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The role of estrogen in intrusive memories

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ABSTRACT

Intrusive memories are highly vivid, emotional and involuntary recollections which cause significant distress across psychological disorders including posttraumatic disorder (PTSD). Recent evidence has potentially extended our understanding of the development of intrusive memories by identifying biological factors which significantly impact on memories for emotionally arousing stimuli. This study investigated the role of stress on the development of intrusions for negative and neutral images, and indexed the potential contributions of sex (estrogen and progesterone) and stress (noradrenaline and cortisol) hormones. Whilst viewing the images, half the participants underwent a cold pressor stress (CPS) procedure to induce stress while the control participants immersed their hands in warm water. Saliva samples were collected to index estrogen, progesterone and noradrenergic and cortisol response. Participants (55 university students, 26 men, 29 women) viewed a series of negatively arousing and neutral images. Participants completed recall and intrusions measures 2 days later. Negative images resulted in greater recall and more intrusions than neutral images. In the cold water condition females recalled fewer neutral memories than males. Cortisol increase predicted decreased recall of negative memories in males, and estrogen predicted increased intrusions of negative images in women. These findings are consistent with evidence that circulating levels of ovarian hormones influence memory for emotionally arousing events, and provides the first evidence of the influence of sex hormones on intrusive memories. These results provide one possible explanation for the higher incidence of anxiety disorders in women.

1. Introduction

Intrusive memories are highly vivid, emotional, and involuntary recollections of events that are typically negative or traumatic in nature. They are a common feature of various psychological disorders, including posttraumatic stress disorder (PTSD; (Bryant, O'Donnell, Creamer, McFarlane, & Silove, 2011)), depression (Patel et al., 2007), bipolar disorder (Gregory, Brewin, Mansell, & Donaldson, 2010), obsessive–compulsive disorder (Lipton, Brewin, Linke, & Halperin, 2010), and social phobia (Hackmann, Clark, & McManus, 2000). Across the disorders, intrusive memories share common characteristics in that they are often unwanted, interfere with ongoing cognitive activity, are experienced as nonvolitional, and are difficult to control (Clark & Rhyno, 2005).

Prevailing theories of intrusions posit that (a) these memories are not adequately embedded within a person's autobiographical memory base, increasing the likelihood of triggering unwanted intrusive thoughts (Conway & Pleydell-Pearce, 2000), (b) these memories were encoded in highly sensory-perceptual details which lack contextual grounding, and therefore intrude into consciousness (Brewin, Gregory, Lipton, & Burgess, 2010), (c) lack of conceptual processing results in traumatic information remaining prone to automatic, cued activation (Ehlers & Clark, 2000), or that (d) memories are activated by cues associated with the original traumatic event (Foa, Steketee, & Rothbaum, 1989). A common theme across these models is that the reason the initial memory is encoded in a manner that leads to subsequent intrusive recollections is that the original encoding occurs during stress.

The role of stress has been repeatedly demonstrated in emotional memories, insofar as emotionally arousing events are better remembered than neutral events (Cahill, 2000). The fast-acting sympathetic adrenomedullary system is responsible for the production of adrenaline and noradrenaline leading to increased blood pressure, heart rate, and availability of glucose to the muscles and brain. The slower-acting HPA system involves the production of cortisol by the adrenal cortex, which increases blood sugar levels and metabolism (Tsigos & Chrousos, 2002). Consistent with the notion that arousal plays a role in emotional memories, noradrenergic activation during encoding results in stronger memories for emotional stimuli (McGaugh & Roozendaal, 2009; van Stegeren, 2005). Further, glucocorticoid activation plays a role in emotional memory in that hydrocortisone administration leads to superior memory of emotional, but not neutral, information (Abercrombie, Speck, & Monticelli, 2006). It appears that noradrenergic and

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glucocorticoid systems interact to enhance emotional memories (McGaugh & Roozendaal, 2009). The evidence that this interaction between arousal systems enhances emotional memories has been explained in terms of glucocorticoids being able to pass the blood–brain barrier, thereby facilitating noradrenergic effects in the amygdala (de Quervain, Aerni, Schelling, & Roozendaal, 2009; Roozendaal, Quirarte, & McGaugh, 2002).

There is also accumulating evidence demonstrating that this stress-facilitated emotional memory is influenced by gender and sex hormones (Andreano & Cahill, 2009). Women have better recall of emotional information than men (Bloise & Johnson, 2007; Canli, Desmond, Zhao, & Gabrieli, 2002), and females are more likely to develop disorders related to emotional memory, such as posttraumatic stress disorder, than males (Olff et al., 2007). Sex-related lateralization of amygdala activity has been shown to differentially mediate enhanced emotional memory in men and women (Cahill, Uncapher, Kilpatrick, Alkire, & Turner, 2004). There is also evidence that sex hormones influence emotional memory (Cahill, 2006). In rodent studies, administration of an estrogen antagonist or ovariectomy prevents the impairing effects of pre-training stress on eyeblink conditioning (Wood & Shors, 1998) and reduces sex differences in a fear conditioning task (Gupta, Sen, Diepenhorst, Rudick, & Maren, 2001). These findings suggest that levels of circulating estrogen may mediate the effects of stress in aversive training tasks. In humans, the luteal phase is associated with higher levels of circulating estrogen and progesterone, which in turn may heighten glucocorticoid release due to progesterone binding to receptor sites (Koubovec, Ronacher, Stubsrud, Louw, & Hapgood, 2005). The increase of glucocorticoid release at the time of encoding an emotional experience may consolidate the memory (Pitman, Shalev, & Orr, 2000). In this context it is noteworthy that the mid-luteal phase is associated with stronger recall of emotional memories in both healthy controls (Andreano, Arjomandi, & Cahill, 2008) and trauma-exposed (Bryant, Felmingham, et al., 2011) women. There is also evidence that progesterone levels at the time of encoding predict subsequent emotional memory for negative images (Ertman, Andreano, & Cahill, 2011; Felmingham et al., 2012).

Few experimental studies have examined the role of sex hormones in intrusive memories. There is evidence that women experience more intrusive recollections of emotional stimuli than men (Ferree & Cahill, 2009), and females in the luteal phase are more likely to experience intrusions of experimentally-generated negative stimuli (Ferree, Kamat, & Cahill, 2011) and flashback memories if they experience trauma during the mid-luteal phase (Bryant et al., 2011). Taken together, sex hormones appear to play an important role in memory for emotional material and this issue needs to be further investigated in the development of intrusive emotional memories.

A major goal of this study was to extend previous research by investigating the role of sex hormones on intrusive emotional memories. A further aim was to enhance the ecological validity of the experimental procedure by administering the stress manipulation at the same time as the presentation of the encoded material. Previous studies have administered a cold pressor stress procedure (Andreano et al., 2008) or epinephrine (Cahill & Alkire, 2003) immediately after presentation of the information. To more closely simulate occurrence of encoding during traumatic events, we required participants to immerse their arm in cold water *during* the viewing of the material. Timing of the stressor in relation to the encoding of information has been shown to be influential in terms of subsequent memory insofar as cortisol increase at the time of retrieval impairs memory (de Quervain, Roozendaal, & McGaugh, 1998; Kuhlmann & Wolf, 2005), but enhances emotional memory at the time of encoding or consolidation (Andreano & Cahill, 2006; Kuhlmann & Wolf, 2006). The role of cortisol in encoding appears to be complex, however, in that cortisol increase at consolidation can impair memory (Diamond, Campbell, Park, Halonen, & Zoladz, 2007), and the effect may be modulated by attentional factors at the time of encoding/consolidation (Preuss, Schoofs, & Wolf, 2009). Accordingly, to simulate the co-existence of the stressor at the time of encoding we randomized males and females to either a cold pressor stress or control condition during presentation of neutral and aversive images. Salivary samples of estrogen, progesterone, noradrenaline and cortisol were collected during the experiment. Two days later participants returned and completed a surprise free recall test and a measure of intrusive memories. We hypothesized that there would be more memories recalled and more intrusions for (a) negative than for neutral images, (b) high than low stress, (c) women than men, and (d) levels of estrogen and progesterone will be positively associated with intrusions for negative but not neutral images.

2. Method

2.1. Participants

Fifty-five undergraduate psychology students at the University of New South Wales comprised of 26 men (12 in cold water, 14 in warm water) of mean age = 19.10 years (*SD* = 2.06) and 29 women (13 in cold water, 16 in warm water) of mean age 19.89 years (*SD* = 4.79) were recruited for the study in return for course credit.

2.2. Materials

Negative and neutral color images were selected from a standard set of pictures from the International Affective Picture System (IAPS; (Lang, Bradley, & Cuthbert, 2008)). The IAPS is a widely used picture set that provides normative information for experimental investigations of emotion and attention. Eighteen negative images rated highly on arousal and valence and 18 neutral images rated low on arousal and valence were randomly interspersed in one of two fully randomized orders (with no more than two successive presentations of the same type of image). Images were presented on a video display unit using Microsoft Powerpoint software, and were presented for 5 s per image. Negative images had a mean normative arousal rating of 6.62 (*SD* = 2.25) and mean normative valence rating of 1.66 (*SD* = 1.19). Neutral images had a mean normative arousal rating of 2.33 (*SD* = 1.72) and mean normative valence rating of 4.81 (*SD* = 1.03).

2.2.1. Intrusion questionnaire

To index intrusive memories of the neutral and negative images, respectively, the Intrusion subscale of the Impact of Event Scale (IES; (Horowitz, Wilner, & Alvarez, 1979)) was adapted to index intrusive memories of the presented images. Participants were asked to rate each intrusive item (e.g. "Pictures about it popped into my mind") on a 5-point Likert scale from 0 ("not at all") to 4 ("extremely"). The questionnaire was administered twice in counterbalanced order to assess intrusions for negative and neutral images, respectively. In each questionnaire, participants were instructed to think about the images that they had seen in the previous experimental session (the "emotional" and the "not emotional") and to answer the occurrence of the intrusive experiences in relation to each type of each image.

2.2.2. Depression, Anxiety and Stress Scales (DASS 21)

The DASS 21 was used to quantitatively measure severity of distress across scales of depressive, anxiety and stress symptoms (Lovibond & Lovibond, 1995). The DASS 21 has been demonstrated