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Acute stress and episodic memory retrieval: neurobiological mechanisms and behavioral consequences

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Episodic retrieval allows people to access memories from the past to guide current thoughts and decisions. In many real-world situations, retrieval occurs under conditions of acute stress, either elicited by the retrieval task or driven by other, unrelated concerns. Memory under such conditions may be hindered, as acute stress initiates a cascade of neuromodulatory changes that can impair episodic retrieval. Here, we review emerging evidence showing that dissociable stress systems interact over time, influencing neural function. In addition to the adverse effects of stress on hippocampal-dependent retrieval, we consider how stress biases attention and prefrontal cortical function, which could further affect controlled retrieval processes. Finally, we consider recent data indicating that stress at retrieval increases activity in a network of brain regions that enable reflexive, rapid responding to upcoming threats, while transiently taking offline regions supporting flexible, goal-directed thinking. Given the ubiquity of episodic memory retrieval in everyday life, it is critical to understand the theoretical and applied implications of acute stress. The present review highlights the progress that has been made, along with important open questions.

Keywords: anxiety; declarative memory; hippocampus; medial temporal lobe; prefrontal cortex

Introduction

The ability to store and retrieve memories enables us to span temporal gaps by using information from the past to inform our thoughts, decisions, and actions in the present and to prospectively plan for the future. Memory retrieval may be strongly influenced by current emotional state, especially emotional states induced by acute stress. Given the pervasive nature of psychological stress in everyday life, characterizing the mechanisms by which such stress affects our ability to retrieve information from memory is critical for understanding the effects of stress in educational, legal, and social contexts, and may offer valuable insight into the development of treatments for individuals suffering from stress-related clinical disorders.

Over the past several decades, research in neuroscience and experimental psychology has probed the effects of stress on episodic/conscious memory for the "what," "where," and "when" of everyday events. While much work has explored the effects of acute and chronic stress on memory encoding and consolidation, the extent to which acute stress specifically influences retrieval processes in humans is less well understood. Here, we review the literature on what is known about the effects of acute stress on episodic memory retrieval, with a focus on emerging evidence showing that different stress systems interact at different timescales to drive neural changes across the brain, bias attention, and shift reliance from a goal-directed, episodic memory system to a habit-based memory system.

More specifically, this review (1) draws upon evidence from numerous cognitive neuroscience methods, including neurohormonal manipulations and functional brain imaging, (2) focuses primarily on episodic memory retrieval in humans, and (3) applies theories derived from research in nonhuman animals when interpreting the literature. We begin by reviewing the timescale of neural effects of

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stress, delineating the rapid sympathetic nervous system (SNS) release of catecholamines and the slower hypothalamic–pituitary–adrenal (HPA) axis release of glucocorticoids. We briefly consider the effects of these two stress systems on episodic encoding and consolidation. The bulk of the review then evaluates the effects of stress on retrieval, discussing factors that may modulate the frequently observed retrieval impairments. In addition to the detrimental effects of stress on hippocampal-dependent retrieval, we consider how stress influences attention and prefrontal function, which could further influence controlled retrieval processes. Finally, we consider recent data suggesting that stress at retrieval upregulates activity in a network of brain regions that enable a reflexive, rapid response to an upcoming threat, while taking offline regions involved in flexible, goal-directed thinking.

Time course of neural effects of stress

Psychological stress (hereafter, stress) has been defined as a reaction to situations that are characterized by (1) novelty, (2) uncertainty, and/or (3) uncontrollability,[1] or (4) a threat to the social self (e.g., status, reputation).[2] These four characteristics predict the stress response and the corresponding release of related stress hormones in humans.[3] A stressor may also include negative situations that capture attention and attenuate cognitive resources (e.g., poverty).[4–6] Paralleling the definition of stress, anxiety has been defined as the response to uncertain or unpredictable threat, "a response which encompasses physiological, affective, and cognitive changes."[7] Given that the uncertainty about an uncontrollable negative future event is aversive and tends to elicit stress responses, anxiety-like behavior, and neural activity,[8,9] the uncertainty and anticipation model of anxiety[10] proposes that anticipatory neurobiological and psychological responses under conditions of uncertainty about a future threat are generally adaptive, but abnormalities in these processes (e.g., amygdala hyperactivity) may underlie psychopathologies such as anxiety disorders, and may amplify the effects of stress on cognition.

During stress exposure, physiological responses drive activation of two stress systems: (1) the rapid SNS release of the catecholamines epinephrine and norepinephrine, which, in turn, drive amygdala activation;[11,12] and (2) the slower HPA axis release of glucocorticoids[13] (cortisol in humans), which can exert faster nongenomic effects (i.e., interacting with membrane receptors) and slower genomic effects on the brain (i.e., altering gene transcription).[14–17] Together, the activation of these stress systems affects neural activity throughout the brain,[12,18,19] most notably in the hippocampus, amygdala, striatum, and prefrontal cortex (PFC). Critically, the distinction between these two stress systems, and their respective time courses, is an important factor in understanding the mechanisms underlying the neurobiological and cognitive effects of stress on episodic memory (Fig. 1).

Rapid catecholaminergic response to emotional stimuli

On the shortest timescale, the occurrence of a transient, emotionally arousing event (e.g., spotting a snake on the path ahead) can capture attention[20] and elicit sympathetic arousal, enhancing memory for the event. Similarly, exposure to a stressor initiates rapid activation of the SNS, release of catecholamines, and subsequent noradrenergic basolateral amygdala (BLA) activation and is the first wave in a series of neuromodulatory changes induced by stress.[19] Extensive evidence suggests that emotional arousal enhances episodic memory by activating the BLA, which modulates encoding and consolidation processes in the medial temporal lobe (MTL).[21] In one landmark study, increased activity in the amygdala during the encoding of emotional films predicted enhanced subsequent recall for the films.[22] Findings from nonhuman animals further demonstrate that the initial exposure to an emotionally arousing situation induces noradrenergic BLA activation through the activation of vagal afferents to the nucleus of the solitary tract (NTS).[11,23] Noradrenergic cells in the NTS project to the BLA both directly and indirectly via the locus coeruleus,[11] and noradrenergic activity in the BLA modulates the function of the caudate nucleus, hippocampus,[24] and PFC,[25] among other brain regions. Converging evidence for the role of the amygdala in enhancing memory for arousing versus neutral stimuli has been found in participants during the viewing of emotional scenes,[26] words,[27] and objects.[28] Critically, blocking sympathetic arousal with propranolol and selective damage to the amygdala bilaterally[29,30] reduces this emotion-induced memory enhancement, demonstrating

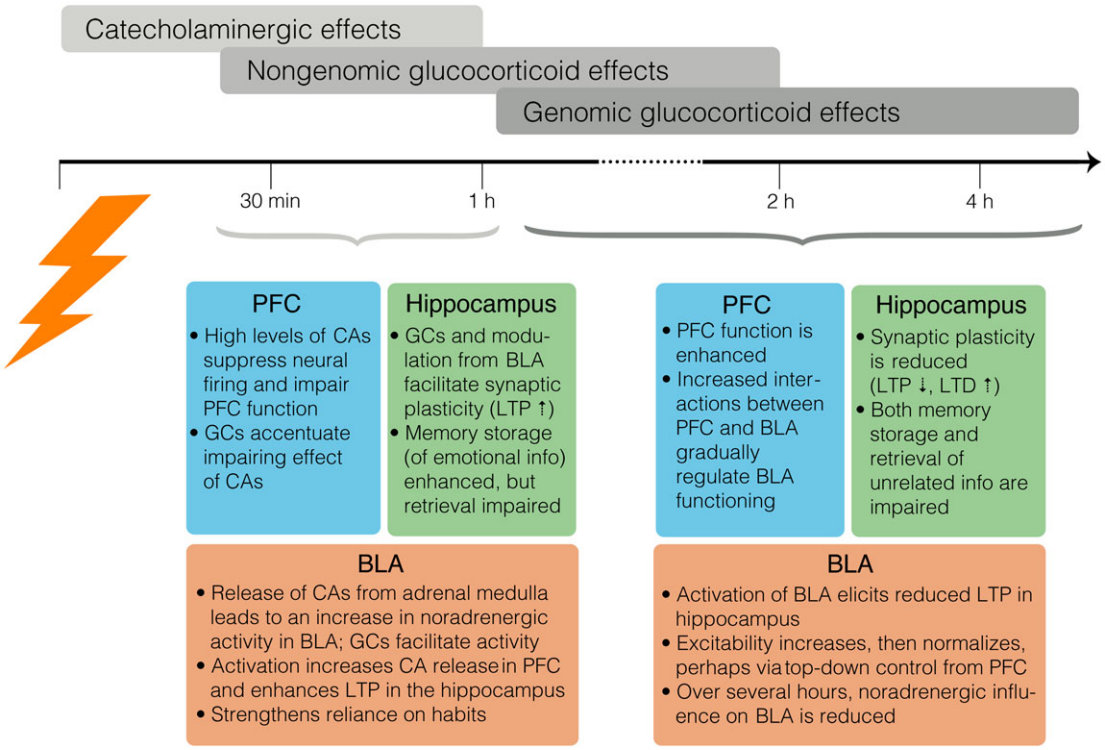

Figure 1. A schematic representation of the effects of stress over time. Approximately 20 min after the onset of a stressor, stress-induced catecholamine and nongenomic glucocorticoid actions interact to increase functioning of the BLA, while enhancing hippocampal plasticity and disrupting prefrontal function. During this time window, memory storage of the stressor and novel emotional information is facilitated, but retrieval of unrelated information is impaired. One to 2 h after exposure to the stressor, cortisol levels decrease and slower genomic glucocorticoid actions begin to reduce dorsal hippocampal plasticity and to modulate amygdala and prefrontal function; these processes impair both storage and retrieval of unrelated information. CA, catecholamine; GC, glucocorticoid; BLA, basolateral amygdala; PFC, prefrontal cortex.

the importance of the SNS–amygdala pathway in enhancing episodic memory for emotional stimuli.

Release of glucocorticoids and interactions with catecholaminergic activation

While rapid, relatively transient activation of the SNS, elicited by the brief presentation of an emotional stimulus or exposure to a stressor, can enhance memory and initiate a cascade of noradrenergic activity in the BLA, acute stress can also influence memory several minutes later by triggering an increase in glucocorticoid levels. Perception of a stressful stimulus leads to the release of hormones from the hypothalamus and pituitary gland, in turn, triggering the release of the glucocorticoid hormone cortisol (corticosterone in rodents) from the adrenal cortex.[3] Relative to SNS effects, activation of the HPA axis occurs over a longer period of time, with cortisol levels peaking at 20–40 min following stressor onset and a return to baseline cortisol levels typically occurring 40–60 min following stressor termination.[13,31]

Decades of research demonstrate that the hippocampus is critical for the successful encoding and retrieval of episodic memories.[32–35] Following the initial discovery that the rat hippocampus has a dense concentration of glucocorticoid and mineralocorticoid receptors (GRs and MRs)[36–39] and parallel findings that the human hippocampus expresses high levels of GR and MR mRNA,[40] much of the extant literature examining stress effects on memory has focused on the link between the hippocampus and the HPA axis.[41–43] High levels of glucocorticoid hormones in brain structures with dense GRs are particularly harmful to neural function, because glucocorticoids bind to GRs, impairing metabolism, cell survival, and neuronal morphology (with the caveat that much of this work in rodents has been conducted on male rats[44]).[45]

As a result, hippocampal-dependent memory processes are particularly affected by stress-induced glucocorticoid release.[46]

Early nongenomic glucocorticoid actions and catecholaminergic interactions

Glucocorticoids released in response to a stressor can exert fast nongenomic and slow genomic effects.[47] Following HPA activation in response to stress exposure, glucocorticoids cross the blood–brain barrier and bind to GRs throughout the brain, particularly in the hippocampus, amygdala,[39] and PFC.[48] Combined with stress-induced catecholaminergic activation of the BLA, glucocorticoids also influence noradrenergic activity in the amygdala, which is critical for mediating stress effects on memory approximately 20–60 min after stressor onset.[24,49,50] It is thought that this relatively fast interaction of catecholamine and nongenomic glucocorticoid actions in the amygdala modulates processing in other brain regions, including the hippocampus, PFC, and caudate nucleus, effectively encouraging a "memory formation mode,"[12] such that the initial glucocorticoid effects benefit the encoding of the current stressor or other prioritized[44,51] (e.g., salient, goal-relevant) events. Specifically, moderate levels of stress enhance learning via increased hippocampal long-term potentiation (LTP) shortly after stress exposure;[44] however, retrieval of previously learned information may be impaired because the encoding of the stressful event putatively competes with and suppresses retrieval of unrelated information.[12,52]

Overall, the retrieval impairments observed following a stressor may stem from (1) a computational trade-off between encoding of novel, nonoverlapping representations (pattern separation) and retrieval of stored information from partial cues (pattern completion) in the hippocampus (see Ref. 53 for preliminary evidence that arousal enhances pattern separation); (2) hippocampal synaptic competition, in which inactive synapses (e.g., representing previously encoded information) are depotentiated when LTP increases in other synapses (e.g., encoding the arousing information);[54] and/or (3) biased attention toward arousing information, thereby increasing the probability that the arousing information will be encoded[44,54] and limiting attentional resources for retrieval (see discussion below).

While stress-induced glucocorticoids undoubtedly affect neural processing by way of hippocampal function, stress modulates other brain regions, including the PFC. Stress-induced release of catecholamines reduces neural firing in the PFC of nonhuman primates,[25] while simultaneously strengthening functioning in the amygdala,[11] striatum,[55] and primary sensory cortex.[56] In turn, amygdala activation drives arousal systems and is fundamental in increasing catecholamine release in the PFC.[57] Research in nonhuman primates provides evidence that high levels of acute uncontrollable stress (e.g., loud noise) impair prefrontal cognitive function through disruption of catecholamine (e.g., dopamine) levels.[58] More recent data in humans demonstrate that viewing an aversive film impairs subsequent working memory performance, putatively by reducing dorsolateral PFC activity[59] and frontal theta activity.[60] Moreover, increases in glucocorticoids in the PFC strengthen the catecholaminergic impairments in working memory performance,[61] suggesting that negative effects of stress on prefrontal function might be enhanced approximately 20 min after stressor exposure, once glucocorticoids have been released.

Later genomic glucocorticoid actions

Approximately 1–2 h after exposure to a stressor, catecholamine levels normalize and the slower gene-mediated actions of glucocorticoids come into play. Specifically, the binding of glucocorticoids to GRs leads to gradual changes in gene transcription that alter proteins affecting neural function.[62] These genomic actions of glucocorticoids inhibit synaptic plasticity in the hippocampus,[15,62] increasing LTD and putatively raising the threshold for LTP induction (metaplasticity),[47] potentially reducing interference and enhancing long-term storage/consolidation of recently encoded stressful or prioritized memories (memory storage mode).[12,44] During this time, encoding of new neutral information and retrieval of old information may be impaired, in part due to stress-induced hippocampal LTD.[54,63] A study in humans provided preliminary evidence that delayed effects of cortisol (administered 3 h before a memory-encoding task) led to decreased activity in the hippocampus, angular gyrus, and middle frontal gyrus during the task,[64] suggesting that memory-related processing might be impaired even hours after a stressor

subsides.[12,15,65] On the other hand, work in rodents suggests that exposure to an acute stressor potentiates PFC glutamatergic transmission 4–24 h after stress exposure, leading to a facilitation in working memory.[66] Similarly, cortisol administration 4 h before a working memory task in humans resulted in increased activity in the dorsolateral PFC and improved working memory performance.[67] These findings are largely consistent with the hypothesis that delayed glucocorticoid genomic actions enhance processing in the executive control network,[19] although further work is needed to more precisely specify the temporal window of glucocorticoid-driven delayed genomic effects on neural mechanisms and memory and to determine whether these effects are modulated by the severity of the stressor.

Effects of chronic stress

Prolonged exposure to glucocorticoids (e.g., due to chronic stress over a period of weeks to years) can be especially harmful, leading to shrinkage of pyramidal neurons in the hippocampus and in the frontal, pre/postcentral, and cingulate gyri in nonhuman primates.[68] Chronic stress can impair long-term memory, putatively by inducing abnormal changes in basal cortisol levels and diurnal rhythms,[69] thereby reducing hippocampal volume and causing cell death.[70] Individuals experiencing chronic stress, such as those with posttraumatic stress disorder (PTSD), often demonstrate long-term memory impairments;[71] and patients with high basal cortisol levels, such as those with Cushing's syndrome and depression, show reduced hippocampal volume and impaired cognition.[72–74] In addition, there is also evidence suggesting that acute and reversible glucocorticoid effects during memory retrieval may contribute to the memory deficits observed in conditions of chronically elevated glucocorticoid levels (e.g., prednisone treatment).[75]

Stress effects on episodic encoding and consolidation: selective enhancement of memory for high-priority stimuli

In general, acute stress–induced release of glucocorticoids enhances episodic memory, particularly for emotional experiences.[76–78] For instance, psychosocial stress before encoding selectively enhances subsequent recall of emotional words, but impairs recall of neutral words.[77,78] Interactions between the amygdala and MTL structures are critical for enhancing encoding of emotional episodic memories.[23,79,80] In healthy individuals, functional connectivity between the amygdala and hippocampus,[81,82] or between the amygdala and MTL cortical regions,[83,84] enhances subsequent memory for emotional material. Reciprocal interactions between the amygdala and MTL are thought to modulate the initial encoding of the memory trace, as well as its consolidation over time.[85] In contrast, the negative influence of stress on the encoding of neutral items is often related to the cortisol response, such that, as levels of cortisol increase during encoding, the ability to correctly recall neutral words decreases.[86]

Stress also affects memory consolidation, as moderate levels of stress experienced immediately after encoding serves to enhance subsequent free recall for arousing[87,88] (and, to some degree, neutral)[89–91] material. Specifically, there appears to be an inverted-U function between levels of cortisol elicited by a stressor and subsequent hippocampal-dependent memory performance, such that moderate levels of stress enhance, but high or low levels impair, recollection (i.e., recognition based on retrieval of event-specific associations) of studied material.[90,92] On the other hand, moderate to high levels of postencoding stress can linearly enhance subsequent familiarity (i.e., a relatively rapid feeling of having encountered an item, without recall of specific information associated with the learning event), perhaps indicating a shift in the response curve, such that even higher levels of stress are necessary to impair familiarity.[89,90]

As is suggested by the preceding discussion, there are conflicting findings as to whether stress (encoding or postencoding) differentially affects emotional and neutral information. Several studies revealed that stress before learning selectively enhances subsequent memory for emotional material,[76–78] whereas other studies observed enhancing effects for both types of information.[93] Similarly, postencoding stress either selectively enhances memory for emotional material[87,88] or, as observed in a growing number of studies, facilitates memory for both emotional and neutral information.[89–91] One possible explanation for these conflicting findings is that stress and/or general arousal either at encoding or during consolidation enhances memory selectively for information with high priority, specifically perceptually salient or goal-relevant stimuli (i.e., arousal-biased competition).[51] Given that

emotional material tends to capture attention when simultaneously presented with neutral stimuli,[94] the emotional information would be relatively prioritized during encoding or consolidation, resulting in enhanced subsequent memory. However, to the extent that neutral items are also prioritized via top-down mechanisms, these items should also show stress-induced encoding or consolidation enhancement. Future studies directing participants' attention toward certain aspects of arousing and neutral stimuli might further our understanding about how bottom-up and top-down mechanisms during encoding/consolidation under stress modulate subsequent memory.

Stress effects on episodic retrieval: glucocorticoids impair hippocampal-dependent memory

In contrast to the predominantly enhancing effects of stress on encoding and consolidation, episodic retrieval is generally impaired by stress.[12,43] At the neural level, retrieval studies have focused primarily on how stress-induced glucocorticoids affect hippocampal function. Specifically, when glucocorticoid levels are selectively elevated during a retrieval task, hippocampal-dependent retrieval performance in rodents[49,95–97] and humans[43,98,99] is impaired.

Insights from findings in nonhuman animals

A study by de Quervain, Roozendaal, and McGaugh provided some of the first evidence that stress and glucocorticoids impair retrieval of long-term, hippocampal-dependent spatial memory in rodents.[95] In this study, rats were trained in a water maze and then tested 24 h later. It was found that receiving stress-inducing paw shocks 30 min before testing reliably increased corticosterone levels and impaired spatial memory of the location of the platform in the water maze. Exposure to a predator before retrieval induced similar memory deficits (however, note that stress exposure in this study occurred immediately after learning and thus might have also influenced synaptic consolidation).[97] Lending further support to the idea that glucocorticoids mediate the effects of stress on memory retrieval, blocking the synthesis of corticosterone by administering metyrapone before stress exposure reduced subsequent corticosterone levels and attenuated the stress-induced retrieval impairment.[95]

While these findings mainly implicate HPA-mediated effects on the hippocampus in impairing retrieval, subsequent work revealed that concurrent noradrenergic activation of the BLA is necessary to impair retrieval.[24] Specifically, lesions of the BLA[49] or infusion of beta-adrenoceptor antagonists into the BLA[49] block the retrieval impairments induced by glucocorticoids in the hippocampus. These findings from rodents lead to the prediction that stress should impair retrieval if the stressor, or perhaps the stimulus materials themselves, elicit sympathetic arousal and activate the BLA, along with HPA-mediated glucocorticoid release. For instance, while de Quervain and colleagues found memory impairments in rodents administered corticosterone before testing,[95] the experience of completing the maze submerged in cold water in itself was likely stressful,[100] perhaps eliciting sympathetic arousal and producing memory-retrieval impairments.

Findings from humans

In humans, the primary factors mediating glucocorticoid effects on memory retrieval are (1) the type of test used to probe memory (e.g., free recall, cued recall, recognition); (2) the manner in which glucocorticoids are elevated (e.g., cortisol administration, psychological stressor), as well as the levels of glucocorticoids elicited and the temporal relationship between glucocorticoid increases and the memory test; and (3) the emotional content of the material to be remembered.

Recollection versus familiarity

Stress-related impairments of episodic retrieval tend to be greater on tests requiring free recall relative to cued recall[101–103] and cued recall relative to recognition.[104,105] That is, retrieval tasks that provide relatively few retrieval cues and require generation of the learned material are more affected by stress than tasks that provide more retrieval cues. With respect to recognition memory, the dual-process view of memory retrieval delineates two processes, recollection and familiarity,[106,107] in which recollection entails recognition based on retrieval of event-specific associations (e.g., "I *remember* seeing that Golden Retriever puppy at the farmers' market last Sunday") and is more reliant on hippocampal-dependent pattern-completion mechanisms. On the other hand, familiarity consists of a relatively rapid, undifferentiated feeling of having encountered an item (e.g., "I *know*

I've seen that puppy before") and is thought to rely on MTL cortical structures, such as the perirhinal cortex.[108] Given the dense concentrations of GRs and MRs specifically in the hippocampus,[40] and stress-mediated modulation of hippocampal LTP[109] and subsequent LTD,[54] hippocampal-dependent recollection (including hippocampal-mediated cortical reinstatement)[110] might be relatively more impaired under stress, whereas cortically based item familiarity might be spared.

The effect of glucocorticoids in the hippocampus during memory consolidation might be dose shifted relative to the effect in MTL cortical structures, such that relatively low levels of cortisol influence hippocampal function but higher levels of cortisol are necessary to affect processing in cortical regions.[90] A similar relationship may also be present during retrieval—moderately elevated cortisol levels might impair free recall and, to some extent, cued recall and recollection-based recognition, with a further increase in cortisol potentially being necessary to produce familiarity-based recognition impairments. While the majority of studies manipulating cortisol levels exogenously (and thereby eliciting greater levels of cortisol than psychosocial stressors; see next section) have failed to find effects of cortisol on recognition,[98,99,111] it might be the case that a greater level of sympathetic arousal and noradrenergic activation of the amygdala is also necessary to impair recognition.

On the other hand, it might be the case that recognition is a sufficiently easier task, and according to the Yerkes–Dodson law,[112,113] stress might have a linear effect on familiarity (such that higher levels of stress boost recognition) while exerting a curvilinear effect on recollection performance (such that performance is best at moderate levels but impaired at low or high levels). This second account is consistent with Easterbrook's hypothesis that the effect of stress on performance depends on the complexity of the task, such that only the most cognitively demanding tasks would suffer a "disintegration" under high levels of stress.[114] Indeed, recognition appears to be spared from stress effects in studies where stress elicits both low[105,115] and high[99,104,111] levels of cortisol.

However, the lack of stress effects on recognition might also stem from the following factors: (1) the near ceiling performance on the recognition test (e.g., 94% hit rate[98] and ~95% corrected hit rate[115] observed in control groups; one study[116] showed $d' = 2.1$ in the control group, but another[111] reported a corrected hit rate of ~35.5% in the control group); and (2) recognition tests have typically followed the free-recall tests[99,115–120] (however, see Ref. 98, in which task order was randomized across subjects, and Ref. 111, in which recognition was the only memory task). Consistent with these possibilities, effects of stress on recognition were observed in one recent study that solely assessed recognition memory, quantifying performance using the sensitivity index d' (i.e., taking into account both the hit and false alarm rates).[65] In that study, a pretest stressor produced a significant decline in recognition ($d' = 0.95$) relative to the moderate performance level of the control group ($d' = \sim 1.25$). Further studies are needed to elucidate the effects of retrieval-phase stress on recognition memory performance and to more directly relate any effects to changes in hippocampal and MTL cortical function.

As with recognition, the effects of stress on cued recall also are mixed, with some studies reporting stress-induced retrieval impairments[88,104,105,121] and others finding no effect.[101–103,122–124] Of the studies finding no significant effect of stress on cued recall, three studies suggested that the stress group underperforms relative to the control group,[101,103,123] one found mixed effects depending on menstrual cycle,[102] and one found greater performance in the stress group.[124] Notably, in studies that observed an impairment, the cued-recall test was the first memory test following the stressor[88,105,121] (see Ref. 98, where cued recall and recognition task order was counterbalanced across participants). In contrast, when cued recall was tested after free recall, no effect of stress was typically observed[101–103,123] (see Ref. 124). One possible account of these apparent test-order effects is that participants may become more relaxed after performing the free-recall task, decreasing sympathetic arousal, and thereby reducing the effects of stress on a subsequent cued-recall task (see Ref. 123). Alternately, with the exception of one study,[88] studies observing stress-induced impairments on cued recall have employed a paired-associate task, such as learning word pairs of abstract, unrelated nouns,[98] pairs of both unrelated and moderately related words,[105] or images of faces paired with verbal descriptions.[121] In these studies, participants were cued with one element from the studied pair and asked to recall the associated

element (e.g., word, verbal description). In contrast, the majority of studies that failed to observe an effect of stress on cued recall used a word-stem completion task, in which participants were cued with the first two or three letters of each studied word and asked to complete the word stems with the previously studied words.[101–103,122] Such tests provide greater cue support and also allow for non-declarative (e.g., priming) influences on performance, both of which appear more robust to the effects of stress.[105]

Type of glucocorticoid induction

In humans, stress effects on episodic retrieval are typically studied by examining how the stress-induced cortisol response modulates behavior and neural function, with stress being operationalized with a variety of methods. A number of studies directly probed the effects of the cortisol response on retrieval by exogenously administering cortisol[75,98,99,101,102,111,121–123,125–129] (or metyrapone to suppress the morning rise in cortisol[119,130]). Other studies sought to endogenously manipulate cortisol levels using exposure to pain (i.e., the cold-pressor task (CPT))[88,116,131,132] or psychosocial stress (e.g., public speaking, performing difficult cognitive tasks).[65,103,105,115,117,118,120,124,133–140] The use of stress-induction methods has implications for understanding the effects of stress on retrieval, specifically because different methods (1) trigger different levels of cortisol, (2) evoke different levels of noradrenergic activity, and (3) produce more or less variable stress responses across individuals.

In general, exogenous administration of cortisol tends to elicit the highest levels of salivary cortisol (typically over 50 nmol/L) and produce the most consistent retrieval impairments in both men[75,99,104,125,129] and women.[75,99,101,102,121,128] While the administration of cortisol in and of itself might not prompt the noradrenergic activation of the BLA that is putatively necessary to provoke a retrieval impairment,[24] it is possible that the testing situation is sufficient to increase arousal. This possibility is corroborated by the finding that creating a non-arousing testing situation attenuates the memory impairments caused by preretrieval cortisol administration.[123] In studies where cortisol levels were manipulated exogenously, memory was typically tested about 1 h after cortisol administration (Fig. 2) to allow for cortisol to enter the brain and reach peak levels, although some studies tested memory sooner.[121,125]

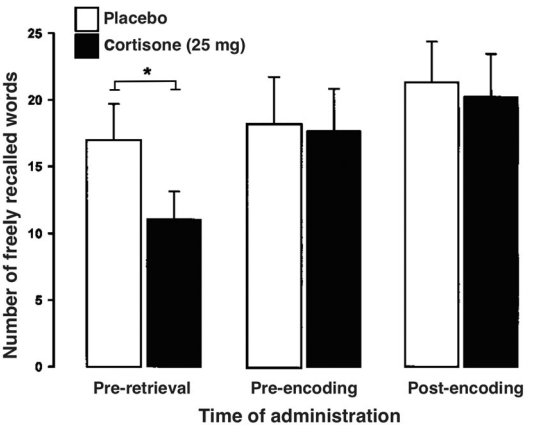

Figure 2. **Cortisone administered orally 1 h before a delayed free-recall test impaired free recall. Memory was not affected if cortisone was administered pre- or postencoding. While cortisone produces levels of salivary cortisol similar to those induced by psychological stress, cortisone administration does not directly modulate noradrenergic activity; consequently, concurrent noradrenergic activity may not be sufficient to modulate memory around the time of encoding in this study. However, the observed effect of cortisone at the time of retrieval suggests that (1) glucocorticoids may be sufficient to produce retrieval impairments or (2) the retrieval experience in itself elicits noradrenergic activity, which interacts with the effects of glucocorticoids. This study was conducted in healthy humans. Adapted, with permission, from Ref. 99.**

Neuroimaging results suggest that memory impairments following cortisol administration are tied to cortisol-induced reductions in MTL[104,111] and right superior frontal cortical[111] activity; more studies are required to fully understand how these neural findings translate to behavior. Using a variety of stimuli, including related[125] and unrelated[75,99] nouns, noun pairs,[104] word–number associations,[127] face–description pairs,[121] and autobiographical memory,[126] increasing levels of administered cortisol tends to impair free recall and cued recall (when the task was not word-stem completion),[104,121,127] while leaving recognition unaffected.[99,104,111] Further, as predicted by the Yerkes–Dodson law,[112,113] abnormally low levels of cortisol, manipulated by suppressing the morning rise in cortisol, also impaired free recall of text[119,130] and pictures[119] learned 3 days earlier, but had no effect on recognition (see discussion above). In other words, stress appears to impair memory specifically when glucocorticoids are at very low or

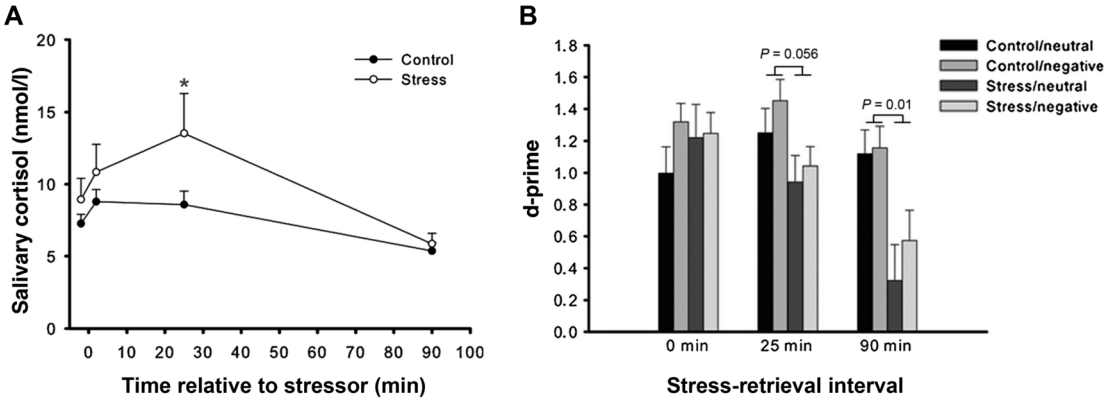

Figure 3. Psychosocial stress 25 or 90 min before retrieval impairs recognition memory. (A) Salivary cortisol concentrations of stress and control groups with a 90-min interval between stress and the recognition memory task. Cortisol concentrations increased 25 min after exposure to the socially evaluated cold-pressor task (SECPT) in the stress group and returned to baseline after 90 minutes. (B) Recognition memory performance for valenced (neutral and negative) words as a function of group and stress-retrieval interval. Exposure to psychosocial stress had no effect immediately after the stressor, but impaired recognition 25 and 90 min after the stressor. There was not a significant group-by-valence interaction. This study was conducted in healthy humans. Adapted, with permission, from Ref. 65.

high levels, regardless of the type of stimuli being recalled.

On the other hand, acute psychosocial manipulations of stress, such as the Trier Social Stress Test (TSST)[141] and the socially evaluated cold-pressor task (SECPT),[142] as well as the CPT (submerging one's hand in ice-cold water for several minutes),[143] elicit more moderate levels of cortisol (typically 8–20 nmol/L) when testing retrieval approximately 20–30 min after exposure to the stressor (however, see Ref. 144, in which memory was tested within ∼5–20 min of CPT). Studies using these endogenous manipulations of stress have generally produced more null findings[124,133,136] or even memory enhancements under stress.[137,144] The inconsistency in these results can be explained, in part, by examining individual differences in response to the stressor; while the stressor may elicit cortisol responses for some individuals, other individuals show little or no effect. For instance, in several studies, the stress caused by the anticipation and delivery of a public speech (i.e., the TSST) impaired memory recall only in the subset of participants that showed a cortisol response.[105,115] Moreover, an increase in elicited cortisol negatively predicts memory performance,[115,134] indicating that this acute psychosocial stress manipulation may only impair memory if a sufficient amount of cortisol is elicited by the stressor. This might also explain why some TSST studies have failed to find effects, especially when the speech-delivery portion of the manipulation is excluded.[124] Similarly, CPT studies report stress-induced retrieval impairments to be reliant on sufficient cortisol increases.[116]

The influence of glucocorticoid levels on retrieval performance also may be moderated by age. Specifically, when examining the effects of the TSST on elderly participants, higher levels of cortisol (∼20 nmol/L) elicited by the stressor led to retrieval impairments,[105] but relatively lower levels of cortisol levels (∼12 nmol/L) did not.[118] In contrast, similar low levels of cortisol in children produced retrieval impairments,[139] suggesting that higher levels of glucocorticoids may be required to cause detrimental effects in older individuals.

Temporal relationship between glucocorticoid increase and memory testing

A recent study using the SECPT suggests that the timing between stress exposure and memory testing has an influence on performance (Fig. 3).[65] Here, participants were tested immediately after the stressor or either 25 or 90 min later. Memory retrieval (measured with a recognition test) was impaired for both neutral and negative words 25 min poststress, when cortisol levels were at their peak. Strikingly,

a retrieval impairment was also observed 90 min poststress, when cortisol levels had returned to baseline; this later impairment was hypothesized to be driven by gene-mediated cortisol actions, putatively protecting the consolidation of the stressful event.[65]

In addition to the gene-mediated effects of cortisol on synaptic plasticity discussed above, recent evidence from humans demonstrates that the slower genomic effects of cortisol reduce blood oxygen level–dependent (BOLD) activity in memory-related regions, including the hippocampus, middle frontal gyrus, and left angular gyrus, 3 h after cortisol administration.[64] Thus, it is a compelling possibility that stress-mediated reductions in activity in these regions drove the memory-retrieval impairment observed 90 min after the SECPT.[65] However, identifying the precise neural mechanisms subserving these findings is a question for future research. How long after a stressor does retrieval remain impaired? What factors might mediate the rate of recovery? Results from rodents suggest that glucocorticoid effects on retrieval are diminished after 4 h;[95] however, whether this timing holds true in humans remains an open question.

Interactions with emotional content

Stress-related retrieval impairments may be particularly strong for emotionally arousing relative to neutral stimuli,[101,103,116,117,128] although the findings have been mixed.[65,75,88,99,104,115,125,127,129,138] While exogenous administration of cortisol largely leads to retrieval impairments for highly arousing positive and negative stimuli and for low-arousing neutral stimuli[75,99,104,125,127,129] (however, note Refs. 101 and 128), psychosocial stress or the CPT can result in selective retrieval impairments for arousing material[103,116,117,140] (however, note Refs. 65, 88, 115, 120, and 138).

As discussed above, a possible explanation for these seemingly contradictory findings is across-study differences in dose level. That is, the psychosocial and CPT stress inductions in some studies may have failed to produce robust hippocampal-dependent retrieval impairments because of lower cortisol levels elicited by the stressor. Alternatively, given the evidence from lesion patients demonstrating that recollection of autobiographical emotional information is partially dependent on the amygdala,[145] and neuroimaging evidence that amygdala activity and functional connectivity between the amygdala and hippocampus is critical for recall of emotional materials,[146,147] it is possible that the sympathetic arousal elicited by acute stress manipulations produces selective retrieval impairments for emotional stimuli by disrupting amygdala function and/or interactions between the amygdala and hippocampus.

Effects on reconsolidation

The finding that stress during retrieval generally impairs episodic memory also raises the question of whether an acute stressor at retrieval affects the process of retrieval or the memory trace itself. Tollenaar and colleagues probed memory performance under stress 1 week after encoding and reassessed memory 1 week later and found that cortisol administered during the initial retrieval session impaired free recall[a] and that this effect was still observable after a wash-out period of 1 week.[129] Here, it is unclear whether (1) the retrieved memory traces were altered under stress, (2) the unretrieved memories were weakened,[148] or (3) the initial retrieval served as an additional encoding episode for each retrieved item, thereby enhancing memories for the successfully retrieved memories in the control group.[149] Alternatively, preliminary evidence suggests that stress may also exert negative effects during reconsolidation,[150,151] that is, the time when retrieved memories enter a labile state after reactivation, before restabilizing.[152–154] For example, exposure to acute stress (SECPT) shortly after recalling autobiographical memories can result in impaired memory for reactivated neutral events 1 week later.[150] Since the stressor was administered after retrieval, these results cannot be attributed to the retrieval-as-encoding hypothesis mentioned above. Thus, if stress during retrieval persists into the reconsolidation period, it might create enduring stress-induced impairments through disruptive effects on reconsolidation; it remains an open question how stress effects on reconsolidation may differ from (the largely enhancing[89–91]) effects observed on initial consolidation.

[a]Note that a cued-recall test (probing memory for half the items) was also administered after the initial free-recall test; cued-recall performance was numerically reduced in the stress group.

Stress effects at retrieval: shifts in attention and impairment of prefrontal cortical function

In addition to stress-induced glucocorticoid effects on hippocampal and amygdala function, episodic retrieval impairments may also emerge from "competitive encoding" of novel information related to the stress exposure.[12,52] During exposure to a stressor, increased hippocampal synaptic plasticity may encourage a memory-formation mode[12] devoted to increasing the likelihood that the stressful event is encoded, while suppressing retrieval of unrelated information. In addition to a computational trade-off between encoding and retrieval in the hippocampus, this competitive encoding of the stressor may also be driven by attention. Specifically, when there is no direct relation between the stressor and the material to be remembered, attentional resources may be diverted to the stressor, leaving limited attention available for the retrieval task.

Cognitive control, top-down attention, and memory retrieval

While a retrieval cue may sometimes be sufficient to trigger relatively automatic hippocampal pattern completion and enable recollection of specific associated knowledge, at other times retrieval is more difficult and effortful, such as when competing memories interfere with retrieval.[155,156] In these instances, performance may be increasingly reliant on a frontoparietal cognitive control network that aids hippocampal-dependent retrieval. Specifically, controlled retrieval may serve to (1) strategically elaborate on the cues available to guide retrieval and/or (2) evaluate the products of memory retrieval in order to resolve conflict between competing memory representations or judge their task relevance.[157–160] Consistent with the notion that the PFC aids in the implementation of controlled retrieval strategies (e.g., generating additional retrieval cues when the presented retrieval cues are insufficient to trigger hippocampal pattern completion), patients with PFC lesions tend to show greater impairments on tasks in which fewer retrieval cues are presented at test (e.g., free recall, cued recall, relative to tests of recognition memory).[161] Interestingly, stressed participants demonstrate a similar pattern of retrieval impairments, such that acute stress appears to have larger effects on free-recall and cued-recall tasks (see above), perhaps in part because of catecholamine and glucocorticoid disruptions of PFC function.[58,59]

Further, retrieval tasks that require effortful, controlled recollection processes, such as free recall or source memory decisions, are often attentionally demanding. Performance on such tasks can be disrupted if top-down attention is commanded by a concurrent task during retrieval.[162] Fernandes and Moscovitch[163] propose that memory tests sensitive to interference from divided attention, such as free recall of categorized word lists,[164] list discrimination,[165,166] and source monitoring,[149,167] tend to be sensitive to frontal lobe damage[168] and aging.[169] Others have argued that memory impairments due to divided attention are specific to encoding, leaving retrieval processes relatively protected.[170] When a memory-retrieval task and a concurrent task (e.g., a continuous reaction-time task; CRT) are given, the memory-retrieval task often will be prioritized, such that overall performance remains the same, whereas the response time on the concurrent task increases.[171,172] However, the co-occurrence of a stressor, especially that of an uncontrollable, unpredictable anticipatory threat (e.g., threat of shock),[7] might provide a unique type of divided attention condition in that the affective content of the threat monitoring and/or emotion regulation processes engaged during the threat manipulation could be prioritized above the retrieval task. In other words, performance on a secondary task, such as the CRT, might be considered secondary to the retrieval task, whereas a stressor (e.g., anticipatory threat) might reverse this prioritization, thus leading to impairments in controlled retrieval. From this perspective, memory tasks that can be subserved by the MTL cortical system (e.g., familiarity judgments) and that place lower demands on frontoparietal attentional processes should be less susceptible to disruptions in top-down attention.[163] At present, it remains undetermined whether the divided attention induced by a stressor (especially that induced by anticipatory stress/threat) might disrupt the cognitive control of memory and influence the neural processes underlying controlled recollection of episodic details.

In addition, when recognition or source memory decisions are difficult or uncertain, there is an increase in engagement of the dorsal attention network,[173] including the frontal eye fields, superior parietal lobule, and medial inferior parietal

sulcus.[174–176] Recruitment of the dorsal attention network during uncertain recognition judgments may serve to guide top-down attention, either to the retrieval cues by modulating their representation in the sensory cortex (e.g., visual word form area when viewing a word cue)[175] or to the internally generated mnemonic evidence.[174] In so doing, attention to the retrieval cues and/or to generated mnemonic evidence may help to adjudicate between competing responses or to enable the cues/evidence to eventually trigger hippocampal-dependent pattern completion. It is presently unclear how disruption of the dorsal attention network during uncertain memory decisions might affect memory behavior, and it remains an open question whether stress influences top-down attention during retrieval. Given considerable evidence that hippocampal retrieval function is disrupted under stress, retrieval success may increasingly demand involvement of controlled retrieval processes and top-down attention, mechanisms that themselves may also be impaired by stress.

Stress, divided attention, and the frontal lobe

In general, stress and threat-evoked anxiety are thought to shift information processing toward increased vigilance to sensory input and bottom-up attention to threat-related stimuli, while attenuating goal-directed top-down attention.[177,178] For instance, exposure to emotional stimuli improves visual contrast sensitivity[179] and enhances sensory neural responses associated with allocating attention to incoming information (i.e., increasing the gain on sensory processing).[180] These effects may result from a stress-induced sensitization of the amygdala, which could either directly bias lower-level processing via dense innervation of sensory cortices[181] or indirectly modulate neurotransmitters such as acetylcholine and norepinephrine via excitatory connections from the amygdala to the locus coeruleus.[25] In addition, there is evidence for an indirect influence of the amygdala on sensory cortical regions when stress levels are low, wherein the processing enhancement in sensory cortical regions observed in affective conditioning paradigms may be mediated by frontoparietal attention mechanisms.[56,182]

However, an acute stressor can have extensive detrimental effects on PFC function, leading to catecholaminergic-driven reductions in neural firing and impaired neural tuning in nonhuman primates,[25] reductions in dorsolateral PFC activation during working memory[59] and declarative memory[111] tasks, attenuation of selective attention,[180] and disruption of frontal theta activity.[60] These impairments in prefrontal function are putatively reinforced by synergistic interactions between catecholamine and glucocorticoid actions.[61] In addition, recent work suggests that slower gene-mediated actions of glucocorticoids can also impair activity in the middle frontal gyrus during a memory-encoding task,[64] providing preliminary evidence that prefrontal processing might still be impaired hours after the stressor subsides.[12,15,65] To the extent that tests of episodic retrieval depend on PFC mechanisms—for example, source memory decisions that demand more controlled recollection or tests where retrieval cues are insufficient to trigger pattern completion without additional cue elaboration[158]—acute stress could impair performance by disrupting prefrontal function, in addition to its influences on hippocampal function.

Stress and retrieval: compensatory shifts in neural networks

From an evolutionary standpoint, stressful, threatening events require a reflexive and rapid response to present or imminent threat.[20,25] At the neural level, this may be accomplished by the rebalancing of large-scale neural networks. Under higher levels of stress, an upregulation of activity in the salience network[183] (e.g., amygdala, anterior insula, dorsal anterior cingulate, striatum, inferotemporal cortex) facilitates the detection of threats by enhancing the gain on early sensory input and biasing bottom-up attentional resources toward the threat-related information, while prioritizing habitual (e.g., dorsal striatal) responses. At the same time, the executive control and top-down attention networks (e.g., the frontoparietal cognitive control and dorsal attention networks) are increasingly forced offline.[19,58] Concurrent with this shift, exposure to an acute stressor may reduce regional cerebral blood flow and BOLD activity in MTL regions, including the parahippocampal gyrus[104] and hippocampus.[64,111]

The shift from hippocampal to striatal mechanisms under stress is particularly notable, given decades of research showing that these two systems support distinct types of memory and behavior. In rodents, the hippocampus is particularly critical for spatial learning (e.g., building a map-like representation of the environment that enables

flexible navigation), whereas the dorsal striatum supports learning of habitual, stimulus–response associations (e.g., turn left at the red landmark).[184] Importantly, extant data indicate that differential reliance on stimulus–response learning, rather than hippocampal-dependent representations, is driven by increased BLA activity under stress, putatively mediated by projections from the BLA to the striatum.[55] While there is relatively less work examining these effects at retrieval, recent findings from rodents reveal that activation of the BLA after learning strengthens retrieval of habitual memories (relative to hippocampal-dependent memories) via projections to the striatum[185] or by modulating relative reliance on striatal versus hippocampal systems.[186] This suggests that acute stress before retrieval might increase rigid striatal-driven habitual behavior while impairing performance dependent on hippocampal and prefrontal systems (see Ref. 187).

Recently, human studies suggest that acute stress shifts reliance from flexible, hippocampal-dependent learning and goal-directed behavior to habit-based learning.[188] Although it remains unclear how stress targeted at retrieval might modulate reliance on these neural systems, examining these effects at encoding can provide valuable insight into how stress modulates neural activity and behavior. For example, Schwabe and Wolf[186] leveraged a probabilistic classification task (PCT), which requires learning probabilistic cue–outcome associations from trial-by-trial feedback,[189,190] to probe reliance on hippocampal versus striatal systems during learning under stress. In this task, reliance on a single-cue strategy (and subsequent explicit knowledge about cue–outcome associations) is supported by the hippocampus, whereas reliance on a combination of several cues is supported by the striatum.[191] Schwabe and Wolf found that SECPT stress induction impaired explicit knowledge about the cue–outcome associations and resulted in a habit (multiple-cue) strategy during learning. Further, stress shifted reliance from the hippocampus to the striatum, such that stress decreased hippocampal activity during the PCT, and performance on the task under stress was positively correlated with striatal activity; by contrast, performance was correlated with hippocampal activity in non-stressed controls.[186] These findings are strikingly consistent with those of Foerde *et al.*,[192] in which hippocampal activity tracked performance on the PCT when participants were solely performing the classification task, but striatal activity was positively correlated with performance on the PCT when they were distracted with a concurrent tone-counting task. While the stressor administered in Schwabe and Wolf's study[186] preceded the PCT, and thus is unlikely to have drawn attention away from the PCT, it is possible that a concurrent stressor (e.g., threat of shock) while performing the PCT may result in even greater reliance on striatal versus hippocampal systems.

Further evidence that stress increases reliance on habitual actions while downregulating the cognitive control network comes from Otto and colleagues.[193] Here, participants were presented with a two-stage reinforcement learning task in which the first-stage choice led to one of two second-stage states (each first-stage choice was followed by one or the other second-stage state 70% of the time), and second-stage choices were probabilistically reinforced. While completing the task, participants could either engage in goal-directed learning and make decisions by learning a model of the environment to guide decisions (i.e., model based), or engage in simple stimulus–response learning, in which previously rewarded actions are repeated (i.e., model free). Here, increased cortisol responses to a CPT administered before the task pushed participants (specifically those with low working memory capacity) away from goal-directed behavior, thought to be dependent on prefrontal and hippocampal function, and toward more habitual, automatic choices, thought to be more dependent on striatal systems.[193] Interestingly, recent findings suggest that goal-directed, model-based behavior may involve prospection over upcoming situations,[194] and the hippocampal memory system may be critical for drawing on experience to engage in simulation of upcoming events.[195–197] To the extent that stress impairs both prefrontal and hippocampal function while increasing reliance on striatal systems, stress may have a particularly profound effect on goal-directed behavior.

While extant studies provide compelling evidence that stress upregulates activity in the salience network (notably the amygdala and striatum) and downregulates activity in the cognitive control network and MTL activity during encoding and after outcome devaluation, it remains unclear how stress targeted at retrieval might modulate

reliance on these neural systems in humans. As such, further work is needed to more fully specify whether and how stress at retrieval affects performance dependent on flexible declarative versus rigid stimulus–response memories, as well as the mechanisms underlying any shifts in the neural systems governing performance.

Implications

Understanding the mechanisms through which stress affects memory retrieval has broad societal consequences. From an educational standpoint, much work has investigated how acute stress or anxiety before and/or during test taking influences performance in academic settings. Distraction theories[198] propose that "choking under pressure" results from averting attention to task-irrelevant thoughts (for instance, worries about the situation and current performance and/or potential consequences, such as performing poorly on an exam),[199] and away from the task at hand (i.e., retrieving previously learned task-relevant information). Stress about the outcome of performance can impair skills that rely on working memory and attention, but not skills less dependent on attention.[200] While the case of test anxiety concerns a stressor directly tied to task performance outcomes, an orthogonal stressor (e.g., TSST, threat of shock, aversive noise threat) could coopt attention in a similar manner. Consequently, the behavioral and neural findings regarding stress effects on retrieval could have direct implications for understanding the effects of test anxiety in the classroom. Interestingly, a recent work in the laboratory and in the classroom suggests that an intervention to help regulate feelings of anxiety immediately before taking a test (i.e., describing thoughts and feelings about an imminent examination) can counteract the negative effects of anxiety on performance, allowing more test-anxious students to excel under stress.[201] Such interventions could prove useful in alleviating stress and improving memory retrieval in other real-world settings.

Exposure to stress over a prolonged period of time can have grave consequences for brain structure and function. Individuals suffering from chronic stress (e.g., PTSD patients and patients with high basal cortisol levels, such as those with Cushing's syndrome and depression) show reduced hippocampal volume and can exhibit long-term memory impairments.[71–73,202] Moreover, economic stressors, such as poverty, have deleterious effects on cognition by coopting attention and impairing cognitive control in adults[4] and by exerting profound effects on children's brain development, particularly affecting hippocampal volume.[5] While all stages of memory are likely affected in these individuals, understanding the mechanisms by which stress influences retrieval in healthy adults may reveal possible treatments for those suffering from prolonged exposure to stress. Indeed, stress-induced retrieval impairments are already being leveraged to treat PTSD[203] and specific phobias.[204] For instance, a series of cortisol treatments in PTSD patients over a period of 1 month provides preliminary evidence that blocking retrieval and/or disrupting reconsolidation with cortisol can reduce the intensity of feelings of reliving the event and the frequency of nightmares; intriguingly, these results persisted off-treatment 1 month later.[205] However, other studies have failed to find such effects;[206] therefore, more work is needed to understand the factors mediating the success of these treatments.

On a shorter timescale, situational factors, such as perceived control,[2] mindset about stress[207] leading to appraisals of the stressor as threatening versus challenging,[208] and acute stressors that pose a threat to one's social status,[2] can influence the likelihood of HPA axis activation in response to acute stress, and may thus mediate the effects of stress on memory retrieval. Given the debilitating effects of acute stress on memory retrieval, it may prove fruitful to explore whether changing one's mindset about stress[207] or providing instructions to reappraise one's physiological response to the stressor as functional and adaptive[209] can counteract stress-induced memory impairments.

Conclusions

Extant findings suggest that the primary factors mediating stress effects on episodic retrieval are (1) how memory is probed; (2) the manner in which glucocorticoids are elevated (e.g., cortisol administration, psychological stressor), the levels of glucocorticoids elicited, and the temporal relationship between glucocorticoid increase and memory testing; and (3) the emotional content of the material to be remembered. In general, when glucocorticoid levels are manipulated exogenously, very low or high levels tend to impair hippocampal-dependent recollection tasks, leaving

cortically based familiarity processes, such as item recognition, relatively unaffected. Further, tasks that require controlled retrieval and recruit prefrontal cognitive control and attention mechanisms may be particularly harmed by stress. Going forward, it may be additionally informative to probe the effects of other stressors that coopt attention and increase noradrenergic activity during retrieval (e.g., threat of shock, unexpected salient threats).

In contrast to the largely negative effects of stress on episodic retrieval observed in exogenous glucocorticoid administration studies, stress operationalized using psychosocial stressors or the CPT tends to produce lower levels of glucocorticoids, and the observed stress effects on retrieval can be more variable. In particular, studies administering cortisol exogenously largely reported effects of stress on retrieval of arousing and neutral information,[99,125] whereas studies employing the TSST, SECPT, and CPT to induce stress were more likely to observe no impairment of stress on retrieval[118,131,133,137] or to observe a selective impairment for retrieval of arousing stimuli.[103,116] It may be that when glucocorticoid levels are low, the sympathetic arousal elicited by acute stress manipulations produces selective retrieval impairments for emotional stimuli by disrupting amygdala function and/or interactions between the amygdala and hippocampus.

Basal cortisol levels at the time of test, which are primarily driven by the diurnal cortisol response,[210] may be another factor influencing stress effects on episodic retrieval. While the majority of studies reviewed here were conducted in the afternoon, a few studies were conducted in the morning and did not find significant impairments for neutral material[103,133] (also see Ref. 134). Gender may also moderate stress effects on retrieval. Specifically, while the majority of studies in humans show similar effects of stress on retrieval for males and females[65,75,99,105,121,127,140] (see Refs. 115, 120, and 131), gender may moderate the stress-induced cortisol increase, such that males tend to show greater changes in cortisol in response to psychosocial stress (particularly in elderly participants).[118,211] The cortisol response elicited by psychosocial stress in young women may be moderated by menstrual cycle phase and use of oral contraceptives;[102] here, women in the luteal phase tended to show a similar stress response to men, but women in the follicular phase or taking oral contraceptives showed a reduced cortisol response.[212] Taken together, gender effects at retrieval should be taken into consideration.

Given the importance of episodic memory retrieval in everyday life, it is critical to understand the theoretical and applied implications of acute stress. In an educational setting, specifying the influences of stress on memory may inform understanding of why some children underperform when faced with a stressful exam. Stress effects on retrieval also have wide-reaching consequences for eyewitness testimony in the courtroom, police interrogations, and clinical treatment of psychiatric disorders. Future neuroimaging studies investigating the neural mechanisms and networks underlying stress effects on retrieval in humans and experiments disrupting stress effects by either administering β-adrenergic antagonists or cortisol suppressors or altering stress mindsets,[207] will enrich our understanding of the interactions between acute stress and memory and guide potential interventions that may enable individuals to overcome life challenges.

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Conflicts of interest

The authors declare no conflicts of interest.

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