

Contents lists available at [ScienceDirect](https://www.sciencedirect.com)

## Journal of Applied Research in Memory and Cognition

journal homepage: [www.elsevier.com/locate/jarmac](http://www.elsevier.com/locate/jarmac)

## Reducing the Consequences of Acute Stress on Memory Retrieval

Amy M. Smith\*, Ayanna K. Thomas

Tufts University, United States

Psychological stress has been shown to impair episodic memory retrieval. Implicated in this memory impairment is the physiological stress response, which interferes with retrieval-related neural processing. An important next step in research is to determine how to improve post-stress memory accessibility. In this review, we first consider methodological differences in studies that have examined stress and memory, as they lend insight into the conditions under which stress does and does not impede retrieval. Motivated by these variations in methodology, we advocate for two potential approaches to intervention. One approach is to employ evidence-based techniques that reduce the physiological stress response. A second approach is to target the processes that occur during initial learning to promote the formation of highly accessible memories. Thus, this review serves to both critically evaluate the methods used to examine the effects of stress on memory retrieval and encourage research on interventions for stress-related memory impairment.

**General Audience Summary**

Psychological stress impairs our ability to remember information. The physiological stress response is implicated in this impairment, as it interferes with neural processing in brain regions that are involved in memory. An important next step in research is to determine how to improve memory in stressful scenarios. In this review article, we advocate for two potential approaches. One approach is to use any of a variety of techniques that help reduce the physiological stress response (e.g., muscle relaxation). A second approach is to use learning strategies that promote the formation of stress-resistant memories (e.g., taking practice tests while learning new information). Discovering interventions for stress-related memory impairment would serve to benefit a host of individuals in their everyday lives, such as professionals in stressful work scenarios and students during high-stakes tests. The interventions described here have not yet been employed as tools for improving memory in the context of psychological stress, and thus we aim to encourage such research in this review.

*Keywords:* Psychological stress, Retrieval, Memory, Cortisol, Intervention

Psychological stress often results in a paradoxical scenario: when we are under pressure to perform our best, we find ourselves performing our worst. This subjective experience of “choking under pressure” has been repeatedly substantiated by memory research. Specifically, over a dozen experiments and a recent meta-analysis have culminated in the consensus that acute incidences of stress temporarily impair memory

retrieval (Shields, Sazma, McCullough, & Yonelinas, 2017). This area of research is rapidly gaining momentum. Two recent papers provided in-depth discussions of the physiological stress response, the empirical literature on the topic, and the theoretical mechanisms that may underlie the detrimental effects of stress on retrieval (Gagnon & Wagner, 2016; Shields et al., 2017). Despite the great strides that have been made to

## Author Note

\* Correspondence concerning this article should be addressed to Amy M. Smith, Psychology Department, Tufts University, 490 Boston Avenue, Medford, MA 02155, United States. Contact: [amy.smith@tufts.edu](mailto:amy.smith@tufts.edu)

better understand how stress impacts retrieval, there has been little discussion of what might be done to mitigate the negative effects that have been observed.

From a practical perspective, discovering interventions for stress-related memory impairment would serve to benefit a host of individuals in their everyday lives. As examples, interventions that target memory accessibility would benefit professionals in stressful work scenarios and students during stressful, high-stakes tests. Such interventions would also serve to test and refine the current theories surrounding the negative effects of stress on memory retrieval. For instance, Schwabe and colleagues (Schwabe, Joels, Roozendaal, Wolf, & Oitzl, 2012) have hypothesized that stress hormones interact in the basolateral amygdala to induce a “memory formation mode” in the stressed brain. When in this state, neural processes related to the encoding and consolidation of information are prioritized at the expense of retrieval. Interventions that yield successful post-stress retrieval would help specify the conditions under which retrieval is and is not impeded by the stress-induced memory formation mode. In their review, Gagnon and Wagner (2016) discussed another neural mechanism by which stress may influence memory, specifically that stress impairs executive functioning. The studies they reviewed demonstrate that stress increases neural activity in areas such as the amygdala and striatum that are associated with reflexive, habitual actions, while simultaneously decreasing activity in regions such as the hippocampus and PFC that support executive functions such as careful, effortful recollection. Demonstrating ways in which memories can be retrieved even when executive resources are impaired would also help refine this hypothesis. With one exception (Smith, Floerke, & Thomas, 2016), researchers have yet to explore ways in which the negative effects of stress on retrieval might be ameliorated. In this piece, our primary goal is to elicit interest in research on interventions for stress-related memory impairment. We will do so by highlighting two evidence-based approaches that have the potential to attenuate the negative effects of stress on retrieval.

### The Scope of the Present Review

In the present review, we use the term *intervention* to refer to a technique that could be used to improve memory accessibility in situations where psychological stress poses a threat to memory retrieval. Generally, the term *intervention* is used in scenarios in which one wishes to modify the outcome of some event. Here, interventions are tools that may modify the memory impairment (outcome) that results from stress (event). Thus, in this context, the term *intervention* may refer to a real-world scenario in which an individual employs a technique to reduce the consequences of stress on her memory, or to an experimental scenario in which a researcher manipulates the use of such a technique in a tightly controlled setting. Because the interventions mentioned in the present review have not yet been examined for their efficacy in stress-and-memory paradigms, the intention of this review is to encourage researchers to explore the use of interventions in experimental settings. By fostering experimental research, we

hope that the broader application of these interventions, such as in clinical or educational settings, will eventually be possible.

The literature reviewed here specifically examines the effects of acute, isolated instances of psychological stress on episodic memory retrieval in healthy adults (for reviews of chronic stress, see Conrad, 2010; Finsterwald & Alberini, 2014). Psychological stress is commonly defined as an uncontrollable and/or unpredictable threat to the physical or social self (Dickerson & Kemeny, 2004). This threat is accompanied by a subjective feeling of mental stress and a physiological response that increases levels of the stress hormone cortisol. Episodic memory refers to memory of events that are associated with a particular time and place. Memory *retrieval* is the phase of episodic memory in which information is recollected after going through the processes of encoding and consolidation. Researchers have examined the impact of inducing stress at various phases of episodic memory (see Gagnon & Wagner, 2016; Schwabe et al., 2012; Shields et al., 2017), but in the wealth of research conducted, retrieval is the only phase of episodic memory that has consistently been negatively affected by stress. Thus, we focus the present review on the deleterious effects of stress on retrieval and the potential for interventions to mitigate those undesirable effects.

### The Physiological Stress Response and Memory Retrieval

In their recent meta-analysis, Shields et al. (2017) confirmed a growing consensus: stress impairs memory retrieval. Further, this impairment was greatest for negatively- and positively-valenced stimuli than for neutral stimuli. The detrimental effects of psychological stress on retrieval are, in part, a consequence of the human stress response. The stress response is characterized by different phases of hormone release, the first of which is initiated by the hypothalamus after a threat has been perceived (Everly & Lating, 2013). From here, preganglionic sympathetic nerves carry neural impulses to the adrenal medulla (Raven, Raven, & Chew, 2010). The stimulated adrenal medulla then serves as the postganglionic release point for epinephrine, prompting the “fight-or-flight” response that prepares the body to take defensive action. Though epinephrine cannot cross the blood-brain barrier to directly affect neural activity, increases in epinephrine initiate a chain of stimulation from the vagus nerve to the solitary nucleus in the medulla to the basolateral amygdala (BLA; Williams & Clayton, 2001). The BLA modulates the learning and consolidation of information, particularly emotional information (McGaugh, Cahill, & Roozendaal, 1996). Thus, memory consolidation is often enhanced after stress (e.g., Andreano & Cahill, 2006; McCullough & Yonelinas, 2013; Smeets, Otgaar, Candel, & Wolf, 2008). During a brief period after the onset of stress (<10 min), memory retrieval may also be enhanced (e.g., Hupbach & Fieman, 2012) or otherwise unaffected (e.g., Schonfeld, Ackermann, & Schwabe, 2014), though literature examining retrieval immediately post-stress is sparse.

The second phase of the stress response is longer lasting and occurs via a different mechanism, referred to as the hypothalamic-pituitary-adrenal (HPA) axis (Everly & Lating, 2013). While the hypothalamus activates the adrenal medulla

during the first phase of the stress response, it simultaneously secretes corticotropin-releasing factor (CRF) that stimulates the anterior pituitary. The anterior pituitary then releases adrenocorticotropic hormone (ACTH) into the bloodstream, triggering the synthesis and release of the human stress hormone cortisol from the adrenal cortex. The release of cortisol from the adrenal cortex is gradual, reaching peak levels in the blood approximately 20 min after the initial detection of a threat (Kirschbaum, Pirke, & Hellhammer, 1993). The magnitude of the HPA axis response to stress varies greatly at the individual level (e.g., Kudielka, Buske-Kirschbaum, Hellhammer, & Kirschbaum, 2004; Uhart, Chong, Oswald, Lin, & Wand, 2006), but is largest and most reliable in stress paradigms involving social evaluation (Dickerson & Kemeny, 2004; Skoluda et al., 2015).

The post-stress release of cortisol can have both desirable and undesirable consequences. Cortisol aids in the metabolism of fats, lipids, and carbohydrates to provide the body with the energy needed to deal with the threat at hand. Cortisol also crosses the blood-brain barrier to exert both positive and negative effects on the brain. In particular, cortisol binds heavily to glucocorticoid and mineralocorticoid receptors in the amygdala and hippocampus, (Lovallo, Robinson, Glahn, & Fox, 2010; Reul & de Kloet, 1985), both of which are implicated in memory formation and retrieval. Increased occupation of glucocorticoid receptors in the amygdala and hippocampus perpetuates the enhancement of memory formation that begins during the first phase of the stress response (Schwabe et al., 2012). However, the prioritization of neural pathways involved in encoding and consolidation comes at the cost of retrieval. Once cortisol levels peak after stress, memory retrieval may be impaired for over an hour (for a review see Gagnon & Wagner, 2016). The amygdala plays a key role in the processing of emotional information, which likely accounts for the finding that emotional memories are impaired to a greater degree than neutral memories.

Retrieval may be further hindered by the stress response as cortisol indirectly reduces activity in the PFC. Working memory deficits and associated reductions in PFC activity have been observed after laboratory stress induction (Gärtner, Rohde-Liebenau, Grimm, & Bajbouj, 2014; Qin et al., 2009). In addition to consuming prefrontal cognitive resources, stress can also bias attention toward threatening objects (see Christianson, 1992). Both of these effects take an individual's mental focus off of retrieval-related processing and may serve to further impair memory retrieval.

In a laboratory setting, researchers commonly use any of three procedures to induce psychological and physiological stress in human subjects: the Trier Social Stress Test (TSST), the Cold Pressor Test (CPT), or the Socially Evaluated Cold Pressor Test (SECPT). During the TSST, participants must give a speech and solve difficult math problems while being videotaped and observed (Kirschbaum et al., 1993). During CPT stress induction, participants must submerge their non-dominant arm in ice water for up to 3 min (Hines & Brown, 1936). The SECPT is an adapted version of the CPT, in which participants are videotaped during arm submersion under the guise that the researchers will later analyze their facial expressions (Schwabe, Haddad, & Schachinger, 2008).

Though the majority of studies on the topic have indeed reported detrimental effects of stress on memory retrieval, a handful of studies have reported null or even positive findings. These discrepant results may be explained by variations in methodology. In a standard paradigm, young adult participants learn verbal or pictorial materials under either incidental or intentional study instructions. In some studies, participants take a free recall test immediately after initial learning to further promote storage of the material. Twenty-four or 48 h later, participants return to the lab for stress induction. Between 15 and 30 min thereafter, once cortisol reaches peak post-stress levels, memory is assessed, typically via a free recall test.

In studies that deviated from the standard methodology outlined above, null or even positive effects of stress on retrieval were reported (Beckner, Tucker, Delville, & Mohr, 2006; Hupbach & Fieman, 2012; Li, Weerda, Milde, Wolf, & Thiel, 2014; Pulpulos et al., 2013; Schoofs & Wolf, 2009; Wolf, Schommer, Hellhammer, Reischies, & Kirschbaum, 2002). These discrepant findings can be explained by variations in methodology. For instance, results have been influenced by the age of the population being investigated, as studies that have examined the effects of stress on retrieval in older adults have typically found null effects of stress (Hidalgo et al., 2015; Pulpulos et al., 2013). This may be because age-related neural changes leave the older brain less sensitive to increases in cortisol (Mizoguchi et al., 2009), and/or because older adults more effectively cope with stress than young adults (Hamarat et al., 2001).

The timing of the memory test relative to when stress is induced has also influenced findings. When tested approximately 25 min post-stress during the cortisol peak, studies typically report negative effects of stress on retrieval. However, when memory is tested immediately post-stress, several studies have reported null effects (Hupbach & Fieman, 2012; Schonfeld et al., 2014; Schwabe & Wolf, 2014; Smith et al., 2016; Zoladz et al., 2014) whereas only one has reported significant memory impairment (Lupien et al., 1997).

Post-stress memory performance also differs according to the type of final memory test administered. The majority of researchers who assessed free recall reported some degree of stress-related memory impairment (Buchanan & Tranel, 2008; Buchanan, Tranel, & Adolphs, 2006; Hidalgo et al., 2015; Kuhlmann, Piel, & Wolf, 2005; Oei, Everaerd, Elzinga, van Well, & Bermond, 2006; Quesada, Wiemers, Schoofs, & Wolf, 2012; Schonfeld et al., 2014; Schwabe & Wolf, 2009; Smith et al., 2016). Findings have been mixed regarding cued recall, with two studies reporting significant impairment (Lupien et al., 1997; Smeets et al., 2008), one reporting marginally significant impairment (Tollenaar, Elzinga, Spinhoven, & Everaerd, 2008), and one reporting null effects (Kuhlmann et al., 2005). Only one experiment used fragment completion and found null effects of stress (Lupien et al., 1997). Finally, the studies that assessed recognition performance found either significant impairment (Merz, Wolf, & Hennig, 2010; Schwabe & Wolf, 2014), selective impairment for stimuli with a positive emotional valence (Domes, Heinrichs, Rimmele, Reichwald, & Hautzinger, 2004; Hidalgo et al., 2015), or no effect of stress on recognition

(Beckner et al., 2006; Buchanan & Tranel, 2008; Li et al., 2014; Pulopulos et al., 2013).

Another likely contribution to discrepant findings in the stress-and-memory literature is the use of multiple free recall tests when participants initially learn stimuli. To promote long-term memory, many researchers have administered tests of free or cued recall immediately after participants study stimuli on the first day of testing. Using memory tests in this manner, which is commonly referred to as retrieval practice, has been shown to yield highly durable long-term memories (for reviews see Roediger & Butler, 2011; Roediger & Karpicke, 2006) and is particularly effective when multiple free recall attempts are made. This may explain why two experiments that employed multiple free recall tests during initial learning reported no detrimental effect of stress on memory (Schoofs & Wolf, 2009; Wolf et al., 2002).

These methodological differences are important to consider because they have implications for interventions for stress-related memory impairment. Interventions may be most helpful for young as opposed to older adults, and should aim to assist memory during the second phase of the stress response when cortisol levels have peaked. The memory task being required should also be considered, as more cognitively effortful memory processes such as free recall are more likely to be negatively affected by stress. Finally, the strategies used during the initial learning of information, such as taking free recall tests, may provide useful interventions themselves. We return to these points later in our subsequent discussion of ways in which post-stress memory accessibility may be improved.

### Improving Post-Stress Memory Accessibility

Two potential approaches to intervention emerge from considering the methods used to examine the effects of stress on retrieval and the results that have been found. One approach is to manage one's physiological response to stress so as to lessen the neural influence of stress hormones. The second is to target the processes that occur during initial learning to promote the formation of highly accessible, stress-resistant memories.

Both strategies have the potential to benefit individuals in many aspects of life, but the strategy of choice in a given scenario is sure to differ. In particular, the strategy that is appropriate in a given situation will depend on whether the source of stress is expected or unexpected. Consider a trial attorney who experiences a stress response each time she presents closing arguments, or a soldier who will soon enter into combat and must remember her protocol under those stressful circumstances. In both of these instances, individuals know in advance that they will be stressed *and* will need to remember crucial information. Similarly, the student who is aware that she experiences stress when taking high stakes exams knows that a stress response is to be expected. In all of these scenarios, it may not be feasible to employ a stress-reduction technique immediately after the onset of stress. In such cases in which an upcoming, unavoidable stress response is anticipated, an intervention that focuses on using effective learning techniques to bolster memory in advance would be best suited. On the other hand, interventions that serve to reduce

**Table 1**

*Interventions that Show Potential for Improving Memory Accessibility in the Context of Acute Psychological Stress*

| Intervention                             | Description   |
|--|---|
| Emotional                                |   |
| • Positive reminiscence                  | Recollecting positive autobiographical memories   |
| • Goal-shifting                          | Reframing a task as others-promoting instead of self-promoting  |
| • Somatic relaxation                     | Performing guided muscle relaxation   |
| • Mindfulness                            | Increasing conscious awareness of emotions and their cognitive influence                                      |
| • Cognitive reappraisal                  | Viewing the stress response as adaptive instead of maladaptive  |
| • Cognitive-behavioral stress management | Multiple, clinician-guided training sessions on stress management   |
| Pharmacological                          |   |
| • Mifepristone                           | Glucocorticoid receptor antagonist  |
| • NBI-34041                              | Corticotropin-releasing factor antagonist   |
| • Propranolol                            | $\beta$ -adrenoreceptor antagonist  |
| • Buprenorphine                          | Partial opioid agonist  |
| • Lamotrigine                            | Glutamate release inhibitor   |
| • Alprazolam                             | Benzodiazepine and GABA positive allosteric modulator   |
| • Oxytocin                               | Neuropeptide (stress-related mechanism unknown)   |
| Environmental                            |   |
| • Dogs                                   | Interacting with a friendly dog   |
| • Pornography                            | Viewing erotic photographs  |
| • Music                                  | Listening to music for the purpose of relaxing  |
| Cognitive                                |   |
| • Retrieval practice                     | Self-testing; During learning, attempting to recollect to-be-remembered information without referencing notes |

the stress response would be more useful when a source of stress is unexpected. Some examples include receiving a stressful phone call before giving a formal presentation at work, or encountering an aggressive driver on the road prior to teaching a class. Essentially, in any instance in which we encounter an unexpected stressor prior to needing to retrieve information, techniques designed to reduce the stress response would be most appropriate because the "bolster memory" approach would not be possible. Instead, the downstream effects of stress on memory might be attenuated if stress-reduction techniques are employed soon after the event. Here we will discuss the two approaches to intervention, the ample literature supporting both strategies, and the scenarios in which each strategy may be most appropriate. A summary of the interventions discussed can be found in [Table 1](#).

### Reducing the Stress Response

Understanding the physical mechanism by which stress impairs memory is helpful in determining how to approach the topic of intervention. Stress-related memory inaccessibility is believed to result from increased occupation of glucocorticoid receptors in brain regions that are crucial for retrieval. Thus, reducing the physiological response to stress has the potential to ameliorate the effects of stress on memory. Several different

techniques have been shown to effectively reduce the magnitude of the cortisol response to psychological stress induction. However, to date, none of these strategies has been applied in a stress and memory paradigm.

The strategies that researchers have used in this manner can be categorized according to the mechanism by which they function: emotional, pharmacological, and environmental. Emotional strategies are those that change one's mindset via endogenous cognitive effort. Pharmacological strategies serve to enact physiological changes, and sometimes cognitive changes, through the administration of a drug. Environmental strategies are those that influence one's mindset through exogenous means via the presence of a physical stimulus. We propose that the success of any given class of intervention will depend on the context in which stress is experienced, particularly whether the stressor is expected or unexpected.

**Emotional approaches.** Several interventions that target one's mindset have been shown to reduce the cortisol response to psychological stress. Because many of these strategies do not require any external support from a coach or therapist, they could potentially be employed after the onset of stress. Thus, we speculate that they may be particularly useful as "quick fixes" after one encounters an unexpected source of stress. Interventions of this nature include reminiscing about positive memories (e.g., [Speer & Delgado, 2017](#)), goal-shifting (e.g., [Abelson et al., 2014](#)), somatic relaxation, mindfulness training (e.g., [Cruess et al., 2015](#)), and cognitive reappraisal (e.g., [Jamieson, Nock, & Mendes, 2012](#)).

Engaging in positive reminiscence has been shown to attenuate the cortisol response to stress. When instructed to recall either positive or neutral autobiographical memories immediately after completing the SECPT, participants in the positive group demonstrated a lower post-stress cortisol increase than those in the neural group ([Speer & Delgado, 2017](#)). Similarly, when participants preparing for a fictitious job interview were encouraged to focus on ways in which the job opportunity could positively affect others, post-interview cortisol levels were lower when compared to a group who did not receive these goal-shifting instructions ([Abelson et al., 2014](#)). Both of these studies suggest that the stress response is influenced by conscious and active cognitive processes (e.g., retrieval and/or reframing).

Also shown to positively impact the cortisol response to stress through conscious cognitive effort are somatic relaxation training, which guides individuals through a series of muscle relaxation statements, and mindfulness training, which encourages individuals to be consciously aware of their emotions and to not allow their emotions to have a significant impact on their subsequent thoughts ([Cruess et al., 2015](#)). That is, participants who engaged in somatic relaxation prior to a stress manipulation demonstrated a lower cortisol response as compared to a control group. Further, participants who received mindfulness training who also reported feeling less stressed during stress induction also demonstrated lower post-stress cortisol levels.

Although cortisol has not been measured in cognitive reappraisal studies designed to examine the impact of reappraisal on stress reduction, cognitive reappraisal also shows promise. In one study, participants were given reappraisal instructions that

encouraged participants to view the body's response to stress as an adaptive one that helps successfully address stressors ([Jamieson et al., 2012](#)). Similar to mindfulness training, reappraisal of the body's stress response accompanied a lower cardiovascular response to stress, comparing participants who used reappraisal to those who did not. Another demonstration of the value of rethinking the stress response comes from a study in which participants completed a questionnaire assessing stressful life events and coping strategies for dealing with stress several weeks before laboratory stress induction ([Crum, Salovey, & Achor, 2013](#)). Of the individuals who demonstrated a heightened cortisol response to stress, those who endorsed a "stress-is-enhancing" mindset had a lower cortisol response to the TSST than those who endorsed a "stress-is-debilitating" mindset. Corroborating the findings regarding cognitive reappraisal, these results suggest that encouraging individuals to view the stress response as beneficial may reduce the cortisol response to stress.

Though not a quick-fix strategy, another example of an effective "rethinking stress" intervention is a cognitive-behavioral stress management course involving cognitive restructuring, problem-solving, self-instruction, and progressive muscle relaxation ([Gaab et al., 2003](#)). Participants in this study attended two seven-hour training sessions on stress management, led by a postdoctoral psychotherapist, and subsequently completed the TSST. As expected, those who received the stress-reduction intervention demonstrated a lower cortisol response to the TSST than a no-intervention control group. This particular intervention shows promise for having a long-term positive impact on stress reactivity, and may be useful for individuals who anticipate an upcoming stressor that may interfere with their memory. For example, students might benefit from stress management training of this nature in the weeks leading up to the SAT test.

In summary, positive reminiscence, goal-shifting, somatic relaxation, mindfulness, cognitive reappraisal, and cognitive-behavioral stress management training all show promise for reducing the cortisol response to stress. When employed prior to a stressful event, these techniques may be of further use for improving memory accessibility. However, emotional interventions require conscious, cognitive effort. Thus, even if a given technique effectively reduces the stress response, memory impairment could still result from the cognitive burden imposed by the technique itself. To our knowledge, none of the studies using the mentioned techniques have reported substandard memory performance. For instance, [Richards and Gross \(2000\)](#) found that use of cognitive reappraisal did not affect participants' verbal or nonverbal memory performance. Nonetheless, future researchers using these strategies should take care to tease apart whether any observed memory impairment is the result of stress-related or intervention-related cognitive burden.

**Pharmacological approaches.** Multiple drug interventions have been shown to effectively reduce the cortisol response to psychological stress. Common to all of these drugs is the fact that they must be administered well before a stressful event, and thus only have the potential to improve post-stress memory in situations in which stress is anticipated. Further, for reasons we

will describe, these drugs vary widely in their potential for use in real-world stressful circumstances.

Several drugs of this nature act on the neural pathways involved in the stress response, namely, the HPA axis and the sympathetic nervous system. For instance, a glucocorticoid receptor (GR) antagonist called mifepristone has been shown to improve memory retrieval in young men when administered under non-stressful conditions (Rimmele, Besedovsky, Lange, & Born, 2013). However, in a separate group of participants in this same experiment, administration of a mineralocorticoid receptor (MR) antagonist called spironolactone resulted in memory impairment. These findings are particularly important because they suggest that memory retrieval is optimized when the occupation of GRs is relatively low and the occupation of MRs is relatively high. A next step in research is to determine whether GR antagonists, and potentially MR agonists, exert positive effects on memory retrieval in the context of psychological stress induction. Future researchers should note that mifepristone is also a progesterone antagonist that is commonly used to terminate pregnancy, and thus is not safe for use with female participants (Cadepond, Ulmann, & Baulieu, 1997).

Similarly targeting the HPA axis, a CRF antagonist called NBI-34041 has been shown to attenuate the cortisol response to stress. Specifically, male participants treated with daily doses of NBI-34041 for two weeks prior to the TSST demonstrated a reduced cortisol response to stress when compared to a placebo group who also underwent stress induction (Ising et al., 2007). Recall that CRF is released by the hypothalamus during a stress response, resulting in the cascade of hormones that ultimately results in the secretion of cortisol. By antagonizing CRF receptors, NBI-34041 has the potential to stop the HPA-axis response to stress at its source.

By targeting the stress response of the sympathetic nervous system, the beta-adrenergic antagonist propranolol may also improve post-stress memory retrieval. Research suggests that retrieval may only be impaired when stress causes simultaneous elevations in both cortisol and catecholamines (Roozendaal, Barsegyan, & Lee, 2008). Thus, although propranolol does not influence cortisol levels, by reducing the influence of epinephrine on the stressed brain it may consequently improve retrieval. In an experiment in which both propranolol and glucocorticoids were pharmacologically manipulated, individuals who only received glucocorticoids demonstrated memory impairment whereas those who received both drugs did not (de Quervain, Aerni, & Roozendaal, 2007). However, it remains to be determined whether propranolol would similarly protect memory retrieval in the context of psychological stress induction, such as the TSST. In terms of application, propranolol is not presently available over the counter in the United States, which limits its utility as an intervention for those who do not need to treat the heart and circulatory conditions for which it is commonly prescribed.

Several drugs that do not act directly on systems related to the physiological stress response (i.e., the HPA axis and the sympathetic nervous system) have also demonstrated utility in lowering post-stress cortisol levels. When administered 1.5 h before the TSST, buprenorphine, an opioid agonist/partial agonist used to

treat severe pain and opioid addiction, has been shown to reduce post-stress cortisol levels (Bershad, Jaffe, Childs, & de Wit, 2015). Via its interaction with opioid receptors, buprenorphine reduces the amount of ACTH released during a stress response, thereby reducing the amount of cortisol released. Similarly, lamotrigine, which is a drug used to treat bipolar disorder (Makatsori et al., 2004), and alprazolam (Xanax), a benzodiazepine used to treat anxiety disorders (Fries, Hellhammer, & Hellhammer, 2006), have also been shown to reduce the cortisol response to the TSST. However, all three of these drugs can be accompanied by a host of side effects and are typically only prescribed by a medical doctor. Further, though its effects on memory are unknown, buprenorphine in particular has been shown to reduce attentional focus (MacDonald, Gough, Nicoll, & Dow, 1989), increase fatigue, and increase reaction time (Saarialho-Kere, Mattila, Paloheimo, & Seppälä, 1987). In light of the potential side effects, we suggest that these pharmacological interventions may be best reserved for clinical use as is currently the case. However, future research could help determine whether low doses might still reduce the cortisol response to stress and cause fewer side effects.

Finally, intranasally-administered oxytocin is potentially another pharmacological means by which to intervene on the stress response. In a recent meta-analysis, Cardoso, Kingdon, and Ellenbogen (2014) found that oxytocin attenuated the cortisol response to laboratory stressors that activated the HPA axis, including all four studies that specifically used the TSST to induce stress. Though the physiological mechanism by which this occurs is not yet understood, intranasal oxytocin shows promise as a safe, easily administered pharmacological intervention for memory impairment resulting from psychological stress. Though it is administered intranasally, it should be noted that presently the effectiveness of oxytocin is contingent on being administered 30–90 min prior to a stressful event (see Cardoso et al., 2014).

In summary, GR and CRF antagonists, beta-adrenergic antagonists, opioid agonists, a few mood-altering drugs, and oxytocin may be useful for buffering the cortisol response to psychological stress. As with emotional interventions, researchers should use caution when manipulating drug use in experiments examining the effects of stress on memory. Pharmacological interventions undoubtedly have the potential to interact with cognitive functions, including memory.

**Environmental approaches.** There have been far fewer studies examining the efficacy of environmental manipulations at decreasing the cortisol response to psychological stress. The handful of studies that do exist suggest techniques that have limitations in real-world implementation or have not yielded robust findings. For instance, research has demonstrated that playing with a friendly dog prior to the TSST resulted in lower cortisol levels for children with a disorganized attachment disorder than playing with either a toy dog or a friendly human (Beetz et al., 2015). Researchers have also found that the cortisol response to the TSST can be attenuated in college-aged men when they view erotic photographs prior to stress induction (Creswell, Pacilio, Denson, & Satyshur, 2013). Though both of these studies provide early evidence for techniques that may be efficacious

in the context of stress, the implications of these findings are presently limited to specific populations: children with disorganized attachment in the former study, and young men in the latter study. Further, these interventions have practical limitations. Many stressful scenarios would not provide the appropriate context in which to interact with a dog or view erotic pictures.

One environmental intervention that may be easier to implement is listening to music, although the findings on the topic have been mixed. Most research has occurred in naturalistic settings (for a review, see [Chanda & Levitin, 2013](#)). For example, choosing to listen to music for purposes of relaxation has been shown to lower cortisol levels in college students ([Linnemann, Ditzen, Strahler, Doerr, & Nater, 2015](#)). Similarly, in a laboratory setting, listening to music during ([Rickard & Knight, 2001](#)) and after ([Khalifa, Bella, Roy, Peretz, & Lupien, 2003](#)) stress induction has been shown to attenuate post-stress increases in cortisol. However, one study found that 10 min of relaxing music before the TSST actually increased post-stress cortisol levels relative to a control group ([Thoma et al., 2013](#)). This discrepancy calls for further research on the cortisol-reducing power of music. In a world in which smartphones and MP3 devices are readily available, music shows great potential as a stress-reduction technique that could be easily implemented in anticipation of a stressful event or as a quick-fix solution after an unexpected stressor.

In summary, friendly dogs, erotic photographs, and music may help reduce the physiological response to psychological stress and, in turn, improve post-stress memory performance. However, at this stage, all of these techniques face limitations that need to be addressed in future research. As with emotional and pharmacological approaches to intervention, researchers investigating the utility of environmental approaches should consider the cognitive consequences of the interventions themselves. For example, dogs and erotic photographs have the potential to distract attention away from a memory test and incidentally impair performance.

### Creating Stress-Resistant Memories

A second approach to promoting post-stress retrieval success is to use strategies during initial learning that strengthen memory representation and increase memory accessibility. Though retrieval is impaired soon after the onset of stress, it is not rendered completely dysfunctional; many memories are still accessible under stress. For instance, one is unlikely to forget her home address under stressful conditions since this information is well-learned. As opposed to managing the physiological stress response in order to avoid memory inaccessibility, this approach to intervention targets initial learning with the goal of creating highly retrievable memories that are robust to stress. This strategy may be particularly useful when preparing for scenarios in which a stress response is both foreseeable and unavoidable. Further, this strategy may be better able to address the issue of greater post-stress memory impairment for emotional than neutral information (see [Shields et al., 2017](#)). Whereas interventions that reduce the physiological stress response are likely to indiscriminately improve memory for all to-be-remembered

information, interventions that bolster memory through effective learning could be used to selectively enhance the emotional memories that are most vulnerable to stress.

As previously discussed, the studies that examined the effects of psychological stress on memory retrieval varied greatly in the procedures employed during initial learning of stimuli. Participants were typically either given nonspecific instructions (incidental learning) or were told to memorize the stimuli for a later memory test (intentional learning). In about half of the studies, participants also completed one or more recall tests during this encoding phase. Thus, researchers did not directly manipulate the learning strategies that participants used during encoding. When given instructions to “memorize” stimuli, it is impossible to determine whether participants chose to study using less effective strategies such as rote rehearsal or highly effective strategies such as mental imagery (e.g., [Smith, Barresi, & Gross, 1971](#)). Thus, the body of research on stress and memory does not adequately address whether all memory representations are subject to the detrimental effects of stress or whether only those of a certain quality are vulnerable.

In a first step toward addressing this issue, [Smith et al. \(2016\)](#) used a highly effective, memory-bolstering technique to promote memory accessibility under stress. As in previous studies, they employed a two-day method in which participants learned stimuli and returned the next day to complete the TSST and a subsequent memory test. All participants were initially presented with a series of words and pictures. For half of participants, these stimuli were then presented three successive times, mirroring the conventional “restudying” approach to learning. The other half of participants engaged in retrieval practice, in which they completed three successive free recall tests for the stimuli. To reiterate, retrieval practice has consistently yielded better long-term memory performance than the former strategy of restudying (for reviews, see [Karpicke, Lehman, & Aue, 2014](#); [Roediger & Karpicke, 2006](#)). Replicating the wealth of previous studies, among individuals who engaged in restudying, those who were stressed recalled fewer items than those who were not stressed. However, the results were different for those who engaged in retrieval practice: stressed and non-stressed participants demonstrated similar recall and outperformed both restudy groups. Thus, when retrieval practice was used to boost memory accessibility, the typical impairing effects of stress were no longer observed.

Though [Smith et al. \(2016\)](#) were the first to directly pit conventional restudying against retrieval practice in a stress and memory experiment, previous researchers used study/test cycles during initial learning and reported similar results ([Schoofs & Wolf, 2009](#); [Wolf et al., 2002](#)). These studies suggest that when testing is employed during initial learning, stress is less likely to impair retrieval. Hence, successful post-stress retrieval may be contingent on whether memory representations are adequately strengthened during initial learning. Retrieval practice has emerged as one means by which this may be accomplished.

As noted in a recent commentary, the idea that certain learning techniques may improve post-stress memory accessibility calls for new theoretical and applied perspectives on the topic

of stress and memory (Wolf & Kluge, 2017). Researchers may consider looking to theoretical models of memory to determine why some memories, like those strengthened by retrieval practice, are still accessible when we are stressed. The results from studies examining how stress influences retrieval suggest a negative relationship between the cognitive demands of memory tests and the amount of information retrieved under stress. For example, as mentioned in our discussion of the methodological differences, stressed individuals tend to underperform on free recall tests but not recognition tests. This pattern of results suggests that conscious, effortful recollection is more likely to be compromised under stress than automatic, familiarity-based retrieval. Further research is needed to directly examine the contributions of automatic and controlled memory processes during post-stress retrieval.

The finding that retrieval practice, in particular, strengthens memory against psychological stress also raises the question of whether other highly effective learning strategies could yield a similar outcome. It is unclear whether the efficacy of retrieval practice in this context owes to a mechanism that is specific to this strategy, or to a mechanism that more generally promotes memory accessibility as other mnemonic techniques do. The episodic context account is currently the most compelling and strongly supported theory used to explain the robust testing effect (e.g., Criss & Shiffrin, 2004; Jang & Huber, 2008; Whiffen & Karpicke, 2017). This account is based on the premise that each attempt at retrieving a desired memory happens in a novel context. For example, a given retrieval attempt may occur at a different time, in a different physical location, and/or while in a different mental state than earlier attempts. Thus, during retrieval practice, each retrieval attempt updates the retrieved memory with new contextual information (Karpicke et al., 2014). On a final memory test, an individual who has engaged in retrieval practice therefore has multiple contextual cues available for guiding his or her memory search. One direction for future research would be to examine whether the detrimental effects of stress on retrieval can be explained by a lack of access to helpful contextual cues of this nature.

Researchers may also consider moving forward by examining the efficacy of other strategies that, like retrieval practice, improve long-term memory relative to rote memorization (for a review of strategies see Dunlosky, Rawson, Marsh, Nathan, & Willingham, 2013). One example of such a technique is interactive imagery, which involves imagining to-be-remembered stimuli interacting with each other in a meaningful way (Bower, 1970, 1972). Optimally, future researchers will better characterize the types of memories that remain accessible in the context of acute stress and will identify a host of study strategies that promote post-stress memory accessibility. Such research will inform our understanding of memory representations and will have direct implications in the classroom, where students and educators will be able to use evidence-based teaching and learning practices that result in stress-resistant memories.

As a final note, future researchers may also wish to examine whether stress differentially affects episodic and semantic memory. In contrast to episodic memory, which encompasses memory for events that are associated with a specific time and

place, semantic memory refers to our general knowledge for which we have no source information (e.g., the Earth revolves around the Sun). The literature reviewed in the present piece solely examined episodic memory, whereas the effects of stress on semantic memory are less understood. In the only study to examine semantic memory, Merz, Dietsch, and Schneider (2016) induced stress using the SECPT and measured subsequent performance on a true/false test involving statements of scientific concepts that are typically acquired during childhood (e.g., a moving bullet loses speed). Relative to a non-stressed control group, stressed individuals did not demonstrate differences in true/false accuracy. This finding raises a host of questions that could be addressed in future research. First is the question of whether Merz et al. (2016) found null results because semantic memory for scientific concepts is immune to stress, or because low-demand memory tests like their true/false test tend to be unaffected by stress. This could be addressed in an experiment examining the effects of stress on free recall of semantic memories. Future researchers may also consider examining whether these findings hold true for other types of semantic memory (e.g., properties of objects) and for semantic memories that vary in how recently they were acquired.

## Conclusions

A wealth of literature suggests that psychological stress impairs memory retrieval. This memory impairment is likely the byproduct of the physiological stress response, which reduces neural activity in retrieval-related brain regions. Given this robust finding, we encourage researchers to consider developing interventions to improve memory accessibility in the context of a stressful event. One approach to intervention may be to use various emotional, pharmacological, or environmental techniques to attenuate the physiological response to stress. Another potentially complimentary approach may be to use evidence-based learning strategies to improve memory accessibility in the presence of stress. We hope that the topics discussed here motivate research on interventions for stress-related retrieval impairment, and we caution researchers to approach the topic of intervention with careful scrutiny of the methodological variations we have discussed. Considering the frequency with which people experience acute psychological stress in everyday life, many stand to benefit from this budding area of inquiry.

## Conflict of Interest Statement

The authors declare no conflict of interest.

## Author Contributions

Amy Smith conducted the literature search for the present review and drafted the manuscript. Ayanna Thomas provided feedback and contributed to revisions of the manuscript.

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Received 1 July 2017;

received in revised form 25 September 2017;

accepted 25 September 2017

Available online xxx