Acute Stress Effects on Statistical Learning and Episodic Memory

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Abstract

■ Stress is widely considered to negatively impact hippocampal function, thus impairing episodic memory. However, the hippocampus is not merely the seat of episodic memory. Rather, it also (via distinct circuitry) supports statistical learning. On the basis of rodent work suggesting that stress may impair the hippocampal pathway involved in episodic memory while sparing or enhancing the pathway involved in statistical learning, we developed a behavioral experiment to investigate the effects of acute stress on both episodic memory and statistical learning in humans. Participants were randomly assigned to one of three conditions: stress (socially evaluated cold pressor) immediately before learning, stress ~15 min before learning, or no stress. In the learning task, participants viewed a series of trial-unique scenes (allowing for episodic encoding of each image) in which certain scene categories reliably followed one another (allowing for statistical learning of associations between paired categories). Memory was assessed 24 hr later to isolate stress effects on encoding/learning rather than retrieval. We found modest support for our hypothesis that acute stress can amplify statistical learning: Only participants stressed ~15 min in advance exhibited reliable evidence of learning across multiple measures. Furthermore, stress-induced cortisol levels predicted statistical learning retention 24 hr later. In contrast, episodic memory did not differ by stress condition, although we did find preliminary evidence that acute stress promoted memory for statistically predictable information and attenuated competition between statistical and episodic encoding. Together, these findings provide initial insights into how stress may differentially modulate learning processes within the hippocampus. ■

INTRODUCTION

From a conflict at work to a train delay, our daily lives are filled with stressful events, or acute stressors. Acute stress has powerful and widespread effects on cognition, influencing attention (Chajut & Algom, 2003), decision-making (Starcke & Brand, 2012), executive functioning (Shields, Sazma, & Yonelinas, 2016), and memory (Shields, Sazma, McCullough, & Yonelinas, 2017). Such effects are frequently characterized as negative; for example, acute stress can impair both the formation (Shields et al., 2017) and retrieval (Gagnon & Wagner, 2016; De Quervain, Roozendaal, & McGaugh, 1998) of episodic memories (particularly for neutral/non-stress-relevant information).

These negative stress effects on memory are thought to reflect acute stress-induced impairments of the hippocampus, a region critically involved in episodic memory. For example, acute stress exposure leads to reduced synaptic plasticity and damage to rodent hippocampal neurons (Chen et al., 2020; McEwen, Nasca, & Gray, 2016; Cazakoff & Howland, 2010; Chen, Yang, Huang, & Hsu, 2010; Kim & Diamond, 2002), as well as reduced medial temporal lobe blood flow (Noack, Nolte, Nieratschker, Habel, & Derntl, 2019; De Quervain et al., 2003) and changes in hippocampal functional connectivity (Goldfarb, Rosenberg, Seo, Constable, & Sinha, 2020; Vaisvaser et al., 2013) in humans. In addition, the hippocampus has a high density of glucorticorticoid receptors (Reul & de Kloet, 1985; McEwen, Weiss, & Schwartz, 1969) and thus is very sensitive to elevations in the stress-related hormone cortisol. Cortisol levels have been directly linked to reduced hippocampal plasticity in rodents (Kim & Diamond, 2002), as well as the modulation of hippocampal-dependent memory across species (Kaouane et al., 2012; De Quervain et al., 1998, 2003; Roozendaal, 2002). Furthermore, in contexts in which different types of memory representations can be used, stress biases behavior away from the use of hippocampal-dependent episodic memory and toward striatal-dependent stimulus–response (S-R) learning strategies (Goldfarb & Phelps, 2017).

Multiple frameworks have sought to explain these deleterious effects of stress on memory via its detrimental effects on the hippocampus (e.g., Schwabe, Hermans, Joëls, & Roozendaal, 2022; Goldfarb & Phelps, 2017; Diamond, Campbell, Park, Halonen, & Zoladz, 2007; Lupien, Maheu, Tu, Fiocco, & Schramek, 2007; but see Goldfarb, 2019). However, these theories ignore a critical

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feature of hippocampal function: The hippocampus is not a homogeneous structure dedicated to episodic memory (Sherman, Turk-Browne, & Goldfarb, 2024; Duncan & Schlichting, 2018; Shohamy & Turk-Browne, 2013; Henke, 2010). Instead, the hippocampus also supports a distinct mnemonic process of statistical learning. Whereas episodic memory reflects the discrete representation of a single experience, statistical learning reflects a more generalized representation integrated across related experiences (Sherman, Graves, & Turk-Browne, 2020). Critically, episodic memory and statistical learning are thought to rely on distinct pathways within the hippocampus, with episodic memory depending on the trisynaptic pathway (TSP; connections from entorhinal cortex to hippocampal subfield CA1 via intermediate connections in subfields CA3 and dentate gyrus [DG]) and statistical learning depending on the monosynaptic pathway (MSP; a direct, recurrent connection between entorhinal cortex and CA1). These pathways contain the necessary circuitry to represent episodic versus statistical encoding, respectively (Schapiro, Turk-Browne, Botvinick, & Norman, 2017), and empirical data support these anatomical distinctions (Molitor, Sherrill, Morton, Miller, & Preston, 2021; Schlichting, Gumus, Zhu, & Mack, 2021; Schlichting, Zeithamova, & Preston, 2014). We note that the kind of *relational* statistical learning we discuss here—requiring the integration across temporally adjacent visual events—may be distinct from other kinds of statistical extraction that may not necessarily require the hippocampus. For example, there is evidence that perceptual (Rungratsameetaweemana, Squire, & Serences, 2019), motor (Reber & Squire, 1998), and cross-situational (Warren, Roembke, Covington, McMurray, & Duff, 2020) regularities can be acquired by patients with hippocampal damage.

The functional heterogeneity of the hippocampus raises the possibility that stress could have dissociable effects. Indeed, both the density of glucocorticoid receptors (Wang et al., 2013; Sarabdjitsingh, Meijer, & de Kloet, 2010; Morimoto, Morita, Ozawa, Yokoyama, & Kawata, 1996; Seckl, Dickson, Yates, & Fink, 1991) and stress-induced changes in neuronal function differ across hippocampal subfields. For example, acute stress exposure or administration of glucocorticoids impairs long-term potentiation in TSP structures including DG and CA3 in rodents (Chen et al., 2010; Pavlides, Watanabe, & McEwen, 1993), leads to neuronal damage in primate CA3 (Stein-Behrens, Mattson, Chang, Yeh, & Sapolsky, 1994; Sapolsky, Uno, Rebert, & Finch, 1990), and is linked to decreased neurogenesis in primate DG (Gould, Tanapat, McEwen, Flügge, & Fuchs, 1998). In contrast, stress/glucocorticoids do not impair long-term potentiation in CA1 (Yamada, McEwen, & Pavlides, 2003), and have been linked with facilitated firing of CA1 neurons (Vandael et al., 2021; Karst et al., 2005; Karst & Joëls, 2005; but see Kavushansky, Vouimba, Cohen, & Richter-Levin, 2006). Together, these findings indicate that stress may negatively affect regions associated with the TSP but spare or even enhance regions associated with MSP. This would be consistent with reports of stress-induced impairments in episodic memory (Shields et al., 2017) and raises the novel hypothesis that stress may enhance statistical learning in humans. A recent human study provides initial evidence for stress-related learning enhancements: Acute stress promoted the extraction of probability-based statistical regularities in a motor sequence learning task (Tóth-Fáber, Janacsek, Szőllősi, Kéri, & Nemeth, 2021), although, as noted above, such motor sequence learning tasks do not necessarily require the hippocampus (Janacsek et al., 2020; Gobel, Parrish, & Reber, 2011; Reber & Squire, 1998).

To investigate how acute stress differentially impacts hippocampal-dependent episodic memory and statistical learning, we tested the effects of a laboratory-based acute stressor on a task designed to assess both processes. To isolate stress effects to the initial encoding/learning, we used a 2-day design with encoding on Day 1 and retrieval on Day 2. We also assessed acute stress actions at multiple time intervals; although a delay between stress and encoding often impairs recognition or recall, stress immediately before encoding can enhance memory (Shields et al., 2017; Zoladz et al., 2011; Joëls, Pu, Wiegert, Oitzl, & Krugers, 2006). These dynamic effects are associated with the timecourse of neuroendocrine stress responses, encompassing rapid sympathetic nervous system activation (evident at a short temporal interval) and relatively slower hypothalamic–pituitary–adrenal axis responses, which increase levels of the glucocorticoid hormone cortisol around 15–20 min poststressor (Schwabe et al., 2022; Hermans, Henckens, Joëls, & Fernández, 2014). As much of the rodent neuroanatomical precedent was informed by direct manipulation of glucocorticoids, we anticipate that stress effects on statistical learning will be stronger with a 15-min delay between stress and learning, and that these effects on behavior may relate to cortisol levels.

We therefore recruited three groups in our 2-day design: (1) no stress exposure, (2) acute laboratory-based stressor immediately before learning (to target sympathetic nervous system responses), and (3) acute stressor 15 min before learning (to elevate cortisol in advance). On Day 1, all groups completed the corresponding stress/control procedure before viewing a sequence of images. This sequence allowed for both statistical learning and episodic encoding and has previously been shown to involve the hippocampus (Sherman & Turk-Browne, 2020). We assessed statistical learning both online on Day 1 (RTs during learning task) and offline on Day 2 (pair familiarity test); retention of episodic memory was also assessed on Day 2 (item recognition test). Together, these data begin to elucidate the differential effects of stress across hippocampal learning processes, highlighting novel and textured ways in which acute stress might affect human learning and memory.

METHODS

Participants

One hundred forty-six individuals were recruited from Yale University and the New Haven community. All participants provided informed consent, and all experimental procedures were approved by the Yale University Institutional Review Board. Eleven participants were excluded for not completing the study (8 opted out during the stress induction; 3 cancelled before Day 2), yielding a usable sample size of 135 (81 female participants, 53 male participants, 1 declined to provide their sex; age range: 18–42, mean age = 23.2). The 135 participants were randomly assigned to one of three stress groups (n = 45 per group; see more details below). The sample size of 45 per group was chosen based on power analyses (to achieve 80% power) both from a study that examined interactions between statistical learning and episodic memory in a similar task (d = .42; Sherman & Turk-Browne, 2020) and from a study that examined the impact of a similar acute stressor on episodic memory (d = 0.62; Goldfarb, Mendelevich, & Phelps, 2017).

All participants were fluent in English, had a BMI between 18 and 35, did not have a current *DSM-V* diagnosis of substance use disorder, and were not currently taking psychiatric, beta-blocker, or corticosterone medications. All female participants were not peri- or postmenopausal, pregnant, or lactating, and did not have a hysterectomy. Female participants completed a menstrual cycle questionnaire, and 37% reported taking some form of hormonal contraceptive.

Procedure

The study employed a between-participants design to probe the effects of acute stress on statistical learning and episodic memory. Participants were pseudorandomly assigned to a control group (no stress) or one of two stress groups (stress-immediate and stress-delayed) such that the three groups were matched on age, sex, race, and Perceived Stress Scale score.

The full experimental procedure is shown in Figure 1A. Briefly, each participant came to the laboratory for two sessions on consecutive days (24 hr apart). On Day 1, participants underwent the acute stress induction (or control) procedure, followed by the learning task. Participants in the no stress and stress-immediate conditions completed the learning task immediately after stress/control induction, whereas participants in the stress-delayed condition underwent a rest period before the learning task. On Day 2, participants completed two tests. These tests were administered on the subsequent day to isolate the effects of stress on learning/encoding rather than memory retrieval, as acute stress can have opposing effects at these timepoints (Goldfarb, Tompary, Davachi, & Phelps, 2019; Goldfarb, Mendelevich, & Phelps, 2017; Shields et al., 2017; Roozendaal, 2002).

Both sessions were conducted between 12:00 and 6:00 p.m. to control for circadian fluctuations in cortisol (Lupien et al., 2007). To maintain consistent context, both sessions were completed within the same experimental testing room and by the same experimenter. All computer-based tasks were built in Python using PsychoPy libraries (Peirce, 2007).

Stress Induction and Salivary Cortisol

Before any experimental procedures, participants acclimated to the environment for 10 min (during which they completed a series of intake questionnaires); this acclimation period allowed for cortisol levels to stabilize to baseline, as physiological correlates of stress tend to increase upon entering a new environment (Linden & McEachern, 1985).

Following the acclimation period, participants underwent the stress or control procedure. To induce an acute stress response, participants in the two stress groups underwent the Socially Evaluated Cold Pressor Test (SECPT; Schwabe & Schächinger, 2018). The SECPT is a validated, laboratory-based, combined physiological/psychosocial stress induction procedure that combines novelty, unpredictability, and uncontrollability (Mason, 1968). Participants submerged their left arm in a bucket of ice water for 3 min (mean temperature = 1.73C, SD = 0.61), while being socially evaluated. The social evaluation consisted of (i) being monitored by a neutral-affect experimenter wearing a laboratory coat and (ii) being video-recorded. Video recording was conducted on a tablet with a front-facing camera, so that participants viewed themselves being recorded. Participants were told that the video recording would be used to evaluate their facial expression and that they should look into the camera the entire time and not speak. All participants (as well as the experimenter) wore face masks in compliance with health and safety regulations for the duration of the experiment, including during stress induction. Participants were not informed of how much time remained in the SECPT, and there were no visible clocks or timers in the room. Participants were required to keep their arm submerged for the full 3 min. Participants in the no stress control condition underwent a matched control task with warm water (mean temperature = 37.89C, SD = 1.11) and no social evaluation (neither monitoring nor video recording).

Upon completion of the SECPT (or control task), participants rated the subjective unpleasantness of the task (0 = not at all unpleasant; 10 = extremely unpleasant). Participants in the no stress and stress-immediate conditions then immediately performed the learning task (see below). Participants in the stress-delayed group rested before the learning task, during which they sat silently with

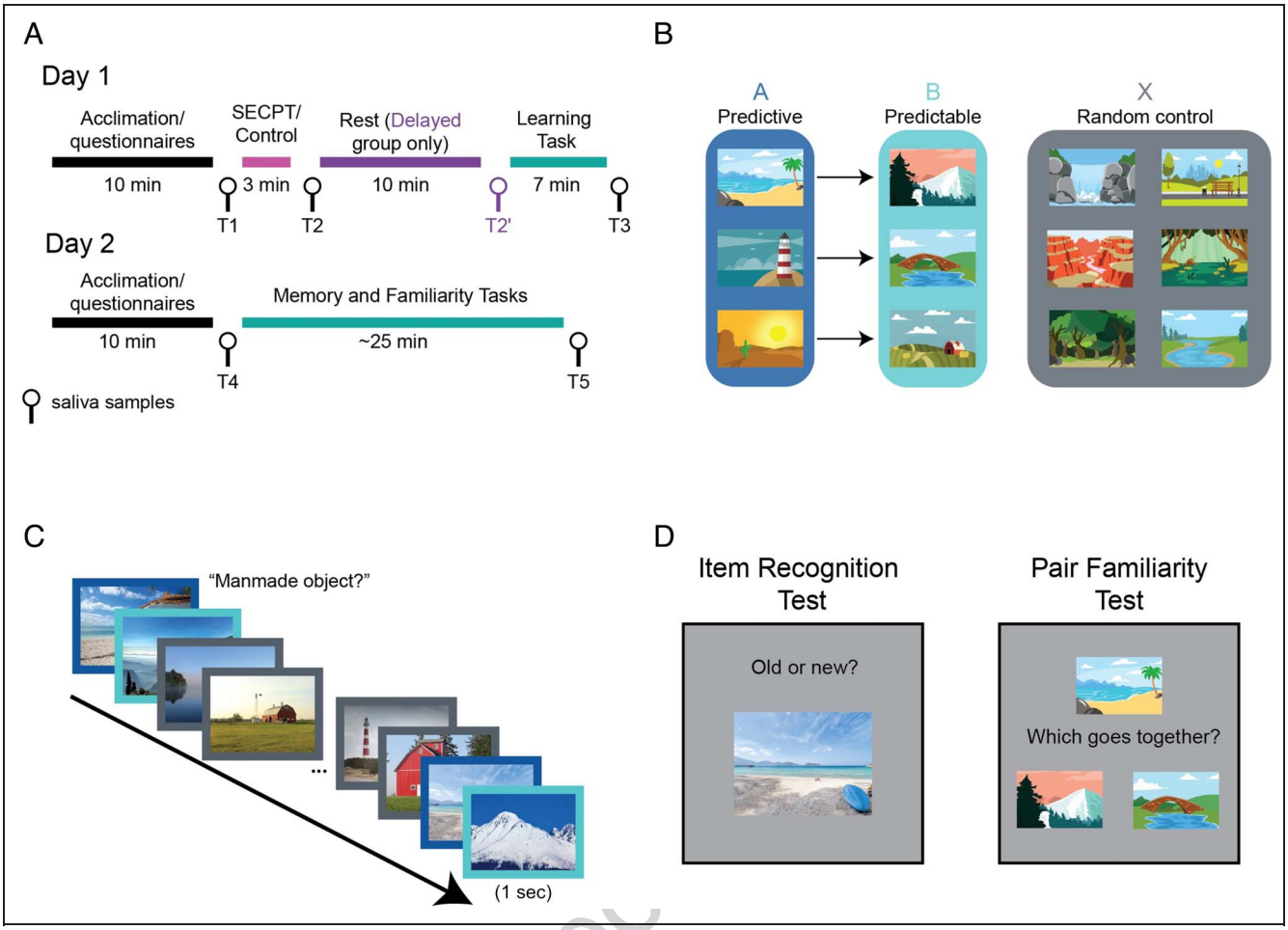

Figure 1. Experimental timeline and tasks. (A) Timeline of experimental procedures on both days. (B) Example scene category pairings for one participant. Three of 12 categories were assigned to Condition A. Each A category was reliably followed by one of three other categories assigned to Condition B to create pairs. The remaining six categories assigned to Condition X were not paired. (C) On Day 1, participants viewed trial-unique scenes drawn from the scene categories (and pairings) in B. They performed a cover task of judging whether there was a manmade object in the scene. (D) On Day 2, participants returned for the test phase. Left: Participants first completed an item recognition test, assessing their memory for each trial-unique exemplar from Day 1 (in addition to novel foils from the same categories). Right: Participants then completed a pair familiarity test, assessing their knowledge of the category pairings from Day 1.

no distractions or electronic devices. This 10-min rest period, together with salivary sampling (see below), created a ~15-min delay between the offset of SECPT and the onset of learning (mean delay = 14.64 min, *SD* = 0.48), allowing for stress-induced increases in cortisol to occur at the start of learning (Goldfarb et al., 2019; Dorey, Piérard, Chauveau, David, & Béracochéa, 2012; Lupien et al., 2007).

Salivary samples were collected throughout both sessions to assess cortisol levels (Figure 1A). At each sample, participants placed a salivette under their tongue for 2 min. Participants were told to refrain from eating or drinking anything other than water in the 2 hr before their participation. Samples were stored in a −20C freezer and were subsequently assayed (via radio immune assay) by the Yale Center for Clinical Investigation. Sixty-one samples (8.5% of the total number of samples; including all samples from $n = 2$ participants) were not successfully assayed because of insufficient sample.

Learning Task

The learning task on Day 1 was based on Sherman and Turk-Browne (2020). On each trial, participants viewed a photograph of a scene for 1000 msec, during which they judged whether it contained a manmade object (Figure 1C). Participants were instructed to respond on a keyboard as quickly and accurately as possible (response mappings of "j"/"k" onto "yes"/"no" were counterbalanced across participants). The scene remained on the screen for 1000 msec regardless of response to equate encoding time. Trials were separated by a 500-msec ISI with a fixation cross.

Each scene photograph was trial-unique, but drawn from one of 12 scene categories (beaches, bridges,

canyons, deserts, fields, forests, lakes, lighthouses, marshes, mountains, parks, and waterfalls; Figure 1B). Each scene category appeared 16 times over the course of the learning task, for 192 trials. The photographs for half of the scene categories always contained a manmade object, and thus all exemplars for a given category required the same response. Participants were informed of this: They were told that they would see photographs of many different "kinds" and that all photographs from a given kind would either have a manmade object or not. An example was given of campgrounds and glaciers (campgrounds would have manmade objects; glaciers would not), which were not categories used in the actual study.

Participants were instructed to pay attention to each scene photograph, as they would be asked questions about the photographs the following day. This instructional manipulation was included to encourage encoding and increase the likelihood that participants would have reliable episodic memory the following day.

Critically, unbeknown to participants, half of the scene categories were paired. Given the category of the first scene in a pair (A category scenes), the category of the second scene (B category scenes) was 100% predictable. The other half of scene categories were neither predictive nor predictable (X category scenes) and were randomly inserted throughout the sequence, with the constraint that they could not be placed between paired categories. Importantly, although the category of the B scenes was 100% predictable, the specific B photograph to appear was never predictable, as all scene photographs were trial-unique. Thus, this task enabled both episodic encoding of each individual scene exemplar, as well as statistical learning of the category pairs.

The assignment of scene categories to A/B/X conditions was randomized for each participant. Within the sequence, category pairs as well as couplets of category pairs could not repeat back-to-back. The 16 repetitions of each category were spread equally across quartiles of the learning task. The overall transition probability between "yes" and "no" responses on the manmade cover task was forced to be statistically indistinguishable from 0.5.

Item Recognition Test

The item recognition test on Day 2 probed episodic memory for each individual photograph encountered during learning. On each trial, one scene was presented and participants indicated whether it was "old" (i.e., presented during the learning task) or "new" (i.e., not previously seen in the experiment; Figure 1D, left). After making an old/new response (using "j"/"k" keys on the keyboard), participants then rated their confidence ("very unsure"/"unsure"/"sure"/"very sure," using the 1–4 keys atop the keyboard). Participants had 5 sec to make each response. All 192 scene photographs from the learning task were shown in addition to 192 foils (16 novel exemplars from each category). The order of the scenes was randomized.

Pair Familiarity Test

The pair familiarity test was designed to probe explicit knowledge of learned scene category pairs. On each trial, a cartoon sketch of one scene category was presented at the top of the screen (cartoons were used to avoid having to present a familiar or novel exemplar). Two other cartoons, depicting two other scene categories, were presented at the bottom of the screen. Participants had 5 sec to choose whether the category on the left (using the "f" key) or right (using the "j" key) side "goes with" the category above (Figure 1D, right).

The cartoon at the top of the screen was either an A category scene (50%) or a B category scene (50%). One of the cartoons below was always the paired category, whereas the other was a within-condition foil. For example, if beach as Category A was reliably followed by mountain as Category B during learning, then another Category B (e.g., field) would serve as the foil. Each category pair/foil combination was tested twice, and both trials contained the same foil. The positions of the true and foil categories were counterbalanced across trials.

Analysis Approach

We employed a linear modeling approach to characterize stress effects on learning and memory while accounting for potentially mediating factors. All statistical analyses were performed in R (Version 4.1.3). For analyses that contained one observation per participant (e.g., accuracy on the pair familiarity test), we used a standard linear model. For models that contained multiple observations per participant, we employed linear mixed effects models using the nlme package (Pinheiro, Bates, & R Core Team, 2022); we included participant as the random intercept and all within-participant main effects as random slopes. Models were evaluated sequentially using the anova function from the stats package. Reported follow-up contrasts were performed using the emmeans package (Lenth, 2022). Logistic regression analyses were evaluated using the Anova function from the car package, using Type 3 tests and the Wald statistic.

Assessing within and between Group Effects

For each behavior of interest, we first assessed differences between conditions by testing the effect of group (no stress, stress-immediate, stress-delayed). In addition to assessing the effect of stress group, we explored main effects within each group (by running a separate model for each group). These within-group analyses allowed us to test whether effects are more prominent in one group in particular. Furthermore, because we hypothesized that there may be a graded effect of stress across the two stress

groups, this approach allowed us to capture trends that may not have been apparent when aggregating across the three groups.

Factors Modulating Stress Effects

Given that stress effects can differ by sex (e.g., He, Beveridge, Vargas, Salen, & Brown, 2023; Guenzel, Wolf, & Schwabe, 2014; Espin et al., 2013) and glucocorticoids may drive stress effects on episodic memory and statistical learning (Bahtiyar, Karaca, Henckens, & Roozendaal, 2020; Goldfarb, 2019), we additionally explored whether learning under stress differed with sex and/or cortisol. We thus ran models predicting each behavior as a function of group, cortisol (see "learning-concurrent" cortisol computation below), and sex, as well as Group × Cortisol and Group × Sex interactions. For these models, we only included participants from the two stress groups, which were designed to elicit changes in cortisol. One participant declined to provide their sex; their sex was coded as "NA" in all sex-based analyses.

Quantifying Cortisol Responses

To assess how cortisol covaried with behavior, we quantified "learning-concurrent" cortisol as the average of participants' pre- and postlearning saliva samples—T2 and T3, respectively, for no stress and stress-immediate, and T2′ and T3, respectively, for stress-delayed (Figure 1A)—and subtracted the baseline sample (T1). To normalize cortisol levels, we log-transformed these values: $mean(log(pre - learning), log(post - learning)) - log(baseline)$ (Goldfarb, Froböse, Cools, & Phelps, 2017). This metric was computed only for participants with three successful assays (baseline, prelearning and postlearning): 110 participants total, $n = 37$ no stress, $n = 34$ stress-immediate, $n = 39$ stress-delayed.

Relationships between Learning and Memory Measures

To assess co-variance across different learning and memory measures, we ran models predicting behavior in one task from behavior in a different task (as well as interaction with stress group). We ran this separately for three combinations of tasks: online statistical learning performance predicting offline statistical learning performance (pair familiarity); online statistical learning performance predicting episodic memory (item recognition); and episodic memory predicting offline statistical learning performance.

RESULTS

Subjective Stress and Cortisol Response

We first evaluated the efficacy of the SECPT stress induction by examining subjective ratings of unpleasantness (Figure 2A). These ratings were significantly modulated by group, no stress mean = 1.41; stress-immediate mean = 7.18; stress-delayed mean = 7.24; $F(2, 132) = 155.6$, $p < .001$. Follow-up tests confirmed that participants in both stress groups (hereafter referred to as "immediate" and "delayed") rated the procedure as more unpleasant than participants in the no stress group, no stress versus immediate: $b = 5.83$, $t(132) = 15.36$, $p < .001$; no stress versus delayed: $b = 5.77$, $t(132) = 15.19$, $p < .001$; the two stress groups were similar to each other, immediate vs. delayed: $b = 0.067$, $t(132) = 0.18$, $p = .98$.

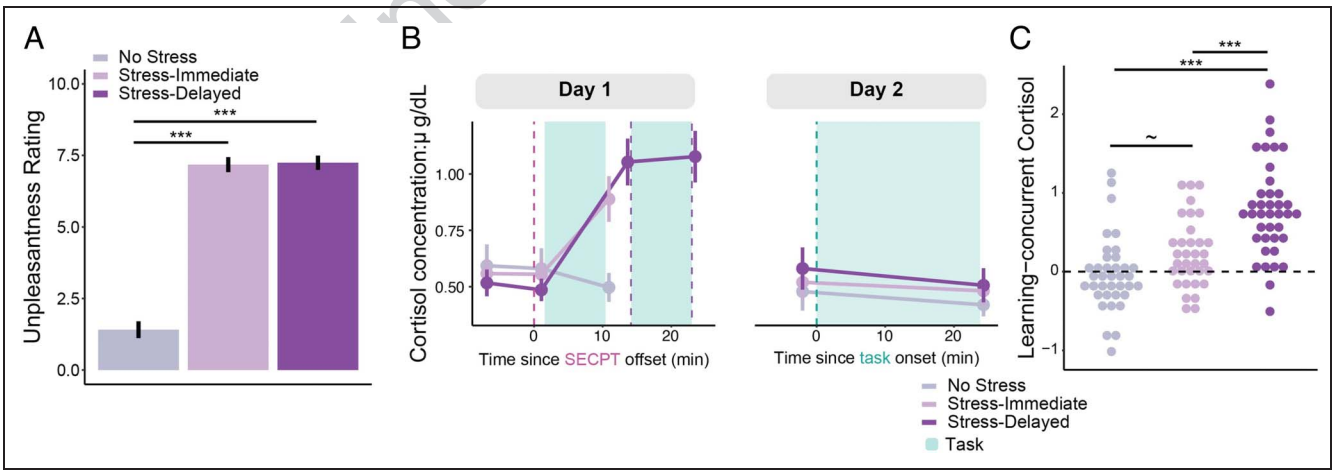

Figure 2. Behavioral and neuroendocrine metrics of stress response. (A) As expected, participants in the two stress groups rated the stressor as more unpleasant than participants in the no stress group. (B) The SECPT led to elevated salivary cortisol responses in both stress groups (peaking 10–15 min poststressor) relative to the no stress group on Day 1 (left), but not on Day 2 (right; as expected, given there was no stressor administered). Left: aligned to offset of SECPT; right: aligned to start of tasks. Shaded green areas indicate when the tasks were performed (learning task on Day 1 and tests on Day 2; the shaded area with the dashed purple border indicates when the delayed group performed the learning task). (C) Salivary cortisol levels before/after learning relative to baseline for each group (each dot is an individual participant). Error bars indicate standard error of the mean across participants. ~$p < .10$; ***$p < .001$.

To assess the influence of SECPT on peripheral cortisol, we compared salivary cortisol levels over the course of Day 1 for the different groups. We expected that cortisol would increase following stress induction in the two stress groups, but not in the no stress group. Furthermore, we hypothesized that there would be higher cortisol levels at the time of learning for the delayed group, given the time needed for the cortisol response to manifest. To test these hypotheses, we modeled cortisol as a function of both group and time (in min) since SECPT (as a continuous variable; Figure 2B, left). The groups did not differ in overall cortisol level, main effect of group: $F(2, 129) = 0.13$, $p = .99$; however, they did show significantly different cortisol trajectories throughout the session, main effect of time: $F(1, 232) = 46.93$, $p < .001$; Group × Time: $F(2, 232) = 22.09$, $p < .001$. Examining each timepoint individually, we found no group differences in salivary cortisol at T1 (baseline) or T2 (immediately post-SECPT; as hypothesized; all $p > .50$). However, at T3 (postlearning), both stress groups had reliably higher cortisol levels than the no stress group, no stress versus immediate: $b = 0.37$, $t(129) = 2.78$, $p = .017$; no stress versus delayed: $b = 0.62$, $t(129) = 4.69$, $p < .001$; the two stress groups did not significantly differ, $b = 0.24$, $t(129) = 1.83$, $p = .16$.

We also examined cortisol trajectories within each group. In the stress-immediate group, cortisol levels were stable from T1 (baseline) to T2, post-SECPT; $b = 0.012$, $t(72) = 0.32$, $p = .95$, indicating that cortisol was not significantly elevated at the start of the learning task. By the end of learning (T3), cortisol was significantly higher than these earlier timepoints (ps $< .001$). In contrast, although cortisol was also stable across T1 and T2 in the stress-delayed group, $b = 0.026$, $t(120) = 0.78$, $p = .86$, levels were significantly elevated at the start of learning, T2′ vs. T1: $b = 0.50$, $t(120) = 6.94$, $p < .001$, and this persisted until after learning, T3 vs. T1: $b = 0.59$, $t(120) = 6.51$, $p < .001$; T3 vs. T2′: $b = 0.090$, $t(120) = 1.46$, $p = .46$.

For later analyses of how cortisol at the time of learning relates to statistical learning and episodic memory behavior, we averaged the pre- and postlearning salivary samples and subtracted the baseline sample (see Methods, Quantifying Cortisol Responses section). As intended, groups differed in this metric, main effect of group: $F(2, 107) = 25.33$, $p < .001$, reflecting increased cortisol during learning, which was strongest in the stress-delayed group, no stress vs. immediate: $b = -0.26$, $t(107) = 2.13$, $p = .089$; no stress versus delayed: $b = -0.82$, $t(107) = 6.95$, $p < .001$; immediate versus delayed: $b = -0.56$, $t(107) = 4.64$, $p < .001$ (Figure 2C).

On Day 2, consistent with our hypotheses (as no stress induction occurred on this day), we did not see any differences in cortisol between groups (Figure 2B, right), main effect of group: $F(2, 127) = 0.39$, $p = .68$; Group × Time: $F(2, 118) = 0.47$, $p = 0.63$. We did observe a main effect of sample, $F(1, 118) = 5.93$, $p = .016$, reflecting a decrease in cortisol over the course of the tests.

Interactions with Sex

We next considered whether stressor efficacy differed by sex. We found no effect of sex on subjective ratings of unpleasantness, $F(1, 128) = 0.095$, $p = .76$, nor an interaction between group and sex, $F(2, 128) = 2.00$, $p = .14$. However, we found a reliable main effect of sex on cortisol during learning, $F(1, 103) = 5.04$, $p = .027$, with higher cortisol levels in male participants. However, we did not observe a Sex × Group interaction, $F(2, 103) = 1.30$, $p = .28$, indicating that the stress induction procedures were effective across male and female participants. Nevertheless, to determine whether learning differences were specific to cortisol, we included sex as a covariate in all analyses of cortisol during learning.

Effects of Acute Stress on Online Measures of Statistical Learning

After the stress (or control) procedure, participants completed the learning task during which they viewed a series of trial-unique scenes with predictable category order (i.e., Category A followed by Category B images; Figure 1B). While viewing this image stream, participants performed a cover task in which they judged whether a manmade object was present or not in each scene. Overall, participants were highly accurate at making this judgment (mean = 0.90, $SD = 0.10$) and accuracy did not differ by stress condition, $F(2, 132) = 0.20$, $p = .82$.

We reasoned that as participants learned the category regularities, they should become faster to respond to predictable (B) compared with unpredictable (A and X) items (Hunt & Aslin, 2001). Furthermore, we hypothesized that stress would enhance statistical learning, leading to more RT facilitation in one or both of the stress groups. Thus, we modeled RT across trials as a function of predictability (B vs. A and X), group (no stress, stress-immediate, stress-delayed), repetition (number of times a given image category was presented), and their interactions, with accuracy (whether participants correctly answered the manmade object question) as a covariate.

We observed a main effect of predictability, $F(1, 24908) = 16.99$, $p < .001$, with faster RTs for predictable items, providing overall evidence of statistical learning. Predictability did not interact with category repetition, $F(1, 24908) = 0.00$, $p = .99$, suggesting that the effect did not emerge linearly over time. We also found main effects of accuracy, $F(1, 24908) = 22.17$, $p < .001$, such that inaccurate responses were slower, and repetition, $F(1, 24908) = 80.31$, $p < .001$, such that participants became faster with practice. There was no main effect of group, $F(2, 132) = 1.06$, $p = .35$, indicating that stress did not affect overall task performance, nor did group interact with repetition, $F(2, 24908) = 1.62$, $p = .20$. Notably, we did not find evidence for our hypothesized interaction between group and predictability, $F(2, 24908) = 0.77$, $p = .46$.

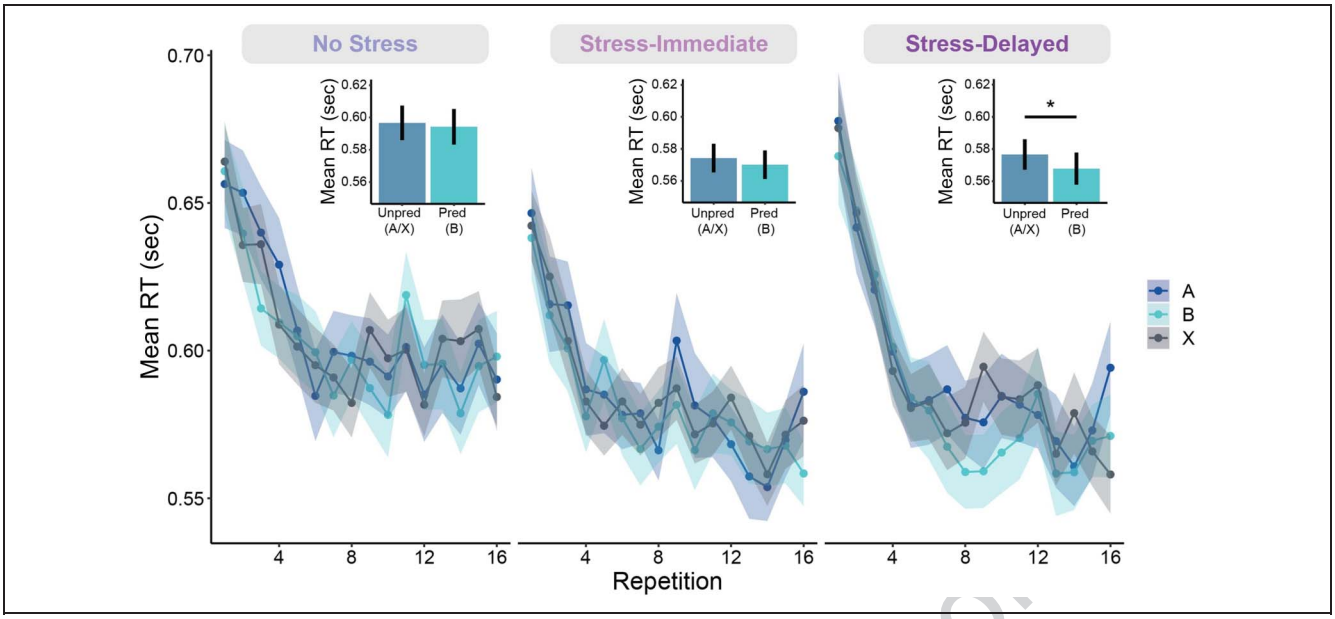

Figure 3. Online statistical learning. RTs (in seconds) during learning as a function of group, trial type (B is predictable whereas A and X are not), and category repetition. Lines/dots correspond to the mean and shading to standard error of the mean across participants. Insets: average RTs (and standard error) for unpredictable (A and X) versus predictable (B) items in the second half of learning (Repetitions 8–16). *$p < .05$.

We next explored online statistical learning within each group (Figure 3); despite the lack of interaction with group, such an analysis allows us to capture learning processes within each of our stress exposure conditions and to characterize more graded trends across the three groups. The predictability effect was significant within the stress-delayed group, $F(1, 8283) = 10.06$, $p = .0015$, and stress-immediate group, $F(1, 8357) = 5.71$, $p = .017$, but not in the no stress group, $F(1, 8266) = 2.58$, $p = .11$.

Last, although we did not observe any interactions between predictability and repetition, we hypothesized that the predictability effects would be most pronounced later on in the sequence, after the opportunity for learning had occurred (Sherman & Turk-Browne, 2020; Hunt & Aslin, 2001). When limiting the analysis to the second half of learning, we observed similar patterns, with the numerically most pronounced learning effects in the delayed group. Specifically, in the delayed group, we observed a main effect of predictability, $F(1, 4141) = 4.25$, $p = .039$,[1] but not in the two other groups, immediate: $F(1, 4170) = 1.36$, $p = .24$; no stress: $F(1, 4152) = 0.036$, $p = .85$ (Figure 3, insets). Together, these results indicate that statistical learning significantly facilitated online RTs, perhaps most strongly when learning occurred ~15 min after stress.

Interactions with Cortisol and Sex

We next modeled interactions of predictability with cortisol level and participant sex in the two stress groups, which were designed to evoke cortisol responses. We found a main effect of cortisol on RTs, $F(1, 67) = 12.50$, $p < .001$, with higher cortisol associated with slower responses. However, cortisol did not interact with predictability or group (ps > .20). There were no overall effects of sex on RTs, $F(1, 67) = 1.33$, $p = .25$, nor did sex interact with predictability or group (ps > .10). Taken together, these results do not provide evidence for cortisol or sex impacting the relationship between stress and online statistical learning.

Effects of Acute Stress on Offline Measures of Statistical Learning

The above results provide modest evidence that stress may enhance statistical learning. That is, although online RTs were facilitated overall for predictable items relative to unpredictable items, this difference was most apparent in the stress-delayed group who encountered the learning task around the time of the peak cortisol response. We next examined statistical learning via the offline pair familiarity test from Day 2. Specifically, we assessed behavioral accuracy in choosing the pair that matched what they had seen in the learning task on Day 1 instead of a recombination of equally familiar items across pairs.

Collapsing across the three groups, performance was marginally above chance, mean = .53, $SD = 0.21$, $t(134) = 1.88$, $p = .063$. There was no main effect of group when considering the three groups together, $F(2, 132) = 1.65$, $p = .20$. However, performance was numerically higher and reliably above chance only in the stress-delayed group, mean = 0.58, $SD = 0.23$, $t(132) = 2.45$, $p = .016$; stress-immediate: mean = 0.53, SD =

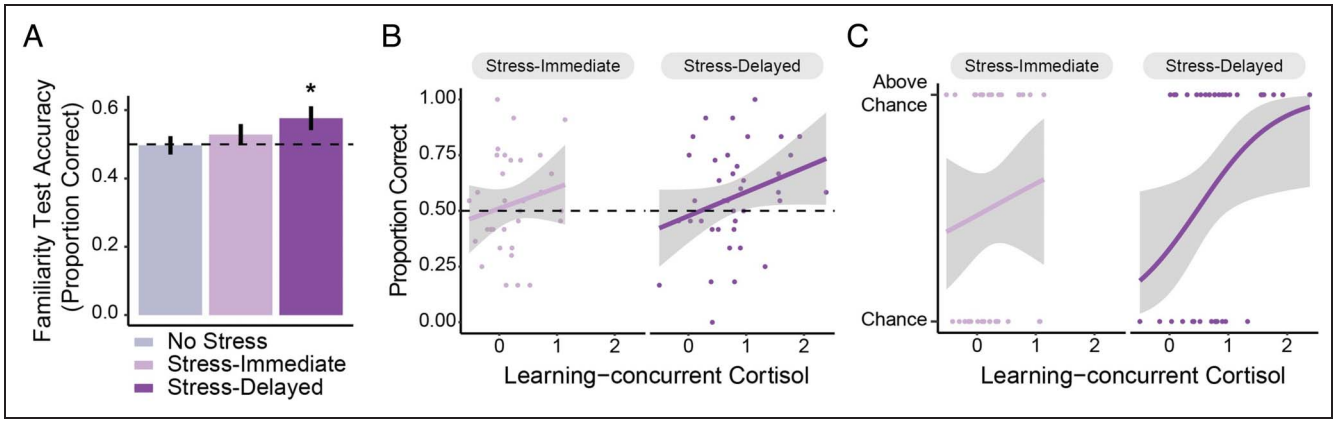

Figure 4. Offline statistical learning. (A) Average (and standard error) pair familiarity test accuracy across participants in each group. Dashed line indicates chance performance (0.5). (B) Linear relationship between pair familiarity test accuracy (proportion correct) on Day 2 and learning-concurrent cortisol on Day 1 for the two stress groups. (C) Logistic relationship between familiarity test accuracy (binary above [> .5] vs. at [< = .5]) chance and learning-concurrent cortisol for the two stress groups. Shading indicates 95% confidence intervals. *$p < .05$.

0.21, $t(132) = 0.90$, $p = .37$; no stress: mean = 0.50, SD = 0.18, $t(132) = -0.096$, $p = .92$ (Figure 4A). This matches the pattern of results from the online measure of statistical learning.

Interactions with Cortisol and Sex

We next assessed whether cortisol level and participant sex in the two stress groups modulated pair familiarity test accuracy. Notably, we found a main effect of cortisol, $F(1, 67) = 5.38$, $p = .023$, such that higher cortisol responses during learning predicted more pair familiarity (Figure 4B). This pattern was consistent across stress, interaction with stress group: $F(1, 67) = 0.63$, $p = .43$, and supports the hypothesis that higher levels of acute stress reactivity correspond to stronger statistical learning.

We also observed a main effect of sex, $F(1, 67) = 5.08$, $p = .027$, and an interaction between group and sex, $F(1, 67) = 10.91$, $p = .0015$. This was driven by male participants performing better on the pair familiarity test, particularly in the immediate group, male versus female participants, $b = 0.33$, $t(67) = 4.07$, $p < .001$.

The above model predicted performance as a continuous measure (accuracy, averaged over trials, yielding a value from 0 to 1). However, performance that hovers around chance (≤ 0.5) may not reflect meaningful variance. Thus, we reran the above analysis using logistic regression to predict which participants were at chance versus above chance. This approach weakened the main effect of cortisol, $\chi^2(1) = 0.86$, $p = .35$, but revealed a marginal Group × Cortisol interaction, $\chi^2(1) = 3.67$, $p = .055$ (Figure 4C), with a positive relationship between cortisol and pair familiarity in the stress-delayed group, $\chi^2(1) = 4.46$, $p = .035$, but not stress-immediate group, $\chi^2(1) = 0.86$, $p = .35$. This analysis also replicated the main effect of sex, $\chi^2(1) = 6.49$, $p = .011$, with male participants more likely to have above-chance memory, although this only marginally differed between stress groups, $\chi^2(1) = 2.72$, $p = .099$.

Together, these results provide further evidence for a positive association between stress and statistical learning, highlighting the role of stress-induced cortisol responses for better learning and retention of regularities.

Effects of Acute Stress on Episodic Memory

Thus far, we have focused on stress effects on statistical learning. However, our task also allowed us to probe episodic memory for each trial-unique scene photograph. To investigate episodic memory, we examined performance during the item recognition test on Day 2. We first assessed memory by computing A', a nonparametric measure of sensitivity that takes into account hit rates and false alarm rates (Grier, 1971). All participants exhibited an A' above 0.5 collapsing across the three predictability conditions (A, B, and X), indicating that participants were able to successfully discriminate previously seen images from foils after 24 hr (Figure 5A). We did not find differences in overall memory performance between groups, A': $F(2, 132) = 1.59$, $p = .21$; hits and false alarms: ps > .4 (Figure 5B).

In addition to assessing overall episodic memory performance, this task enabled us to examine the interaction between episodic memory and statistical learning by assessing the effect of statistical predictability (A vs. B vs. X) on memory. In our prior work, we found that recognition of scene photographs in the same session as encoding was modulated by predictability. Namely, we found a lower hit rate for predictive A items relative to nonpredictive X items (Sherman et al., 2022; Sherman & Turk-Browne, 2020). Accordingly, we next assessed whether similar competition between prediction and encoding would be found when retrieval was measured after a 24-hr delay. We did not find a lower hit rate for A versus X items in the no stress condition (closest to prior studies that did not manipulate stress). Instead, the no stress group seemed to show an impairment in memory for B items not evident in either stress group (Figure 5C). There was no main effect of trial type, $F(2, 264) = 1.52$, $p = .22$, nor a

Group × Trial Type interaction across all three groups, $F(4, 264) = 1.62$, $p = .17$. However, there was a marginal main effect of trial type within the no stress group, $F(2, 88) = 3.03$, $p = .054$, but not either stress group ($ps > .25$), with memory for predictable B items significantly worse than A, $b = 0.045$, $t(88) = 2.46$, $p = .042$, in the no stress group.

We followed up on these patterns in an exploratory analysis. Specifically, because the observed deficit for the no stress group was specific to predictable B items, we collapsed A and X trials (both of which were unpredictable) to increase power. Analyzing the data in this way revealed a marginal Group × Predictability interaction, $F(2, 132) = 3.05$, $p = .051$, such that biases in episodic memory for predictable versus unpredictable items differed based on stress, with the no stress group exhibiting relative impairments in memory for predictable items and the two stress groups exhibiting the numerically opposite pattern.

Interactions with Cortisol and Sex

There were no main effects of cortisol level or participant sex, nor interactions with group or predictability/trial type, on either A' or hit rate measures of episodic memory (all $ps > .10$).

Relationship between Statistical Learning and Episodic Memory Measures

Taken together, our results suggest that acute stress may be positively associated with statistical learning. Participants in the stress-delayed group showed the clearest evidence of statistical learning both online (faster responses to predictable items) and offline (above chance performance in discriminating learned category pairs). Elevated cortisol during learning was also linked to better offline statistical learning. In addition, participants in the two stress groups showed a relative preservation of episodic memory for predictable items, perhaps a reflection of enhanced encoding or consolidation of statistically reliable information. These patterns thus raise questions about whether stress may be similarly acting on these two independent measures of statistical learning.

Furthermore, although we did not find an overall effect of stress on our episodic memory measures, prior work has suggested that statistical learning and episodic memory may trade-off, or compete, with one another (Sučević & Schapiro, 2023; Sherman & Turk-Browne, 2020). This can be assessed by examining how participants' performance on the statistical learning measures related to their episodic memory performance.

Thus, we next explored whether the observed learning and memory metrics might be related to one another, and whether stress exposure modulated these relationships.

Online and Offline Statistical Learning

We first assessed whether our two measures of statistical learning—online facilitation of RTs and offline familiarity of category pairs—were related. We computed each participant's mean difference in RT for unpredictable (A, X) minus predictable (B) items throughout learning. We then modeled pair familiarity test performance as a function of group and online RT differences. Across all participants, we found no main effect of RT difference on pair familiarity, continuous performance: $F(1,129) = 0.89$, $p = .35$; binary above/at chance: $\chi^2(1) = 0.89$, $p = .34$. We also found no interactions between RT difference and group ($ps > .20$). This lack of relationship is consistent with past work (Bays, Turk-Browne, & Seitz, 2015) and was not an artifact of quantifying online statistical learning as the difference in average RTs across the whole learning task;

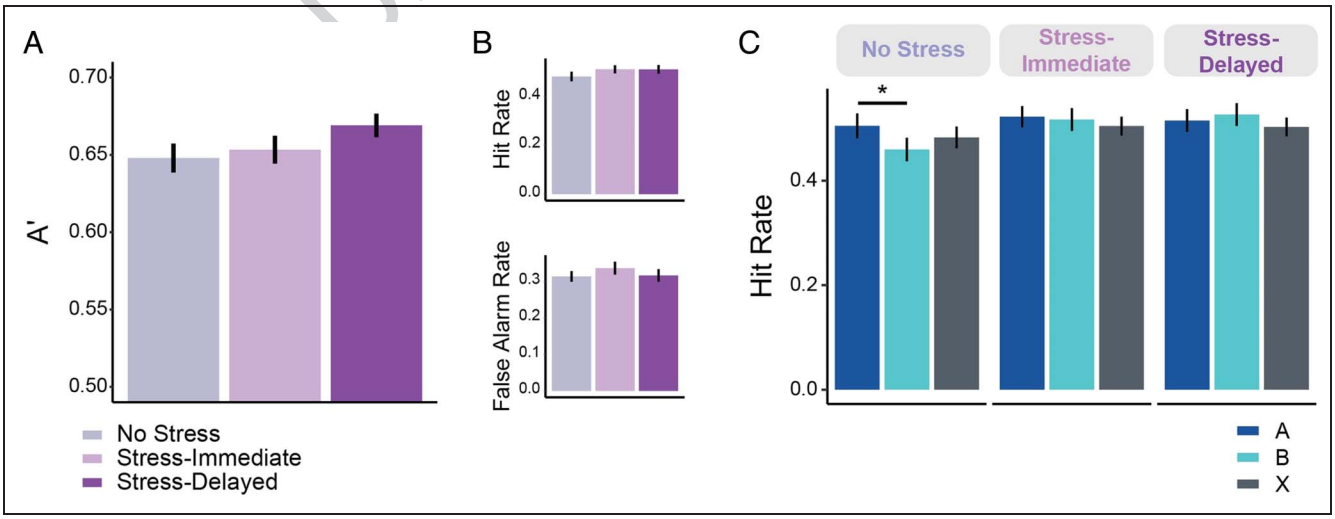

Figure 5. Episodic memory. (A) Average item recognition test performance (A') across participants within group. (B) Top: average hit rate by group. Bottom: average false alarm rate by group. (C) Average hit rate for each trial type (A, B, X) by group. Error bars indicate standard error of the mean across participants. *$p < .05$.

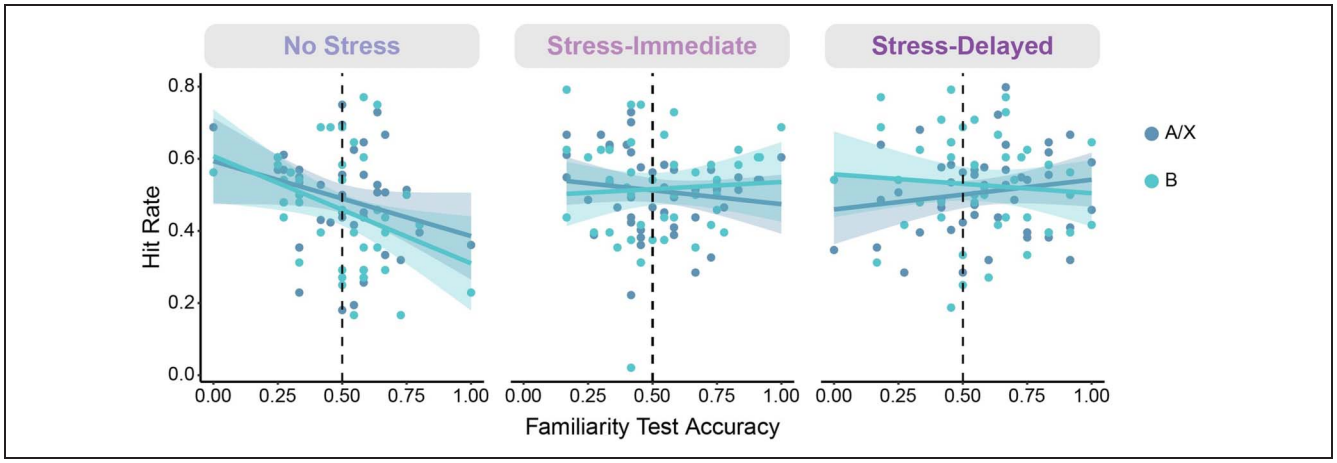

Figure 6. Relationship between accuracy on the pair familiarity test and hit rate on the item recognition test by group, separately for unpredictable (A/X) and predictable (B) items. Each dot is a participant. Solid lines are the linear relationships. Vertical dashed line indicates chance pair familiarity test performance (0.5). Shading indicates 95% confidence intervals.

limiting the analysis to the second half did not reveal any relationships with offline statistical learning. Thus, despite both showing modest benefits of acute stress, we did not find evidence that online and offline measures of statistical learning were related.

Online Statistical Learning by Episodic Memory

We next assessed whether episodic memory was predicted by online statistical learning. We modeled hit rate on the item recognition test as a function of group, predictability (A/X vs. B), and online RT difference (both across all of learning, and for the second half of learning only). There was no main effect of RT difference on hit rate, nor did RT difference interact with predictability or group (ps > .18).

Offline Statistical Learning by Episodic Memory

We last examined relationships between episodic memory and pair familiarity. We modeled hit rate on the item recognition tests as a function of group, predictability (A/X vs. B), and offline pair familiarity test performance. There was no main effect of pair familiarity, $F(1, 129) = 0.91$, $p = .34$. Pair familiarity performance did not interact with predictability, $F(1, 129) = 0.95$, $p = .33$, although there was a marginal interaction between pair familiarity and group, $F(2, 129) = 2.50$, $p = .086$. Furthermore, we observed a three-way interaction between group, predictability, and pair familiarity, $F(2, 129) = 3.77$, $p = .026$, indicating that the relationship between offline statistical learning and episodic memory differed with stress (Figure 6).

In the no stress group, there was a negative relationship between hit rate and pair familiarity across predictability conditions, $F(1, 43) = 5.06$, $p = .030$, such that participants with higher familiarity for category pairs exhibited worse item recognition for individual exemplars.

In contrast, the two stress groups did not show a significant main effect of pair familiarity on hit rate (ps > .30). However, the effects of pair familiarity differed based on whether the exemplars were predictable in the stress-delayed group, $F(1, 43) = 5.38$, $p = .025$, and marginally in the stress-immediate group, $F(1, 43) = 2.88$, $p = .097$. The significant pattern in the stress-delayed group was that participants with higher pair familiarity had worse episodic memory for predictable (B) but not unpredictable (A/X) exemplars. These findings suggest that stress may time-dependently balance competition between statistical learning and episodic memory.

We note that these opposing patterns for predictable versus unpredictable items were not driven by a negative correlation between episodic memory for B items and A/X items; in all three groups, item recognition of B items was highly positively correlated with item recognition of A/X items (ps < .001). Finally, to build confidence in these results and ensure that they were robust to various analysis choices, we ran the analysis in several complementary ways. For example, taking into account the category of the probe as an additional predictor (i.e., relating item recognition memory for beaches to familiarity performance on trials in which beach was a probe) yielded a similar result (three-way interaction, $p = .028$). In addition, coding familiarity as above/at chance (binary) rather than as a continuous variable (ranging 0–1) also yielded a significant three-way interaction ($p = 0.024$). Together, these results underscore the role of stress in modulating the relationship between episodic memory and statistical learning.

DISCUSSION

Here, we explored how acute stress influences statistical learning and episodic memory, two key learning processes supported by the hippocampus (Schapiro et al., 2017). Consistent with our hypothesis, we found preliminary evidence that acute stress could enhance some aspects of

statistical learning. Specifically, participants in the stress-delayed group (who had the highest levels of cortisol during learning) exhibited the clearest evidence of statistical learning, as measured via both online and offline measures. We also found that higher cortisol levels during learning were beneficial for offline retention of regularities the next day. Although we found no main effect of acute stress on episodic memory (contrary to our hypothesis), we found initial evidence that stress modulated the relationship between statistical predictability and episodic encoding, preventing episodic memory impairments that were evident in the no stress group.

We interpret these findings with caution, given inconsistent main effects and interactions with stress condition. Nevertheless, we note that these modest effects were consistent across multiple uncorrelated behavioral measures of learning, providing an important initial contribution to our understanding of how acute stress can influence statistical learning and bias behavior adaptively.

Stress Effects on Statistical Learning

We measured statistical learning in two ways. First, we measured learning online, as indicated by facilitated RTs to predictable items in a sequence. Second, we measured learning offline, 24 hr later, by asking participants whether they were explicitly familiar with learned category pairings.

Across these two complementary metrics, statistical learning benefits were strongest with stress, specifically the stress-delayed group. Indeed, this was the only group for which online performance was significantly modulated by predictability and offline performance was reliably above chance. Furthermore, we found that both measures of statistical learning in the stress-immediate group were numerically between the no stress and stress-delayed groups, perhaps suggesting a graded effect modulated by the temporal dynamics of the unfolding stress response (Lupien et al., 2007).

One potential explanation for these time-dependent effects of stress are changes in cortisol levels during learning. By manipulating time since stress, these levels were graded such that they were highest in the stress-delayed group, then stress-immediate, then no stress. Indeed, we found some evidence that cortisol mediated the relationship between stress and statistical learning, as higher learning-concurrent cortisol responses predicted better performance on the offline statistical learning test (particularly in the stress-delayed group). This may suggest that cortisol promotes the consolidation of regularities, as offline measures were collected the next day. This notion is in line with prior rodent work suggesting that post-encoding cortisol (thought to affect memory consolidation) promotes the generalization of, or integration across, episodic memories (Bahtiyar et al., 2020), and such generalization is thought to be fundamental for statistical learning (Schapiro et al., 2017). Notably, we did not find a relationship between cortisol and online statistical learning; instead, we found that cortisol was associated with overall slowing of RTs (irrespective of predictability condition). This finding, although challenging to interpret given mixed effects of acute stress and cortisol on RT (Raio, Konova, & Otto, 2020; Shields, Ivory, & Telzer, 2019; Goldfarb, Mendelevich, & Phelps, 2017), underscores the importance of considering relative differences in RT (i.e., the difference between predictable and non-predictable trial types), rather than global changes, as evidence of learning.

Despite finding successful statistical learning under stress in both online and offline measures, it is noteworthy that these two metrics were uncorrelated. Although the lack of a cross-measure relationship may seem surprising, prior work has similarly found a lack of correlation between online and offline measures of statistical learning (Kiai & Melloni, 2021; Bays et al., 2015), indicating that they may be capturing different subcomponents of statistical learning (Bogaerts, Siegelman, Christiansen, & Frost, 2022; Siegelman, Bogaerts, Kronenfeld, & Frost, 2018; Batterink & Paller, 2017). This raises the possibility that stress may benefit these different statistical learning computations via distinct mechanisms. For example, as noted above, learning-concurrent cortisol was associated with stronger offline, but not online, learning, suggesting a benefit to consolidation. Future work could help clarify stress effects on different subcomponents of statistical learning, as well as the mechanisms by which these subcomponents are impacted, by using tasks that target different statistical representations (Liu, Forest, Duncan, & Finn, 2023; Forest, Finn, & Schlichting, 2022).

To date, only one other study to our knowledge has examined the influence of acute stress on statistical regularities (Tóth-Fáber et al., 2021). In that study, participants underwent the SECPT before a motor sequence learning task. They found that participants in the stress group exhibited faster RTs to predictable motor sequences relatively early in learning, suggesting faster extraction of regularities. Importantly, such motor-based sequence learning tasks are thought to rely on striatal mechanisms (Janacsek et al., 2020), which are known to be enhanced by stress (Goldfarb & Phelps, 2017). Thus, although our behavioral findings are largely consistent with this report, our results suggest a more general role for stress in enhancing detection of regularities in the context of relational forms of statistical learning, which are thought to rely on the hippocampus (Sherman & Turk-Browne, 2020; Covington, Brown-Schmidt, & Duff, 2018; Schapiro, Gregory, Landau, McCloskey, & Turk-Browne, 2014; Schapiro, Kustner, & Turk-Browne, 2012; cf. Marlatte, Belchev, Fraser, & Gilboa, 2024).

Stress Effects on Episodic Memory

We hypothesized that stress might impair episodic memory, consistent with prior empirical work in humans (Shields et al., 2017; Payne et al., 2007) and with our neural

framework, in which acute stress has been shown to impair the structure and function of hippocampal subregions involved in episodic memory (Chen et al., 2010; Gould et al., 1998; Stein-Behrens et al., 1994; Pavlides et al., 1993; Sapolsky et al., 1990). However, we observed no overall effect of stress on episodic memory, and if anything observed a numerically opposite pattern, with the best memory performance in the stress-delayed group (a pattern mirroring what we observed across our statistical learning measures). This null finding is concordant with prior demonstrations that memory for neutral, nonstress-relevant information, such as the scene photographs in this study, is largely unaffected by prelearning stress (Shields, Hunter, & Yonelinas, 2022; Goldfarb et al., 2019; Zoladz et al., 2011; Domes, Heinrichs, Rimmele, Reichwald, & Hautzinger, 2004). Future work employing emotionally salient stimuli may yield greater sensitivity to stress effects on episodic encoding (and perhaps trade-offs between episodic memory and statistical learning).

Although we observed no main effect of stress on memory, we did find initial evidence that stress may modulate the relationship between statistical learning and episodic memory. Participants in the no stress group showed impaired episodic memory for *predictable* (B) items, a deficit that was not apparent in the two stress groups. This was surprising, given our prior findings (with no stress manipulation) that episodic memory was impaired for *predictive* (A) items. This impairment for predictive items was theorized to be driven by reduced encoding of the distinctive features of A items while the category of A was used to predict the category of B (Sherman et al., 2022; Sherman & Turk-Browne, 2020). Thus, we might have hypothesized that the no stress group in the current study would exhibit this same pattern. One key difference in the current study is that episodic memory was tested after a 24-hr delay, rather than immediately after encoding in the prior studies (Sherman et al., 2022; Sherman & Turk-Browne, 2020). This procedural change was necessary in the current study to allow acute stress to dissipate before memory was tested, to isolate effects on encoding rather than retrieval (as stress can have opposite effects at these timepoints; Shields et al., 2017). The differing pattern of episodic memory results, from impairment of predictive (A) items previously to impairment of predictable (B) items here, raises several interesting questions for future research, including about how competition between statistical learning and episodic memory decays over time and changes as a result of consolidation.

Despite these impairments in episodic memory without stress, participants exposed to stress before learning appeared to be spared the impairment in episodic memory for predictable items. It is possible that enhanced statistical learning under stress allowed for improved episodic encoding or consolidation of predictable B items (although we note that B memory was not significantly greater than A and/or X within the stress groups). Although no prior work to our knowledge has assessed the effect of stress on the consolidation of predictable information, our finding may perhaps be consistent with theories arguing that stress may "tag" useful information for subsequent consolidation (often discussed in the context of emotional information; e.g., Payne & Kensinger, 2018, but perhaps also relevant to statistically meaningful content).

Analyses probing the relationship between measures provide further indication that stress may mitigate competition between episodic memory and statistical learning. In the absence of stress, there was a negative association between episodic memory (hit rate) and offline statistical learning (pair familiarity). This finding is consistent with the idea that the shared reliance of these processes on the hippocampus and output pathways may create interference (Sherman et al., 2024; Sučević & Schapiro, 2023; Sherman & Turk-Browne, 2020; Schapiro et al., 2017). However, this general trade-off was not apparent under stress, suggesting that statistical learning can persist even without significant costs to episodic memory. Instead, the relationship between memory metrics under stress was nuanced, varying with time since stress and with the predictable nature of the memoranda. These findings suggest that stress may alter the mechanisms by which hippocampal representations interact. Our findings suggest that different time-varying components of the stress response may modulate memory for predictable versus unpredictable events. Further targeted work, for example, using pharmacological manipulations, is needed to directly assess this hypothesis.

Implications for the Hippocampus

Our hypotheses were inspired by both nonhuman studies demonstrating divergent effects of acute stress or glucocorticoid exposure across hippocampal pathways (Vandael et al., 2021; Chen et al., 2010; Van Gemert et al., 2009; Karst & Joëls, 2005; Pavlides et al., 1993), as well as human studies and neural network models highlighting hippocampal processes supporting statistical learning and episodic memory (Covington et al., 2018; Schapiro et al., 2014, 2017). Given that statistical learning is thought to rely heavily on subfield CA1 (via the MSP), which is spared or enhanced under stress or glucocorticoids in rodents, we hypothesized that stress would enhance statistical learning. However, effects in rodents have been mixed (e.g., Kavushansky et al., 2006; Karst & Joëls, 2005), and rodent and human hippocampal subfields differ in key ways, including in glucocorticoid receptor density (Wang et al., 2013; Szot et al., 2005; Seckl et al., 1991). Furthermore, although our task was designed to probe hippocampal-dependent statistical learning (Covington et al., 2018; Schapiro et al., 2014), some forms of statistical learning do not appear to require the hippocampus (Warren et al., 2020; Rungratsameetaweemana

et al., 2019; Reber & Squire, 1998; see also Marlatte et al., 2024). Thus, the early bridge provided by the current behavioral findings will need to be augmented by future studies that probe stress effects on human hippocampal subfields. This can be accomplished using high-resolution fMRI of the hippocampus. Notably, we recently found that glucocorticoid administration enhanced connectivity between hippocampal subfields during learning in healthy humans (Sherman, Harris, Turk-Browne, Sinha, & Goldfarb, 2023). However, as this study only probed episodic memory, further work is needed to understand the hippocampal mechanisms by which stress and glucocorticoids modulate statistical learning.

A General Role for Stress in Promoting Integrative Learning?

Our findings resonate with a recent proposal that stress may enhance gradual, integrative, or generalization-based learning processes across a range of brain regions (Sherman et al., 2024; Schwabe et al., 2022). For example, stress has been associated with biases away from episodic memory and toward S-R learning, which relies on the gradual learning of an association between a cue and a response to receive a desired outcome (e.g., Goldfarb, Shields, Daw, Slavich, & Phelps, 2017; Vogel et al., 2017; for reviews, see Goldfarb & Phelps, 2017; Vogel, Fernández, Joëls, & Schwabe, 2016). Although the neural substrates supporting S-R learning and statistical learning are decidedly different (relying on the striatum and hippocampus, respectively), both representations rely on learning temporal contingencies (i.e., to uncover which response leads to the desired outcome, given a particular cue). Furthermore, both types of associations require repeated experience, allowing individuals to separate out what reliably co-occurs from what co-occurs by chance. Thus, rather than framing stress as biasing away from hippocampal and toward striatal memory (Goldfarb & Phelps, 2017), the current findings accord better with an alternative, process-based perspective that stress may promote the learning and use of regularities (whether that be S-R associations or statistically learned temporal contingencies; Sherman et al., 2024). Such a bias may be adaptive: Acting based on regularities may be cognitively less demanding and thus may serve to preserve cognitive resources under stress.

In line with these ideas, our finding that stress enhances learning processes thought to be dependent on the MSP of the hippocampus in humans raises novel hypotheses about other kinds of learning that may be enhanced by stress. For example, other kinds of integrative learning, such as transitive inference and category learning, have also been associated with the hippocampus (Schlichting et al., 2014, 2021; Schlichting, Guarino, Schapiro, Turk-Browne, & Preston, 2017; Mack, Love, & Preston, 2016), particularly MSP (Sučević & Schapiro, 2023; Schapiro et al., 2017). This framework may perhaps explain previous behavioral findings that stress can enhance memory for linked episodes (Grob, Milivojevic, Alink, Doeller, & Schwabe, 2023). Further exploring the potential benefits of stress on these hippocampally mediated learning processes could help to inform frameworks of how acute stress acts on integration and suggest ways in which this inescapable part of daily life can be harnessed to enhance memory.

Limitations and Conclusions

As discussed throughout, there are several caveats and limitations to the current study. First, our sample was majority (60%) female participants. Although a notable change, as much stress research has exclusively focused on male participants (Shansky & Murphy, 2021), this imbalance (together with the fact that the magnitude of cortisol responses also differed by sex) makes it tricky to disentangle modulatory contributions of sex and glucocorticoids to stress effects on learning. Second, this study leveraged a between-subjects design. This was important for assessing stress effects on statistical learning, which is less amenable to a within-subject stress manipulation because learning one structure can interfere with learning a second structure (Yu & Zhao, 2015; Gebhart, Aslin, & Newport, 2009; Jungé, Scholl, & Chun, 2007). Nevertheless, this may have decreased our sensitivity to detect stress effects. Finally, we included three experimental groups to test exploratory questions about how the timing of stress may impact statistical learning. Although our sample size within each group was determined by a power analysis for key within-group effects, future work with larger groups of no stress and stress-delayed (which had the strongest effects) may lead to increased power to detect group-level differences.

Despite these limitations, the current study marks an important first step toward uncovering the effects of stress on hippocampal learning in humans. Our findings point to a novel, potentially adaptive role for stress to enhance some forms of hippocampal learning and raise hypotheses about how stress may affect different hippocampal subregions. This view is in line with the idea that stress can organize our memories adaptively (Goldfarb, 2019), allowing for the prioritization of what will be most relevant for the future. More generally, our study highlights how carefully examining behaviors associated with different types of memories may help to explain divergent stress effects across and within neural systems and provide new insights into how stress constrains learning and memory.

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Data Availability Statement

The data associated with this article are available at the following OSF page: https://osf.io/h3kmx/.

Author Contributions

Brynn E. Sherman: Conceptualization; Formal analysis; Investigation; Methodology; Software; Visualization; Writing—Original draft; Writing—Review & editing. Isabella Huang: Investigation; Resources; Validation; Writing—Review & editing. Elaine G. Wijaya: Investigation; Validation; Writing—Review & editing. Nicholas B. Turk-Browne: Conceptualization; Methodology; Supervision; Writing—Review & editing. Elizabeth V. Goldfarb: Conceptualization; Funding acquisition; Methodology; Supervision; Writing—Review & editing.

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Diversity in Citation Practices

Retrospective analysis of the citations in every article published in this journal from 2010 to 2021 reveals a persistent pattern of gender imbalance: Although the proportions of authorship teams (categorized by estimated gender identification of first author/last author) publishing in the *Journal of Cognitive Neuroscience (JoCN)* during this period were M(an)/M = .407, W(oman)/M = .32, M/W = .115, and W/W = .159, the comparable proportions for the articles that these authorship teams cited were M/M = .549, W/M = .257, M/W = .109, and W/W = .085 (Postle and Fulvio, *JoCN*, 34:1, pp. 1–3). Consequently, *JoCN* encourages all authors to consider gender balance explicitly when selecting which articles to cite and gives them the opportunity to report their article's gender citation balance. The authors of this paper report its proportions of citations by gender category to be: M/M = .297; W/M = .319; M/W = .099; W/W = .286.

Note

1. This model failed to converge when including random slopes for predictability, repetition, and accuracy; we thus ran the model without the random slope for accuracy, but we note that the results are comparable regardless of which random slope was excluded.

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