Low lifetime stress exposure is associated with reduced stimulus–response memory

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Exposure to stress throughout life can cumulatively influence later health, even among young adults. The negative effects of high cumulative stress exposure are well-known, and a shift from episodic to stimulus–response memory has been proposed to underlie forms of psychopathology that are related to high lifetime stress. At the other extreme, effects of very low stress exposure are mixed, with some studies reporting that low stress leads to better outcomes, while others demonstrate that low stress is associated with diminished resilience and negative outcomes. However, the influence of very low lifetime stress exposure on episodic and stimulus–response memory is unknown. Here we use a lifetime stress assessment system (STRAIN) to assess cumulative lifetime stress exposure and measure memory performance in young adults reporting very low and moderate levels of lifetime stress exposure. Relative to moderate levels of stress, very low levels of lifetime stress were associated with reduced use and retention (24 h later) of stimulus–response (SR) associations, and a higher likelihood of using context memory. Further, computational modeling revealed that participants with low levels of stress exhibited worse expression of memory for SR associations than those with moderate stress. These results demonstrate that very low levels of stress exposure can have negative effects on cognition.

Stressors occurring over the life course exert a cumulative impact on human health (McEwen 1998; Lupien et al. 2009). Even among preclinical samples of young adults, higher levels of lifetime stress exposure have been associated with adverse health outcomes (Toussaint et al. 2016), changes in reactivity to acute stress (Elzinga et al. 2008; Lovallo et al. 2012; Seery et al. 2013), and increased risk for psychopathology (Lloyd and Turner 2008). Stress-related psychopathologies may be driven in part by stress-induced memory biases. Specifically, an imbalance between flexible, rapidly acquired contextual associations (which depend on the hippocampus; Bunsey and Eichenbaum 1996; Burgess et al. 2002) and rigid, slowly acquired stimulus–response associations (which depend on the striatum; Graybiel 1998; Bayley et al. 2005; Yin and Knowlton 2006) has been theorized to contribute to disorders like addiction and post-traumatic stress disorder (PTSD; McDonald et al. 2004; Goodman and Packard 2016). For example, preferential use of stimulus–response memory could facilitate habitual drug-seeking behavior. However, the effects of lifetime stress exposure—especially very low levels of lifetime stress—on the relative use of contextual and stimulus–response memory are not yet known.

Prior research has suggested that the relative engagement of these memory systems may be sensitive to lifetime stress exposure. Across species, high levels of recent acute stress (Kim et al. 2001; Packard and Wingard 2004; Schwabe et al. 2007; 2010; Elliott and Packard 2008; Schwabe and Wolf 2012; Leong and Packard 2014) and chronic stress (Schwabe et al. 2008; Ferragud et al. 2010; Taylor et al. 2014) have been shown to facilitate preferential engagement of striatal rather than hippocampal memory. Importantly, remote stressors are also associated with a bias toward striatal memory (Schwabe et al. 2012; Patterson et al. 2013), indicating that stressors experienced throughout life may modulate memory systems. Further, periods of chronic stress can lead to lasting morphological changes that would facilitate this shift between memory systems. Chronic stress has frequently been shown to impair the structure and function of the hippocampus (McEwen 1999; Lupien et al. 2007) and has recently been shown to enhance the structure and function of the striatum (Dias-Ferreira et al. 2009; Taylor et al. 2014). Thus, just as chronic stress early in life can influence working memory in adulthood (Evans and Schamberg 2009), it may also modulate long-term memory systems.

Although these results lead to strong predictions regarding the effects of high levels of lifetime stress exposure, the possible effects of very low stress are less clear. Understanding the influence of low levels of stress on cognition is critical, as low lifetime stress exposure can lead to negative health outcomes and
would expect low stress participants to preferentially engage context and striatal memory. In this case, we would expect that very low stress participants would show impaired context memory. Thus, if only one memory system could be used, low stress participants would show impaired context memory. Therefore, we hypothesized that the least- and most-stressed participants from the population would differ in their ability to encode and retrieve contextual and SR associations.

In this study, we investigate the influence of low levels of lifetime stress exposure on contextual and stimulus–response memory. We measured cumulative lifetime stress experiences in a large cohort of undergraduate students at a 4-year university, a sample previously shown to have relatively low stress exposure (Breslau et al. 1991; Anders et al. 2012). To compare participants with very low stress exposure to those with moderate stress exposure, we recruited individuals from the top and bottom of this distribution. We assessed participants’ lifetime stress exposure using a comprehensive online interviewing system, and their memory using a recently developed task that concurrently and comparably measures contextual (hippocampal) and stimulus–response (SR; striatal) memory by assessing their respective influences on attention in visual search (Goldfarb et al. 2016). We hypothesized that the least- and most-stressed participants from the population would differ in their ability to encode and retrieve contextual and SR associations. Specifically, if the relationship between lifetime stress and context memory followed the same trajectory as acute stress and hippocampal memory, then we would expect that very low stress participants would show impaired context memory. Thus, if only one memory system could be used, low stress participants would preferentially engage SR memory. On the other hand, if the relationship between lifetime stress and stimulus–response memory followed the same pattern as lifetime stress and addiction risk, we would expect that very low stress would be associated with impaired SR memory. In this case, we would expect low stress participants to preferentially engage context memory.

Materials and Methods

Participants

Participants (N = 893) completed the Stress and Adversity Inventory for Adults (STRAIN) online for course credit. This population consisted of healthy, young (in the final laboratory sample, M = 19.7 yr, SD = 1.2) participants who were completing full-time coursework at the time of assessment. Based on previous power analyses (Goldfarb et al. 2016), we invited STRAIN-screened participants into the laboratory until 35 participants from the bottom 25% and 35 participants from the top 25% of the distribution completed the laboratory study (Supplemental Table S1; see STRAIN below for details). Two additional laboratory participants were excluded due to failure to follow task instructions (N = 1) and incorrect coding of STRAIN responses (N = 1). Participants in the low- and moderate-stress groups did not differ with respect to age (P > 0.25) or gender (P = 0.19) (Supplemental Table S1). The laboratory session was completed for monetary compensation within a few months of the STRAIN (M = 79 d). Participants provided written informed consent for both components. All procedures were approved by the New York University Committee on Activities Involving Human Subjects.

Materials

STRAIN

Lifetime stress exposure was assessed using the Stress and Adversity Inventory for Adults (Adult STRAIN). The STRAIN employs a sophisticated interviewing methodology that includes extensive branching logic to assess a person’s lifetime experience of 96 different acute and chronic stressors. If a respondent indicates that he or she has experienced a particular stressor, the branching logic prompts follow-up questions to assess the frequency, timing, duration, and perceived severity of the reported stressor. As such, the STRAIN provides extensive information on stressor exposure, the stressfulness of that exposure, when it occurred, and how long it lasted. The two main indices used in the present analyses were participants’ lifetime stressor count and overall stressor severity, calculated as the sum of perceived severities of all reported stressors. Early life stress exposure was calculated by summing stressor counts and severity scores for all stressors occurring before age 18, and recent stressors were defined as those that were either ongoing or experienced in the 3 mo prior to assessment. The STRAIN has good predictive validity, as evidenced by prior research showing that the main stress exposure indices from the STRAIN strongly predict several different health outcomes (Bower et al. 2014; Toussaint et al. 2016; Dooley et al. 2017). The Adult STRAIN also has high reliability, with a test–retest correlation of r = 0.92 over 2 wk.

In order to compare individuals with low lifetime stress to those with moderate stress exposure, we computed the overall stressor severity score for each participant (M = 30.9, range = 0–124) and recruited participants from the top and bottom 25% of this distribution to participate in the search task. Using a latent class analysis (Supplemental Fig. S1; Supplemental Text), we determined that the distribution of severity scores was better described by two latent classes than by one class, and that participants from the top and bottom of the distribution fell into distinct classes. These findings provide statistical support for dichotomizing the stress severity score and treating the participants from the top and bottom of the distribution as separate groups (MacCallum et al. 2002).

Participants from the bottom of the distribution (N = 35 from the bottom 25% of our population) had experienced fewer than 4 major stressors on average (range = 0–11), which places them at the extreme low-end of a larger population. However, participants reporting the highest stress severity (N = 35 from the top 25%) experienced an average of 29 lifetime stressors (range = 18–50), which equates to a moderate level of lifetime stress exposure on the STRAIN (high stress participants, similar age group: M = 42 stressors, range = 25–83; G. M. Slavich and G. S. Shields, unpublished data), consistent with previous reports of relatively low stress exposure in this population (Anders et al. 2012). We thus refer to these groups as Low Stress (LS) and Moderate Stress (MS), respectively.

Multicued search task

To measure hippocampal and striatal memory we used a recently developed visual search task (Fig. 1). The multicued search task builds on the contextual cueing task, in which repeated spatial contexts facilitate search performance. This “contextual cueing” effect has been extensively replicated (e.g., Chun and Jiang 1998, 2003; Greene et al. 2007; Manelis and Reder 2012; Giesbrecht et al. 2013) and shown to critically involve the hippocampus (Chun and Phelps 1999). The multicued search task also includes probabilistic stimulus–response (SR) associations, designed to measure striatal memory. Previous research has demonstrated that, in a group of participants not screened for stress exposure, the multicued task can lead to performance benefits...
moved. They were asked to indicate the quadrant in which the “T” had appeared (testing memory for CC and SR associations), and the direction of the “T” (SR). Finally, they completed a probe test (40 trials, Fig. 1, right). During this phase, participants were told that multiple “Ts” would appear on each trial, and to respond to the “T” they found first. Some trials included both CC and SR cues, each of which indicated the “T” would appear in a distinct quadrant (competitive, 12 trials) or in the same quadrant (collaborative, 4 trials). Additional trials with no memory cues (12 with “Ts” in distinct quadrants, 12 with “Ts” in the same quadrant) were randomly interleaved. As in the search phase, participants received feedback regarding reaction time (RT) and accuracy on every trial. Finally, participants were asked to verbally report any learned associations.

Results

Influence of lifetime stress exposure on relative expression of multiple memory systems

We first examined whether lifetime stress exposure, like acute stress, influenced which form of memory would be preferentially expressed. To do this, we analyzed performance during probe test trials in which participants could use either CC or SR memory (Fig. 1, right), focusing on the first trial in order to limit the influence of new learning. Lifetime stress exposure led to distinct memory biases—specifically, the majority of LS participants (71.4%) used CC rather than SR memory, whereas the majority of MS participants (68.6%) used SR rather than CC memory ($\chi^2$,$N=$70 = 9.69, $P = 0.004$) (Fig. 2). This pattern persisted throughout the probe test, with most LS (62.8%) expressing CC memory and most MS (54.3%) expressing SR memory. To understand how these memory biases developed, we examined how participants learned CC and SR associations.

Influence of lifetime stress exposure on memory-guided search

Day 1

Overall, visual search performance did not differ between the low- and moderate-stress groups (Accuracy—MS: $M = 96.8\%$, LS: $M = 96.1\%$, $t_{68} = 1.06$, $P > 0.25$; RT—MS: $M = 1.47$ sec, LS: $M = 1.38$ sec, $t_{68} = 1.23$, $P = 0.22$; Fig. 3A). Participants in these two groups also did not differ in performance on No Cue trials

Figure 1. Search task to measure multiple memory systems. During the search phase (left), participants implicitly learned associations with mnemonic cues that could help them respond to the target. On contextually cued (CC) trials, repeated spatial patterns provided a cue for the location of the target. On stimulus–response (SR) trials, the color probabilistically cued the approximate target location and motor response. During the probe test (right), the two mnemonic cues were combined, each predicting a distinct target location and motor response.

Figure 2. Proportion of participants choosing context or stimulus–response cued target during the first trial of the probe test. More Moderate Stress participants chose the target cued by the stimulus–response association, whereas more Low Stress participants chose the target cued by the context association.
Low lifetime stress multiple memory systems

Figure 3. Search task performance. (A) Learning during the search task on Day 1 (Epoch 1–6) and retention on Day 2 (Epoch 7–8) for Low Stress (left) and Moderate Stress (right) participants. (B) Memory-guided search during the end of Day 1 (left) and Day 2 (right). Positive values indicate faster reaction time (RT) when using a memory cue compared with no memory cue. (*** P < 0.001; (**) P < 0.01; (‘) P < 0.05. (C) STRAIN variables predict SR performance during learning (left) and retention (right). Seventy of acute stressors negatively correlated with SR performance in Low Stress participants during learning and retention. Full list of predictive STRAIN variables in Supplemental Table S2. (CC Contextually cued, (SR) stimulus–response cue, (LS) Low Stress, (MS) Moderate Stress.

(Accuracy—t(134) = 1.12, P > 0.25; RT—Main Effect of Group: F(1,68) = 2.5, P = 0.12, n^2 = 0.035; Group × Epoch: F(1,68) = 1.19, P = 0.28, n^2 = 0.017). Further, there were no differences in accuracy between trial types, demonstrating that participants could perform the task with and without memory cues, and that differences in RT are not due to speed/accuracy tradeoffs (Supplemental Table S2). As in previous studies (Chun and Jiang 1998; Goldfarb et al. 2016), we measured the influence of memory on search as performance on trials with memory cues relative to trials with no mnemonic cue (No Cue trials) during the second half of the experiment. To enable comparison with Day 2 performance, we focus on the last two epochs of Day 1.

Lifetime stress exposure led to differences in learning and retrieval of SR associations. Although MS participants showed significant SR learning at the end of Day 1 (t(134) = 2.12, P = 0.041), LS participants did not (t(134) = −0.83, P > 0.25). These patterns were consistent throughout Day 1 (MS: Cue [No Cue vs. SR] × Time: F(3,170) = 2.58, P = 0.042, Huyhn–Feldt corrected, n^2 = 0.071; LS: Cue × Time: F(3,170) = 1.45, P > 0.21). As SR cues were 80% valid, we could also assess development of SR associations by comparing performance on valid to invalid trials. We observed a significant Group × Cue [SR-Valid vs. SR-Invalid] interaction throughout Day 1 (F(1,68) = 4.21, P = 0.044, n^2 = 0.058), showing that SR memory differed between MS and LS participants (Supplemental Fig. S2).

In contrast, the stress groups did not differ in learning and retrieval of CC associations. Both groups showed significant CC learning during the last two epochs (faster RT on CC than No Cue trials; LS: t(134) = 2.25, P = 0.031; MS: t(134) = 6.71, P < 0.001), MS participants showed significant CC learning throughout Day 1 (Main effect of Cue [No Cue vs. CC]: F(1,134) = 20.36, P < 0.001, n^2 = 0.37), while LS showed the same pattern (although not significant; F(1,24) = 2.56, P = 0.12, n^2 = 0.07), with no significant difference between stress groups (Group × Cue: F(1,68) = 1.3, P > 0.25).

Day 2

The above results persisted 24 h later (Fig. 3). Again, there was no significant difference between stress groups in overall search performance (Accuracy—MS: M = 97.9%, LS: M = 97%; t(134) = 1.51, P = 0.14; RT—MS: 1.13 sec; LS: 1.11 sec; t(134) = 0.49, P > 0.25) or performance on No Cue trials (Accuracy—t(134) = 1.01, P > 0.25; RT—F(1,68) = 1.16, P > 0.25, n^2 = 0.017). Although MS participants continued to show SR memory expression (faster on SR than No Cue; t(134) = 2.59, P = 0.014), LS participants still did not (t(134) = 0.13, P > 0.25). Both groups retained CC memory on Day 2 (faster on CC than No Cue; LS: t(134) = 3.14, P = 0.003; MS: t(134) = 5.58, P < 0.001).

In the explicit memory tests immediately following search, neither stress group showed above chance (25%) memory for the cued “T” location on CC trials (LS: M = 27.5%, t(134) = 0.89, P > 0.25; MS: 27.9%, t(134) = 1.07, P > 0.25), or the cued “T” orientation on SR trials (50% chance; LS: 52.9%, t(134) = 0.7, P > 0.25; MS: 54.3%, t(134) = 0.9, P > 0.25). However, MS participants were significantly above chance in recalling the cued “T” location on SR trials (37.9%, t(134) = 3.43, P = 0.002), whereas LS were not (25.7%, t(134) = 0.21, P > 0.25). Despite this, only one MS participant (2.9%) verbally reported that the “T” usually appeared in a consistent location.

Relationship between types of stress exposure and SR memory

To examine whether specific aspects of lifetime stress exposure explained differences in SR learning and retention (beyond those explained by MS versus LS group), we conducted linear regressions in which Group and different STRAIN variables were used as predictors. SR learning and retention were quantified as the percent difference in RT between accurate No Cue and SR trials during the end of Day 1 and throughout Day 2, respectively. Based on prior research (Bower et al. 2014; Toussaint et al. 2016), we examined the frequency and perceived severity of acute, chronic, early life, and adulthood stressors as predictors of SR learning and retention in separate regressions (Supplemental Table S3).

For both learning and retention, we observed a main effect of acute stressor count (Day 1: β = −4.8, P = 0.017; Day 2: β = −5.81, P = 0.003), acute stressor severity (Day 1: β = −2.8, P = 0.021; Day 2: β = −2.89, P = 0.015) (Fig. 3C), and early life stressor count (Day 1: β = −3.92, P = 0.048; Day 2: β = −5.8, P = 0.003), such that increasing stress was associated with worse SR performance. This relationship was driven by LS participants: for all stress indices listed above, increasing levels of stress negatively predicted SR performance in LS (all Ps < 0.05) but not MS participants (all Ps > 0.11). In other words, among those participants with very low overall stress exposure, those who had experienced more (or more severe) stressors showed worse SR performance.
Computational model: Understanding differences in SR memory

Thus far, we have demonstrated that individuals who experienced moderate levels of lifetime stress exposure show faster RT in the presence of SR cues relative to trials with no memory cues, but those who experienced low levels of lifetime stress exposure do not show this RT benefit. We also showed that low stress participants do not differ in RT based on whether the SR cue is valid or invalid, although moderate stress participants show this distinction. It is possible that the stress groups differed in another dimension of task performance that led to this result. Further, if the groups did specifically differ in SR memory, it remains unclear what component of SR memory was altered in low stress participants.

To address these questions, we created a computational model to characterize dynamics influencing RT on each trial of Day 1. This allowed us to examine the contribution of different memory systems in terms of trial-by-trial RT adjustments reflecting learning, complementary to the epoch-wise analyses presented above. We modeled RT on every trial as reflecting a nonspecific improvement with total time on task, accompanied by trial-specific contributions of three learning processes: priming of stimulus locations (regardless of cue type), and learning based on history with CC and SR cues.

As reported previously (Maljkovic and Nakayama 1996), RT provided evidence of location priming. Participants were significantly faster to find the “T” if it was in the same quadrant (M = 1.33 sec) rather than a different quadrant (1.45 sec) than the previous trial (t(69) = 7.63, P < 0.001). A similar process occurred on SR trials: participants were significantly faster to find the “T” when it was in the same quadrant (SR-Valid; 1.39 sec) rather than a different quadrant (SR-Invalid; 1.44 sec) than the last SR trial (t(69) = 2.24, P = 0.028). Thus, RT could reflect memory for the “T” location on the previous trial and, on CC or SR trials, memory based on history with CC and SR cues.

Specifically, for every trial t, we modeled RT as follows:

\[
\log(\text{RT}_t) = \beta_0 + (\beta_{\text{num}} \times \log(t\text{Num}_t)) + (\beta_{\text{prime}} \times w^{\text{prime}}_q) + \beta_{\text{SR}} \times (\beta_{\text{SR}} \times w^{\text{SR}}_q + ICC_t \times (\beta_{\text{CC}} \times w^{\text{CC}}_q) + \epsilon_t,
\]

where ISR and ICC are binary indicators of whether trial t was a CC or SR trial and q indicates the correct quadrant.

The vectors \( \vec{w} \) updated on every relevant trial following a prediction-error based Rescorla–Wagner updating rule (Rescorla and Wagner 1972), with a stepsize determined by a corresponding learning rate (\( \alpha_{\text{prime}}, \alpha_{\text{SR}}, \) or \( \alpha_{\text{CC}} \); details in Supplemental Text).

The \( \alpha \)'s and \( \beta \)'s, all free parameters that we fit to best explain each subject’s RT timeseries, govern the acquisition and expression (respectively) of the learned associations that guide search. Accordingly, this model embodies two distinct (but not mutually exclusive) hypotheses that could explain the difference in performance between MS and LS participants.

One possibility is that MS participants were better at using the \( \alpha_{\text{SR}} \) predictions to facilitate RT on SR-cued trials, which would be shown by a significantly lower \( \beta_{\text{SR}} \). Another possibility is that MS participants were faster to update location expectations on SR-cued trials, which would be reflected by a significantly larger learning rate \( \alpha_{\text{SR}} \). We used Bayesian hierarchical modeling (Supplemental Text) to derive group-level estimates of each parameter and thereby to estimate the difference in each parameter between groups. If the change in parameter estimates from MS to LS participants was significantly different from zero, the two groups differed on that parameter.

The model captured the learning trends seen in the data (Fig. 4A). The only parameter that differed significantly between MS and LS participants was \( \beta_{\text{SR}} \), showing that expression of SR learning was reduced in LS participants (Fig. 4B; full parameter list in Supplemental Table S4). That is, although the MS group used location expectations formed on previous SR trials to find the “T” more quickly, the LS group made significantly less use of these SR expectations. However, we did not find evidence that the updating of location expectations differed between groups, as there was no significant difference in learning rate (\( \alpha_{\text{SR}} \)). These results indicate that lifetime stress exposure modulated the use, while not significantly changing the learning rate, of stimulus–response associations.

Discussion

The present data provide some of the first evidence that very low levels of lifetime stress exposure can have negative effects on memory. Although individuals with low levels of lifetime stress did not differ from moderately stressed participants in overall visual search performance or in learning and memory for contextual associations, they did differ in stimulus–response (SR) memory. Individuals who had experienced low levels of lifetime stress made significantly less use of probabilistic stimulus–response associations than those who had experienced moderate levels of stress. These effects were supported by a computational model of task performance, showing that the only parameter that significantly differed between groups was the parameter governing the expression of SR memory.
The results of the probe test, demonstrating that higher levels of stress are associated with increased likelihood of using SR rather than context memory, are consistent with a large body of research. In both rodents and humans, studies have consistently shown that recent chronic (rodent: Schwabe et al. 2008; Ferragud et al. 2010; human: Schwabe et al. 2008) and acute stress (rodent: Kim et al. 2001; Packard and Wingard 2004; Packard 2009; Schwabe et al. 2010; Vanelzakker et al. 2011; Leong and Packard 2014; human: Schwabe et al. 2007; 2013; Schwabe and Wolf 2012; but see Schwabe et al. 2009) causes a shift from expressing hippocampal to striatal memory. However, as only one memory system could be expressed in these tasks, and these systems are known to compete (Poldrack and Packard 2003; Foerde et al. 2006) or compensate (Moody et al. 2004), it was not clear how each form of memory was affected individually (Goldfarb and Phelps 2017). Here, we show that the trade-off between context and SR memory with varying lifetime stress was driven by differences in SR memory.

These results demonstrate that context and SR memory are differentially sensitive to very low levels of lifetime stress. Although expression of SR memory differed between low and moderate stress participants, context memory did not. Our results do not support the hypothesis that very low lifetime stress would, like low levels of acute arousal (McCullough et al. 2015), lead to impaired hippocampal memory in the low stress group. Instead, we found support for our hypothesis that SR memory would be reduced among low stress participants. This result is consistent with prior research showing that higher cumulative stress is associated with increasing odds of alcohol dependence (Lloyd and Turner 2008), which has itself been theorized to result from enhanced striatal memory (McDonald et al. 2004). Thus, it is possible that mechanisms shown to link lifetime stress to addiction risk in preclinical populations (see Sinha 2008 for review) are also relevant to changes in striatal memory.

Despite this group-level effect, we were surprised to find a negative relationship between stressors and expression of SR memory among participants with overall low stress exposure. This may be due in part to the fact that individual stressors occur within the context of a lifetime of events (Seery et al. 2010) and attain greater importance among individuals with overall very few stressful events. One possibility is that maladaptive responses to stressors among those with low stress exposure (Seery et al. 2013; Liu 2015) could contribute to performance deficits. For example, recent work has shown lower striatal BOLD signal in response to stress among individuals with low cumulative adversity (Seo et al. 2014). Given the previously reported relationship between increased striatal signal and SR memory in the present task (Goldfarb et al. 2016), generally dampened striatal reactivity could lead to worse performance. Although future studies are needed to understand the mechanism by which this negative relationship occurs, this finding emphasizes the importance of treating cumulative stress as a continuous as well as dichotomized variable.

Limitations of the present study include simultaneous measurement of contextual and stimulus–response memory. Given potential interactions and competition between these memory systems (Poldrack and Packard 2003; McDonald et al. 2004; Foerde et al. 2006), it is unclear whether the observed reduction in SR expression among LS participants would exist in a task that assessed only SR learning. However, there are rarely cases in everyday life that engage only one memory system. Even in canonical SR tasks, the medial temporal lobe has been shown to contribute to learning (Poldrack et al. 2001), lending the current approach greater ecological validity. Another limitation involves the use of retrospective self-report to assess lifetime stressors. Because we measured (but did not manipulate) lifetime stress exposure, these results do not demonstrate a causal relationship between stress and memory. The validity of using self-report to assess stress exposure has been demonstrated in numerous studies: many life events can be reliably recalled when probed systematically (Brewin et al. 1993), and self-reported stress exposure has been associated with different neural (Seo et al. 2014) and behavioral responses to acute stressors (Seery et al. 2013), as well as different health outcomes (Bower et al. 2014; Toussaint et al. 2016). It is also unlikely that observed differences in learning are the result of systematic biases in self-reported stress exposure. Nonetheless, future research should examine the present associations using independent measures of objective stress exposure. Finally, these data do not address the effects of extremely high levels of cumulative stress exposure. The young undergraduate population used in this study had experienced relatively moderate levels of stress exposure relative to the general population, which is an appropriate sample in which to test the present hypotheses. An additional “high stress” community sample could be added in future research, but caution is warranted, as such a sample would differ in many demographic characteristics and thus potentially confound comparisons between groups. Nevertheless, additional research is needed to understand the effects of the full trajectory of lifetime stress exposure on the use of different memory systems.

In sum, the present study provides preliminary evidence that very low levels of lifetime stress exposure may be associated with impairments in cognitive functions in humans. Relative to participants who had experienced moderate levels of lifetime stress, low stress participants showed reduced expression of stimulus–response memory. This difference was specific to stimulus–response memory, as low stress participants were capable of learning and retrieving context memories. These results raise the question of whether some stress exposure is necessary for good stimulus–response memory, and how very low levels of stress exposure could influence other cognitive processes.

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