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

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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.

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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-generations), and in 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;...
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; Qiu 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 – 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 35°C water. 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 11605 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; Caihl 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...
a complete lack of pain or stress and 10 indicating unbearable pain or stress.

2.2.2.2. Cardiovascular analysis. Heart rate (HR) and blood pressure (BP) measurements were taken immediately before, halfway through and immediately after the water bath manipulation. Cardiovascular activity was measured with a vital signs monitor (Mark of Fitness WS-820 Automatic Wrist Blood Pressure Monitor) placed on the wrist of each participant’s dominant hand.

2.2.2.3. Cortisol analysis. Saliva samples were collected from participants immediately before and 25 min after the water bath manipulation to analyze salivary cortisol concentrations. We chose to examine salivary cortisol levels 25 min following the water bath manipulation because this is the approximate time frame when stress-induced cortisol responses peak. The samples were collected in a Salivette saliva collection device (Sarstedt, Inc., Newton, NC). Participants were asked to place a synthetic swab in their mouths and chew on it so that it would easily absorb their saliva. Following 1 min of chewing, the synthetic swab was collected and placed in the Salivette conical tube and kept at room temperature until the experimental session was completed. The samples were subsequently stored at −20 °C until assayed for cortisol. Saliva samples were thawed and extracted by low-speed centrifugation. Salivary cortisol levels were determined by enzyme immunoassay (EIA; Cayman Chemical Co., Ann Arbor, MI) according to the manufacturer’s protocol. The sensitivity of the assay was 6.6 pg/ml, and the intra-assay coefficient of variation was 3.1%.

2.2.3. Forced confabulation paradigm

The forced confabulation paradigm used in the present study followed that which was developed by Zaragoza and colleagues (Ackil and Zaragoza, 1998; Zaragoza et al., 2001), but with a modified time line.

2.2.3.1. Video presentation. Immediately following the water bath manipulation, participants viewed an 8-min excerpt from the Disney movie Looking for Miracles, which depicts the adventures of two brothers at summer camp. The clip has both action and drama, including, for example, a fight among the campers and an encounter with a deadly snake. Only one participant, who was in the stress condition, reported having seen it "a long time ago." After viewing the video clip, participants sat quietly until the second saliva sample was collected for cortisol analysis, and then they were dismissed for the day.

2.2.3.2. Interview. The next day, participants returned to the laboratory to be interviewed by an experimenter about the video clip they had seen. Before the interview began, participants were instructed to provide an answer to every question, even if they had to guess. Each participant was asked 12 questions. Of those, 8 were true-event questions about events from the video; these were the same for all participants. The remaining 4 were false-event questions about events that had clearly never occurred in the video. Thus, in order to answer the false-event questions, participants had to make up, or confabulate, answers. For example, in going over a scene from the video, the experimenter said, “It [the chair] broke, and Delaney fell on the floor. Where was Delaney bleeding?” This question required a made up response because, although Delaney did fall off a chair in the video, it was clear that he was not injured and no blood was ever shown. When participants resisted answering these questions, the experimenter prompted them to take their best guess until they provided an answer. There were two sets of 4 false-event questions. Each participant was yoked with another participant (i.e., his or her “yoked partner”) assigned to the same condition (i.e., stress or no stress); one of these participants was provided one set of false-event questions, and the other participant was provided the other set. This procedure enabled us to use the answers generated by each participant in his or her yoked partner’s memory test as a control (i.e., the participant who had not confabulated answers to the other set of questions should recognize them as blatantly false during the memory test).

2.2.3.3. Recognition testing. Three days following the interview, participants returned to the laboratory to complete a surprise recognition test. The participants were met by an experimenter (different from the one who conducted the interview) who told them that the interviewer who had asked them about the video had asked some questions about events that never actually happened. Their task, they were told, was to indicate which things they were sure they remembered seeing in the video and which things they had not seen. All participants were asked 22 yes/no questions of the form “When you watched the video, did you see ______?” For each “yes” or “no” response, they also indicated their confidence in their answer using one of the following five verbal descriptors: “not at all confident,” “somewhat confident,” “fairly confident,” “considerably confident,” and “extremely confident.” This response format yielded two measures: assents (i.e., number of “yes” responses) and a confidence score (ranging from 1 to 10, with 1 indicating “extremely confident no” and 10 indicating “extremely confident yes”). For each participant, the test list included four different types of questions: (a) the 4 confabulated items the participant had generated in response to the false-event questions (forced confabulation items), (b) the 4 items the participant’s yoked partner had confabulated in response to the alternate set of false-event questions (yoked control items), and (c) 14 filler items that included 9 questions about things

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Fig. 1. Timeline of the experimental procedures. On Day 1, participants placed their non-dominant hand in cold (stress) or warm (no stress) water for 3 min. Then, participants viewed an 8-min video clip from the movie Looking for Miracles. Saliva samples and cardiovascular measurements were taken at various time points in order to verify the induction of a stress response. The next day, participants were interviewed and asked various questions about the video clip, some of which forced participants to confabulate answers. Three days later, participants completed a recognition test that assessed their memory of the events that actually took place in the video. Three weeks later, participants were emailed and asked to recall as much information about the video as they could.
that actually occurred in the video (true-event items) and 5 questions about things that were neither in the video nor asked about during the interview (new items). All data from the recognition test were converted into probabilities of assents [e.g., p(forced confabulation assent) = # of assents/4] for the purpose of data analysis.

2.2.3.4. Delayed recall testing. Three weeks following the recognition test, participants were contacted via email and sent a questionnaire which asked them to recount, as accurately and in as much detail as possible, the events from the video they had watched. To help orient the participants, the questionnaire provided general descriptions of the major scenes in the video (e.g., the lake scene), and for each, prompted participants to describe such things as what happened, the characters who were there, how they were dressed, what was said, and so forth. Although general prompts were given, participants were in no way cued to recall the specific items they had been forced to confabulate. Seventy participants (83.33%) responded to the email with a description of what they remembered. Two research assistants who were blind to participant condition examined the responses for any indication of (a) the 4 confabulated items the participant had generated in response to the false-event questions [forced confabulation items], (b) the 4 items the participant’s yoked partner had confabulated in response to the alternate set of false-event questions [yoked control items], and (c) other falsely recalled details (new items). All data from the recall test were converted into probabilities, similar to the recognition data, for the purpose of data analysis.

2.3. Statistical analyses

Unless otherwise noted, mixed-model ANOVAs were used to analyze all physiological and behavioral data; the between-subjects factors utilized in these analyses were stress and sex, and the within-subjects factors were question type [(forced confabulation, yoked control, true-event, new) for recognition and recall analyses] or time (for physiological and subjective ratings analyses). For the memory data, our primary interest was to examine the misinformation effect across conditions, which was accomplished by comparing falsely recognized or falsely recalled forced confabulation items with falsely recognized or falsely recalled yoked control items. The purpose of true-event and new items was only to verify that participants had intact memory for the video; thus, these data are not included in the figures and are summarized in the text. Alpha was set at 0.05 for all analyses, and Fisher’s LSD post hoc tests were employed when the omnibus F test revealed a significant effect. Partial η² and Cohen’s d are reported as measures of effect sizes for ANOVAs and pairwise comparisons, respectively.

3. Results

Our initial analyses revealed no significant effects of stress, overall, on memory. Because previous work has shown that stress and its time-dependent effects on learning and memory can be influenced by cortisol response, we divided stressed participants into cortisol “responders” and “non-responders” based on their cortisol response to the CPT. Specifically, stressed participants exhibiting a cortisol increase of at least 2.5 nmol/l following the CPT were considered responders (N = 31; 17 males, 14 females); all other stressed participants were considered non-responders (N = 18; 6 males, 12 females). This cutoff criterion corresponds to an elevation of approximately 1 μg/dl of serum or plasma cortisol and is thought to reflect a cortisol secretory episode that would occur following a stressor (Kirschbaum et al., 1993; Smeets et al., 2012; Zoladz et al., 2014b). For the analyses of subjective ratings and physiological responses to stress, prior to conducting analyses with responders and non-responders as levels of stress, we performed analyses to assess the effect of stress, overall, on each measure. This allowed us to verify the induction of subjective and objective stress responses in stressed participants as a single group.

3.1. Subjective ratings of water bath manipulation

3.1.1. Analysis of stress effects overall

Stressed participants reported significantly greater pain (d = 3.38) and stress (d = 2.29) ratings than non-stressed participants throughout the water bath manipulation (PAIN RATINGS: main effect of stress: F(1,75) = 294.58, p < 0.001, η²p = 0.80; STRESS RATINGS: main effect of stress: F(1,75) = 101.95, p < 0.001, η²p = 0.58). The pain and stress ratings of stressed participants also significantly increased over time (PAIN RATINGS: main effect of time: F(2,150) = 12.63, p < 0.001, η²p = 0.14; Stress × Time interaction: F(2,150) = 8.27, p < 0.001, η²p = 0.10; STRESS RATINGS: main effect of time: F(2,150) = 3.98, p < 0.05, η²p = 0.05; Stress × Time interaction: F(2,150) = 3.98, p < 0.05, η²p = 0.05).

3.1.2. Analysis of stress effects categorized by responder

Responders and non-responders reported significantly greater pain (responders v. non-stressed: d = 3.88; non-responders v. non-stressed: d = 3.78) and stress (responders v. non-stressed: d = 2.32; non-responders v. non-stressed: d = 2.19) ratings than non-stressed participants throughout the water bath manipulation (PAIN RATINGS: main effect of stress: F(2,73) = 143.62, p < 0.001, η²p = 0.80; STRESS RATINGS: main effect of stress: F(2,73) = 50.30, p < 0.001, η²p = 0.58; Table 1). The pain and stress ratings of responders and non-responders also significantly increased over time (PAIN RATINGS: main effect of time: F(2,146) = 12.96, p < 0.001, η²p = 0.15; Stress × Time interaction: F(4,146) = 5.50, p < 0.001, η²p = 0.13; STRESS RATINGS: main effect of time: F(2,146) = 7.90, p = 0.001, η²p = 0.10; Stress × Time interaction: F(4,146) = 2.45, p < 0.05, η²p = 0.06).

3.2. Physiological responses

3.2.1. Heart rate

3.2.1.1. Analysis of stress effects overall. There was no overall effect of stress on HR (main effect of stress: F(1,73) = 0.03, p > 0.86, η²p = 0.00). The Stress × Time interaction was also not significant, F(2,146) = 2.76, p = 0.066, η²p = 0.04, but there was a weak trend revealing that stressed participants had greater HR than non-stressed participants during the water bath manipulation (d = 0.18).

3.2.1.2. Analysis of stress effects categorized by responder. The stress manipulation had no overall effect on HR (main effect of stress: F(2,71) = 0.05, p > 0.95, η²p = 0.001; Table 2).

3.2.2. Mean arterial pressure

3.2.2.1. Analysis of stress effects overall. Stressed participants exhibited significantly greater mean arterial pressure than non-stressed participants (d = 1.15) during the water bath manipulation (main effect of stress: F(1,73) = 11.03, p < 0.001, η²p = 0.13; main effect of time: F(2,146) = 36.48, p < 0.001, η²p = 0.33; Stress × Time interaction: F(2,146) = 26.62, p < 0.001, η²p = 0.27). Males also exhibited

Table 1

<table>
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<th>DV</th>
<th>condition</th>
<th>Min 1</th>
<th>Min 2</th>
<th>Min 3</th>
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<td>Subjective pain and stress ratings of the water bath manipulation.</td>
<td></td>
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<td></td>
</tr>
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<td>Pain ratings (0-10)</td>
<td>Responders</td>
<td>5.94 (0.36)*</td>
<td>6.59 (0.42)*</td>
<td>7.10 (0.41)*</td>
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<td>Non-responders</td>
<td>6.61 (0.52)*</td>
<td>6.27 (0.46)*</td>
<td>6.80 (0.60)*</td>
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<td></td>
<td>No stress</td>
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<td>0.43 (0.12)</td>
<td>0.46 (0.13)</td>
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<tr>
<td>Stress ratings (0-10)</td>
<td>Responders</td>
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<td>5.41 (0.59)*</td>
<td>5.69 (0.60)*</td>
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<td>No stress</td>
<td>0.43 (0.12)</td>
<td>0.43 (0.12)</td>
<td>0.43 (0.11)</td>
</tr>
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</table>

Data are presented as means ± SEM; * p < 0.05 relative to the no stress group.
Table 2
Cardiovascular activity before, during, and after the water bath manipulation.

<table>
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<th>DV/condition</th>
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<th>During</th>
<th>Post</th>
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</thead>
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<tr>
<td>Heart rate (bpm)</td>
<td>Responders</td>
<td>Non-responders</td>
<td>No stress</td>
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<tr>
<td>Responders</td>
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<td>80.32 (3.28)</td>
<td>72.90 (2.47)</td>
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<td>Non-responders</td>
<td>80.00 (3.13)</td>
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<td>74.39 (2.64)</td>
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<td>No stress</td>
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<td>77.24 (2.54)</td>
<td>73.80 (2.00)</td>
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<tr>
<td>Mean arterial pressure (mm Hg)</td>
<td>Responders</td>
<td>Non-responders</td>
<td>No stress</td>
</tr>
<tr>
<td>Responders</td>
<td>95.51 (1.10)</td>
<td>104.38 (5.08)*</td>
<td>94.52 (3.08)</td>
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<tr>
<td>Non-responders</td>
<td>92.22 (2.79)</td>
<td>104.38 (5.08)*</td>
<td>94.52 (3.08)</td>
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<td>No stress</td>
<td>96.70 (1.91)</td>
<td>95.04 (1.63)</td>
<td>91.55 (1.63)</td>
</tr>
</tbody>
</table>

Data are presented as means ± SEM; * p < 0.05 relative to the no stress group.

significantly greater mean arterial pressure than females (d = 0.85) during the water bath manipulation (main effect of sex: $F(1,73) = 17.72, p < 0.001, \eta^2_p = 0.20$; Sex × Time interaction: $F(2,146) = 3.10, p < 0.05, \eta^2_p = 0.04$).

3.2.2.2. Analysis of stress effects categorized by responder. Responders and non-responders exhibited significantly greater mean arterial pressure than non-stressed participants (responders v. non-stressed: d = 1.34; non-responders v. non-stressed: d = 1.13) during the water bath manipulation (main effect of stress: $F(2,71) = 7.15, p = 0.001, \eta^2_p = 0.17$; main effect of time: $F(2,142) = 50.04, p < 0.001, \eta^2_p = 0.41$; Stress × Time interaction: $F(4,142) = 14.07; p < 0.001, \eta^2_p = 0.28$; Table 2). Males also exhibited significantly greater mean arterial pressure than females (d = 0.93) during the water bath manipulation (main effect of sex: $F(1,71) = 21.15, p < 0.001, \eta^2_p = 0.23$; Sex × Time interaction: $F(2,142) = 3.88, p < 0.05, \eta^2_p = 0.05$).

3.2.3. Salivary cortisol

3.2.3.1. Analysis of stress effects overall. Stressed participants exhibited significantly greater cortisol levels than non-stressed participants (d = 1.16) following the water bath manipulation (main effect of stress: $F(1,80) = 7.30, p = 0.01, \eta^2_p = 0.08$; main effect of time: $F(1,80) = 37.08, p = 0.001, \eta^2_p = 0.32$; Stress × Time interaction: $F(1,80) = 44.01, p < 0.001, \eta^2_p = 0.36$; Fig. 2a).

3.2.3.2. Analysis of stress effects categorized by responder. By definition, responders exhibited significantly greater cortisol levels than non-responders (d = 1.12) and non-stressed participants (d = 1.61) following the water bath manipulation (main effect of stress: $F(2,78) = 3.97, p < 0.05, \eta^2_p = 0.09$; main effect of time: $F(1,78) = 81.45, p < 0.001, \eta^2_p = 0.51$; Stress × Time interaction: $F(2,78) = 84.84, p < 0.001, \eta^2_p = 0.69$; Fig. 2b).

3.3. Memory testing

3.3.1. Recognition testing

3.3.1.1. Probability of assents. Overall, participants displayed intact memory for events that actually occurred in the video, as they exhibited a significantly greater probability of assents for true-event questions (M = 0.86) than new (M = 0.09, d = 4.78) or yoked control (M = 0.11, d = 4.83) questions (main effect of question type: $F(3,216) = 181.58, p < 0.001, \eta^2_p = 0.72$). Participants, overall, also displayed a misinformation effect by exhibiting a significantly greater probability of assents for forced confabulation items (M = 0.32) than yoked control items (M = 0.11, d = 0.66). Importantly, there was a significant Stress × Question Type interaction, $F(6,216) = 2.91, p < 0.01, \eta^2_p = 0.08$, indicating that the misinformation effect was present in responders (d = 1.04) and non-stressed participants (d = 1.18), but was absent in non-responders (d = 0.02; Fig. 3a). The absence of a misinformation effect in non-responders was due to their significantly lower probability of assents for forced confabulation items.

3.3.1.2. Confidence ratings. The confidence ratings from the recognition test ranged from 1 to 10, with 1 indicating an “extremely confident no” and 10 indicating an “extremely confident yes”. Overall, participants had significantly greater confidence ratings for true-event questions (M = 8.80) than new (M = 2.78, d = 5.72) or yoked control (M = 3.38, d = 4.76) questions (main effect of question type: $F(3,234) = 301.96, p < 0.001, \eta^2_p = 0.80$). Participants also displayed significantly greater confidence ratings for forced confabulation items (M = 4.94) than yoked control items (d = 0.86). Both of these effects parallel those reported for the probability of assents described above (Fig. 3b). Stress did not have a significant influence on confidence ratings of participants (main effect of stress: $F(2,78) = 2.28, p < 0.11, \eta^2_p = 0.06$), and the Stress × Question Type interaction was not significant, $F(6,234) = 0.61, p > 0.72, \eta^2_p = 0.02$.

3.3.2. Free recall

Because no participant falsely recalled any yoked control item and the recognition effects were primarily attributable to the forced confabulation answers, we conducted a one-way ANOVA on the proportion of times that a forced confabulation item was falsely recalled, with stress serving as the between-subjects factor. Consistent with our recognition test findings, this analysis revealed that non-responders exhibited significantly fewer recall errors for forced confabulation items than responders (d = 0.89) and no stress participants (d = 0.87) (main effect of stress: $F(2,63) = 3.42, p < 0.05, \eta^2_p = 0.10$; Fig. 4).

![Fig. 2](image-url) Salivary cortisol levels before and after exposure to the water bath manipulation. When conducting the analysis with stressed participants as a single group, the results showed that stressed participants exhibited significantly greater salivary cortisol levels than non-stressed participants following the water bath manipulation (a). When conducting the analysis with stressed participants broken down by cortisol response, responders exhibited significantly greater cortisol levels than non-responders and non-stressed participants following the water bath manipulation (b). Data are expressed as means ± SEM. * p < 0.001 relative to no stress (a, b) and non-responders (b).
4. Discussion

The misinformation effect is a robust phenomenon that can be observed across a variety of situations. In the present study, we have replicated this effect by showing that, overall, participants exhibited a significant likelihood of recognizing and recalling confabulated events that never took place. The most important finding, however, is that this robust effect was completely absent in stressed participants who exhibited a blunted cortisol response to the stressor (i.e., non-responders). This was true for both recognition and recall assessments of false memory, which took place 3 days and 3 weeks following the interview, respectively. 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.

4.1. Neurobiological mechanisms underlying observed effects

Previous work has shown that the temporal proximity of stress, relative to learning, plays a major role in pre-learning stress effects on long-term memory. For instance, brief stressors administered immediately before learning appear to enhance long-term memory (Diamond et al., 2007; Vogel and Schwabe, 2016; Zoladz et al., 2011a; Zoladz et al., 2014c), which is believed to result from non-genomic effects of corticosteroids interacting with a rapid increase in norepinephrine (Diamond et al., 2007; Joels et al., 2011; Schwabe et al., 2012). Thus, we hypothesized that stressing participants immediately before viewing a video clip would enhance their memory for that video and protect it from self-generated misinformation the next day. In contrast, we observed no overall effect of stress on the misinformation effect. Rather, the misinformation effect was blocked only in stressed participants who exhibited a blunted cortisol response to the stress. Importantly, responders and non-responders exhibited comparable stress-induced changes in cardiovascular activity, ruling out the possibility of autonomic differences accounting for these effects. However, as illustrated in Fig. 2, non-responders exhibited higher baseline levels of cortisol than responders. Although this difference was not statistically significant, it presents the possibility that non-responders were in a stressed state prior to the experimental session and thus unable to manifest a CPT-induced increase in cortisol levels comparable to that of responders. In response to this possibility, we would emphasize that all participants were provided with the same rest period prior to the initiation of experimental manipulations and that the aforementioned autonomic responses, as well as the subjective data in reported in Table 1, support similar stress-induced increases of stress levels in responders and non-responders.

Taken together, our results suggest that stress-induced autonomic arousal without a concomitant rise in cortisol protected the video memory from subsequent distortion by misinformation. The notion of autonomic arousal benefitting learning is well-documented in the literature. Numerous studies involving stress-induced increases in arousal or the administration of norepinephrine/epinephrine around the time of learning have reported enhancements of long-term memory (Cahill and Alkire, 2003; Gold and Van Buskirk, 1975; McGaugh, 2004). Indeed, we previously reported that brief, pre-learning stress enhanced long-term memory only in stressed participants who exhibited a robust heart rate response to the stress (Zoladz et al., 2014c), and some have reported better post-stress learning and memory performance in cortisol non-responders who still demonstrate stress-induced increases in autonomic activity (Buchanan and Tranel, 2008; Elzinga and Roelofs, 2005; Zandara et al., 2016). Other investigators have reported a more specific association between arousal and false memory development. Hoscheidt and colleagues (Hoscheidt et al., 2014) found that stressed participants who self-reported higher levels of arousal were less likely to fall victim to the misinformation effect. Importantly, though, autonomic arousal did not enhance participants’ learning in the present study, as there were no group differences observed for the recognition or recall of true-event items from the video. It is possible that the absence of such enhancement was due to a ceiling effect, as the average probability of asents for true-event items was 0.86, leaving little room for improvement.

Our data suggest that a stress-induced increase in cortisol counteracted the positive effects of autonomic arousal on false memory generation. Although this is surprising, given the relatively short period...
of time encompassing the stressor and video (approximately 11 min combined), it is not unprecedented. An extensive amount of work has shown that corticosteroids can exert deleterious effects on learning, memory and their presumed neurobiological underpinnings (de Quervain et al., 2009; Wiegert et al., 2008; Wolf, 2009). There is also a wealth of literature discussing a necessary interaction between the sympathetic nervous system (SNS) and the hypothalamic-pituitary-adrenal (HPA) axis for such effects to emerge. Several studies have shown that stress-related increases in glucocorticoid levels impair cognition only when combined with autonomic arousal (de Quervain et al., 2007; Kuhlmann and Wolf, 2006; Roozendaal, 2003; Roozendaal et al., 2004). Similarly, Andrews and colleagues reported that subjective and objective measures of the stress response differ markedly when one of these systems is rendered inactive (Andrews et al., 2012; Andrews and Pueessner, 2013); for instance, in one study, pharmacological reduction of corticosteroid levels significantly increased baseline and stress-evoked cardiovascular activity and significantly increased subjective stress responses. Thus, a differential effect of stress on behavior in individuals exhibiting a robust versus blunted cortisol response to the stress is consistent with other work in this area.

What is undetermined and should be of particular interest for future research is how stress affects memory formation in responders and non-responders at the neurobiological level such that one is more susceptible to false memory development. One study that lends insight into this issue is that performed by Quaedflieg and colleagues (Quaedflieg et al., 2015). These investigators showed that cortisol responders and non-responders exhibited opposite patterns of connectivity changes in amygdala-prefrontal cortex (PFC) and amygdala-hippocampus circuits during and following acute stress. Specifically, responders exhibited increased amygdala-PFC connectivity during stress, while non-responders exhibited decreased connectivity in this circuit. Following the stress episode, responders exhibited decreased amygdala-PFC connectivity and increased amygdala-hippocampus connectivity; this pattern was completely reversed in non-responders. It is possible that different connectivity changes in brain memory systems of responders and non-responders could account for a different quality of memory in each group, with differential susceptibility to misinformation.

Investigators have suggested that stress promotes the encoding of gist, at the cost of details, thus serving an adaptive function to enhance future survival, but also increasing the rate of false recognition (e.g., Payne et al., 2002; Qin et al., 2012). In the present study, non-responders may have been able to encode more details from the video, which made this memory less susceptible to subsequent misinformation. Another possibility is that non-responders had better source monitoring than responders and controls. That is, non-responders may have formed a memory of the video that remained separate from the memory of the interview experience and the confabulated information produced during that session. Then, during testing, non-responders were better able to discern what information was encoded during the initial video exposure and what information was encoded during the interview. Unfortunately, we did not test source monitoring by asking participants what information they remembered from the video and what information they remembered from the interview, but this is something that should be examined in future work.

4.2. Altered reconsolidation as an explanation

A similar, yet alternative, explanation for the present findings is that reconsolidation processes were less prone to disruption in non-responders. For some time, the dogmatic view of memory consolidation was that once a memory trace was laid down, it was permanent and relatively unable to be modified afterwards. However, based on preliminary research in the 1970s and a surge of research over the past 15 years, it is now well-documented that, even after the initial consolidation phase, when memories are retrieved, they return to a labile state and are susceptible to distortion (Schwabe et al., 2014). In the present study, the interview phase represents a time when participants’ memory of the video was reactivated. In theory, when participants confabulated the misinformation about events from the video, these false memories were incorporated into the original, now reactivated, memory trace. In non-responders, however, this reconsolidation of the original memory trace was unscathed. This could be related to non-responders having kept two separate memory traces, one for the video and one for the interview (leading to better source monitoring, as described above), or it could simply be that the reactivated video memory was less susceptible to reconsolidating misinformation. Clearly, future work is warranted to better understand the differences in memory quality across responders and non-responders.

4.3. Conclusions and limitations

In the present study, we have replicated previous work by demonstrating a robust misinformation effect in participants. Most importantly, we found that this misinformation effect was completely absent in stressed participants with a blunted cortisol response. One limitation of the present study is that we did not obtain saliva samples from participants on the interview and testing days, so participant cortisol levels at those times are unknown. Additionally, even though the video that participants viewed may have added external validity to our experiment, it was not highly arousing. It is well-known that stress effects on learning and memory depend on the emotional nature of the learned information (Zoladz et al., 2011b), and eyewitnessed events are often emotionally arousing. Thus, future research in this area should incorporate highly arousing information as the learning material.

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