Hormones and Behavior 93 (2017) 1–8

Contents lists available at ScienceDirect

Hormones and Behavior

journal homepage: www.elsevier.com/locate/yhbeh

Blunted cortisol response to acute pre-learning stress prevents misinformation effect in a forced confabulation paradigm

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ARTICLE INFO

Article history:
Received 1 November 2016
Revised 31 March 2017
Accepted 12 April 2017
Available online xxxx

Keywords:
Stress
Learning
False memory
Cortisol
Norepinephrine

ABSTRACT

Research examining the effects of stress on false memory formation has been equivocal, partly because of the complex nature of stress-memory interactions. A major factor influencing stress effects on learning is the timing of stress relative to encoding. Previous work has shown that brief stressors administered immediately before learning enhance long-term memory. Thus, we predicted that brief stress immediately before learning would decrease participants' susceptibility to subsequent misinformation and reduce false memory formation. Eighty-four male and female participants submerged their hand in ice cold (stress) or warm (no stress) water for 3 min. Immediately afterwards, they viewed an 8-min excerpt from the Disney movie *Looking for Miracles*. The next day, participants were interviewed and asked several questions about the video, some of which forced them to confabulate responses. Three days and three weeks later, respectively, participants completed a recognition test in the lab and a free recall test via email. Our results revealed a robust misinformation effect, overall, as participants falsely recognized a significant amount of information that they had confabulated during the interview as having occurred in the original video. Stress, overall, did not significantly influence this misinformation effect. However, the misinformation effect was completely absent in stressed participants who exhibited a blunted cortisol response to the stress, for both recognition and recall tests. The complete absence of a misinformation effect in non-responders may lend insight into the interactive roles of autonomic arousal and corticosteroid levels in false memory development.

1. Introduction

Pioneering work by Elizabeth Loftus revealed that after a memory of an event had been formed, exposing participants to misinformation about the event led them to subsequently recall this misinformation as having been part of the original event (Loftus et al., 1978). This was coined the “misinformation effect,” and since its observation, researchers have continued to expand the scope of this work. In all of these studies, the misinformation effect has proven to be a robust phenomenon; it occurs in participants of all ages (from preschoolers to older adults), when presented in a variety of different ways (e.g., narratives, post-event questions, imagination, or even self-generation), for both simulated and real-world events and across several different types of memory tests (e.g., recall, recognition, and source-monitoring) (Ackil and Zaragoza, 1995, 1998; Ceci et al., 1987; Drivdahl et al., 2009; Lane and Zaragoza, 2007; Lindsay, 1990; Nourkova et al., 2004; Zaragoza et al., 2011). Additionally, it has been reported that not only can memories for individual items be altered through misinformation, but memories for entire events can be fabricated by participants, either in conjunction with a previously shown witnessed event (Chrobak and Zaragoza, 2008) or within their own life history (Lindsay et al., 2004; Wade et al., 2002).

Studies on false memory formation are important for understanding the accuracy of eyewitness testimony. Research suggests that eyewitness testimony is frequently flawed and filled with errors in details. These inaccuracies, along with the overconfidence often displayed by eyewitnesses, can lead to wrongful identification and even wrongful conviction of innocent persons (Doyle, 2005). Because eyewitness accounts often involve stress, it is important to understand how stress might influence the formation of memories, especially false memories. Over the past several decades, it has become clear that the effects of stress on learning and memory are complex, as stress can enhance, impair or have no effect on learning and memory, depending on several factors (Diamond et al., 2007;

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http://dx.doi.org/10.1016/j.yhbeh.2017.04.003
0018-506X/

Joels et al., 2011; Schwabe et al., 2012; Zoladz et al., 2014a; Zoladz et al., 2011b). One particularly important factor is the temporal proximity of the stressor to the learning experience. Research has shown that when stress occurs around the time of learning (i.e., experienced in the context of learning, Joels et al., 2006) and is of relatively short duration, long-term memory is enhanced (e.g., Diamond et al., 2007; Vogel and Schwabe, 2016; Zoladz et al., 2011a; Zoladz et al., 2014c). On the other hand, when stress is separated from the learning experience (i.e., experienced outside the context of learning) or is of a longer duration, long-term memory is impaired (e.g., Quaedflieg et al., 2013; Zoladz et al., 2011a; Zoladz et al., 2013). Stress appears to exert such time-dependent effects on learning and memory, in part, because of an amygdala-mediated biphasic effect on hippocampal plasticity (Akirav and Richter-Levin, 1999, 2002). Shortly following stress, rising cortisol levels exert rapid, nongenomic effects that, in conjunction with a rapid increase in norepinephrine, are excitatory in nature and enhance hippocampal function (Diamond et al., 2007; Joels et al., 2011; Schwabe et al., 2012). However, as the stress response continues, the rising cortisol begins to exert gene-dependent, inhibitory effects on hippocampal function, which result in impaired learning and memory.

Research concerning stress effects on false memory development has been equivocal. Some studies have shown that stress increases false memory development (Pardilla-Delgado et al., 2016; Payne et al., 2002; Qin et al., 2012); other studies have shown that stress reduces false memory development (Schmidt et al., 2014; Zoladz et al., 2014d); and, still others have reported no effects of stress on false memory formation (Beato et al., 2013; Hoscheidt et al., 2014; Smeets et al., 2006; Smeets et al., 2008). Two relatively recent studies reported that stress or the physiological responses associated with stress result in less incorporation of misinformation into an established memory. Schmidt et al. (2014) found that stressing participants immediately before misinformation exposure led them endorse fewer misinformation items at testing. In another study, Hoscheidt et al. (2014) found that stressing participants immediately before learning had no overall influence on subsequent incorporation of misinformation, but within the stress group, subjective arousal levels were negatively correlated with the endorsement of misinformation items during testing, suggesting a potential role for stress-induced autonomic nervous system activity in blunting the misinformation effect. Because stress exerts the time-dependent effects outlined above, exposure to stress immediately before learning could enhance memory consolidation and prevent false memory development in participants. It is possible that Hoscheidt et al. (2014) did not observe an overall effect of stress because of the duration of the stressor that was administered immediately prior to learning (e.g., 15-min; Trier Social Stress Test). In previous work, we found that exposing participants to the cold pressor test, a brief (3-min) stressor, immediately before learning several word lists from the Deese-Roediger-McDermott paradigm reduced false memory formation (Zoladz et al., 2014d). However, this study involved a within-day paradigm, and we did not assess long-term memory in participants. In the present study, we were interested in applying our ideology to a more realistic learning event – in this case, a video – and examining participants' long-term memory for the learned information. Furthermore, we wanted to create a more realistic way for the false memories to be developed, through an interrogation-like technique. Specifically, we interviewed participants one day after they watched the video and forced them to self-generate misinformation about the events that took place, following the forced fabrication paradigm developed by Zaragoza and colleagues (Ackil and Zaragoza, 1998; Zaragoza et al., 2001). Our hypothesis was that exposing participants to a brief stressor immediately before watching the video would enhance the ensuing memory of the video and protect it from being distorted by the misinformation that was self-generated during the interview.

2. Material and methods

2.1. Participants

Eighty-four healthy undergraduate students (43 males, 41 females; age: $M = 19.04$, $SD = 1.07$) from Ohio Northern University volunteered to participate in the experiment. Individuals were excluded from participating if they met any of the following conditions: diagnosis of Raynaud's or peripheral vascular disease; presence of skin diseases, such as psoriasis, eczema, or scleroderma; history of syncope or vasovagal response to stress; history of severe head injury; current treatment with psychotropic medications, narcotics, beta-blockers, steroids, or any other medication that was deemed to significantly affect central nervous or endocrine system function; mental or substance use disorder; regular nightshift work. Participants were asked to refrain from using recreational drugs (e.g., marijuana) for 3 days prior to the experimental sessions; to refrain from drinking alcohol or exercising extensively for 24 h prior to the experimental sessions; and, to refrain from eating or drinking anything but water for 2 h prior to the experimental sessions. Upon arrival at the laboratory, participants were reminded of the exclusion criteria and study restrictions and verbally affirmed that they had adhered to the requirements. All of the methods for the experiment were undertaken with the understanding and written consent of each participant, with the approval of the Institutional Review Board at Ohio Northern University, and in compliance with the Declaration of Helsinki.

2.2. Experimental procedures

All experimental procedures took place between 1100 and 1700 and began with a 10-min rest period. A timeline of all procedures can be found in Fig. 1.

2.2.1. Cold pressor test (CPT)

Following completion of a short demographics survey and the collection of baseline physiological measures (see Section 2.2.2 below), participants were asked to submerge their non-dominant hand, up to and including the wrist, in a bath of water for 3 min. Those participants who had been randomly assigned to the stress condition (N = 49; 23 males, 26 females) placed their hand in a bath of ice cold (0–2 °C) water, while participants who had been randomly assigned to the control condition (N = 35; 20 males, 15 females) placed their hand in a bath of warm (35–37 °C) water. The water was maintained at the appropriate temperature by a VWR 1160S circulating water bath. To maximize the stress response during the CPT, participants were encouraged to keep their hand in the water bath for the entire 3-min period. However, if a participant found the water bath too painful, he or she was allowed to remove his or her hand from the water and continue with the experiment. Nine participants from the stress condition removed their hand from the water prior to 3 min elapsing ($M = 162.95$ s, $SD = 40.69$), and all participants from the control condition kept their hand in the water for the entire 3-min period. Inclusion of the data from stressed participants who removed their hand from the water early had no significant effect on the observed results. Research has consistently shown that the CPT results in significant increases in subjective (e.g., affect, stress ratings) and objective (e.g., cortisol, autonomic arousal) measures of the stress response (Buchanan et al., 2006; Cahill et al., 2003; Schoofs et al., 2009; Zoladz et al., 2014b; Zoladz et al., 2014c; Zoladz et al., 2015).

2.2.2. Subjective and objective stress response measures

2.2.2.1. Subjective pain and stress ratings. Participants were asked to rate the painfulness and stressfulness of the water bath manipulation at 1-min intervals on 11-point scales ranging from 0 to 10, with 0 indicating