative emotional memory (Marin et al., 2010). In contrast, behavioral stress following memory reactivation resulted in a memory impairing effect (Drexler and Wolf, 2017), which suggests that cortisol administration and behavioral stress have differential effects on memory reconsolidation. However, there is evidence that experiencing stress during memory reactivation may not influence declarative memory but does increase intrusive memories (Cheung et al., 2015). Further, stress following memory reactivation can impair memory for

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negative stimuli encoded five weeks prior (Tollenaar et al., 2008). The discrepancies in terms of declarative memory recall for emotional stimuli may be attributable to the strength of memory, nature of stimuli, and differential modulation of the hypothesized reconsolidation window and related timing of the stressor (i.e., cortisol exposure during vs after memory reactivation). Additionally, the timing of glucocorticoid administration in relation to new learning appears critical in facilitating subsequent memory (de Quervain et al., 2017), with evidence to suggest that delayed glucocorticoid exposure can impair retrieval of memory (Joels et al., 2006). Further, noradrenergic activity appears to play a role in the persistence of emotional memories, with evidence that blocking the noradrenergic system (with propranolol) prior to reactivation eliminates conditioned fear (Kindt et al., 2009), and selectively impairs negative episodic memories (Schwabe et al., 2012). Given the encoding (van Stegeren et al., 2007), and storage of emotionally arousing experiences (van Stegeren, 2008) depend upon the interactive relationship between glucocorticoids & noradrenaline, it is conceivable that a similar relationship may at least in part underlie the reconsolidation of emotional memories as well.

A role for physical exercise in modulating emotional memory reconsolidation arises from evidence that exercise-induced mechanisms underpin stabilisation of memories. In particular, memory stabilisation appears to be time-dependant with the specific activation of molecular mechanisms responsible for learning and memory (Hötting and Röder, 2013; Roig et al., 2013,2016). Additionally, acute aerobic exercise induces significant increases in glucocorticoids (Hötting et al., 2016; Wahl et al., 2010), and blockade of exercise-induced glucocorticoid production attenuates memory retention in animals (Hajisoltani et al., 2011). Similarly, acute exercise activates noradrenaline (Segal et al., 2012; Winter et al., 2007) and plays a crucial role in exercise-induced memory consolidation (Segal et al., 2012). There is increasing evidence in animals (Siette et al., 2014), and humans (Keyan and Bryant, 2017a,b) that acute exercise following encoding of fear memories increases the strength of the memory trace. A recent animal study demonstrated a role for exercise in the reconsolidation of fear memories by demonstrating that wheel running immediately after brief exposure to a previously fear conditioned context subsequently displayed more fear (as indexed by freezing behavior) on a delayed retention test relative to sedentary controls (Siette et al., 2014). Moreover, the distance covered in the wheel running following brief exposure was positively correlated with levels of freezing (Siette et al., 2014), suggesting that more intense exercise following memory reactivation corresponded with increased emotional memory strength. In support of this notion, the dose response of exercise on memory enhancement appears to be critically mediated by brain derived neurotrophic factor (BDNF; Winter et al., 2007), a growth factor implicated in the consolidation (Schulz-Klaus et al., 2013), and recently the reconsolidation of contextual fear memories in animals (Giachero et al., 2013). Given the available evidence, it is possible that exercise plays a role in the reconsolidation of distressing emotional memories, and this may be dependent on the intensity of the exercise and subsequent activation of critical biological mechanisms in implicated in memory reconsolidation.

The current study aimed to extend previous animal research (Siette et al., 2014) by investigating the role of acute exercise in modulating the reconsolidation of emotional memories. An aerobic cycling task was chosen as this mode and level of intensity has been shown to induce substantial learning and memory benefits (Roig et al., 2013), elevate noradrenergic levels (Segal et al., 2012), and hypothalamus-pituitary-adrenal (HPA) responsivity (Brownlee et al., 2005). An analogue trauma (film) paradigm was utilized as it elicits significant stress responses (Cheung et al., 2015), and distressing emotional memories in non-clinical populations (Holmes and Bourne, 2008). On Day 1 of the experiment, participants viewed a trauma film. On Day 3, participants were randomised to either, (a) Reactivation/Exercise (acute exercise immediately following memory reactivation), (b) Reactivation (memory reactivation alone), or (c) Exercise (exercise alone).On Day5 participants completed a surprise cued recall and measure of intrusive memories. Based upon the available evidence that acute stress enhances reactivated emotional memories (Bos et al., 2014; Cheung et al., 2015), and exercise functions to enhance memory, we hypothesised that participants who received both memory reactivation and exercise would display better cued recall and more intrusions on a delayed memory test. We also hypothesized that levels of cortisol and salivary amylase would be positively associated with reconsolidated emotional memories of the trauma film.

2. Method

2.1. Participants

The sample included 54 healthy University of New South Wales undergraduate students (26 female, 28 male) aged between 17 and 36 years (M = 19.48, SD = 3.03) who participated in exchange for course credit. Participants were randomly allocated to a Reactivation/Exercise (n = 18; 11 male), Reactivation/No exercise (n = 18; 9 male), or No Reactivation/Exercise condition (n = 18; 8 male).

2.2. Measures

2.2.1. Depression anxiety and stress scales-21 item version

Baseline depression was assessed using the Depression Anxiety and Stress Scales (DASS; Lovibond and Lovibond, 1995) 21-item version, which indexes depression, anxiety and stress. This measure possesses strong reliability and internal consistency (Lovibond and Lovibond, 1995).

2.2.2. Intrusions questionnaire

Selected items from the intrusion subscale of the Impact of Event Scale (IES; Horowitz et al., 1979) was used to measure intrusive memories of the trauma film. Participants were instructed to rate the degree to which they identified with each item on a five-point Likert scale (0 = *Not at all*, 4 = *Extremely*). The items were *Pictures about it popped into mind*, *Other things kept making me think about it*, and *I thought about it when I didn't mean to*. Items were framed to capture memory occurrences of the film presented to participants initially, and in the intervening two days since the experiment.

2.2.3. Cued recall test

A 25-item questionnaire that has been previously adapted to the car accident film was used to index intentional recall in the current study (Devilly et al., 2007). This questionnaire included 12 items relating directly to the central features (e.g., *How many of the injured victims had dark skin and how many had light skin?*), and 13 items relating to peripheral/surroundings (e.g. *How many police vehicles surrounded in the scene*) of the car accident. Central features of the film were defined as elements directly relating to the victims, whereas peripheral features were defined as elements not directly relating the victims, and therefore elements that captured background details (Devilly et al., 2007).

2.2.4. Current distress

Participants' distress associated with the trauma film was assessed by rating an 8-point Likert scale (0 = *Not at all*, 7 = *Extremely*).

2.2.5. Pre-exercise questionnaire

Participants were asked to indicate if they were currently suffering from any health and/or physical conditions that would prevent them from engaging in strenuous physical activity (1 participant was excluded for this reason). Examples included high blood pressure, asthma, chronic pain, and a current heart condition; endorsement of any condition resulted in exclusion from the study. In addition, participants did not report taking any hormonal contraceptives on this questionnaire.