Reminiscing about positive memories buffers acute stress responses

Authors: Megan E. Speer & Mauricio R. Delgado

Supplementary Results: Behavioral Study

Change in Cortisol over time by Condition and Memory Valence

To measure changes in cortisol across time, we conducted a valence (positive, neutral) x condition (stress, control) x time ANOVA for cortisol across two timepoints relative to baseline. Specifically, this included increases from baseline for timepoint #2 (peak; cort *s*2 – cort *s*1) and increases from baseline for timepoint #3 (recovery; cort *s*3 – cort *s*1). We observed a main effect of valence ($F_{1,130}$ = 7.38, p = .008), a main effect of condition ($F_{1,130}$ = 5.36, p = .022), and a main effect of time ($F_{1,130}$ = 70.3, p < .001), but non-significant interactions for valence x condition ($F_{1,130}$ = 0.29, p = .594), time x valence ($F_{1,130}$ = 2.47, p =.118), time x condition ($F_{1,130}$ = 2.78, p = .098) and time x valence x condition ($F_{1,130}$ = 0.01, p =.981). Similar to the AUCI analysis, we found no significant interactions for cortisol. We then computed condition x valence ANOVAs for baseline-corrected cortisol for the two timepoints separately. Timepoint #2 (peak) showed a significant main effect of valence ($F_{1,130}$ = 7.64, p = .007) and of condition ($F_{1,130}$ = 6.15, p = .014) but no interaction ($F_{1,130}$ = 0.19, p = .664). Timepoint #3 (recovery) also showed a main effect of valence ($F_{1,130}$ = 4.36, p = .039), and approached significance for condition ($F_{1,130}$ = 2.60, p = .11) but no interaction ($F_{1,130}$ = 0.31, p = .579). We then tested our specific hypothesis for stress-positive relative to stress-neutral groups for each timepoint separately and found that both timepoints were trending (timepoint #2: t_{65} = 1.96, p = .051; timepoint #3: t_{65} = 1.87, p = .066), suggesting that similar cortisol differences are found at peak and recovery.

Emotion during Recall as a Mediator between Resiliency and Mood after Recall

We found that trait resiliency mediates the relationship between positive feelings during memory recollection and enhanced mood afterwards in Stress-Positive individuals. It could also be the case that individuals with greater resilience report enhanced mood after recall, but only if they generated stronger positive feelings during recollection. Therefore, we tested whether emotion during recall might mediate the relationship between resiliency and mood after recall in an alternative model. However, resiliency remained a significant predictor of mood whereas the indirect effect was not significant in this model, indicating that emotion during recall was not a mediator (direct effect: B = 0.31, SE = 0.13, $t_{32} = 2.46$, p = .02; indirect effect: B = 0.05, SE = 0.07, bias corrected bootstrapping 95% confidence interval {-0.09 to 0.20}).

Supplementary Results: fMRI Study

Feeling Modulates Ventral Striatum Responses during Positive Memory Recollection

We have previously shown that the ventral striatum (VS) – when functionally defined by monetary gains versus losses – is also sensitive to the valence of autobiographical memory recollection (positive versus neutral)[1]. Since acute stress has been linked to reduced behavioral and neural responsiveness to rewards[2,3], we hypothesized that recalling positive memories that dampen the stress response would engage the VS to a greater extent than recalling neutral memories. To test this, our stress participants performed a surprise card-guessing task for monetary rewards at the end of the scanning session (+40 min after stressor). On each trial, participants had the opportunity to gain or lose money by guessing whether a card's value was higher or lower than the number 5 (adapted from[4]). We then used this task to identify reward-related ROIs by contrasting gains > losses, which revealed activation in the VS bilaterally (Supplementary Fig 1; Supplementary Table 4). We extracted parameter estimates for high (rating of 3 or 4) and low (rating of 1 or 2) feeling memories within the VS ROI, which allowed us to further examine group differences in neural activity as a function of feeling. Interestingly, feeling modulated VS responses only in the positive group, showing greater activity for high relative to low feeling memories (left VS: $t_{21} = 2.48$, $p = .022$; right VS: $t_{21} = 1.99$, $p = .06$), but not for the neutral group (both $p > .24$). This suggests that, when exposed to stress, reminiscing about positive memories may recruit greater VS activity to aid in dampening acute stress responses. Although one limitation of this finding is the lack of a comparison with a non-stress control group, as the design included two stress groups who underwent different memory treatments (positive or neutral recall).

Supplementary Results: Vividness Ratings and Recall Duration by Memory Valence (Positive vs. Neutral)

It is also possible that other factors, such as the level of engagement or interest during memory recall, could be driving our cortisol differences between positive and neutral recollection. To address this issue, we conducted analyses examining a) the duration of memory recall during the task and b) post-experimental vividness ratings of each memory previously recalled in the scanner (i.e., How vivid was the memory or how clearly could you see the particular memory in your mind? Ratings: 1-5; 1 = very slightly or not at all vivid, 5= extremely vivid).

Recall duration and vividness ratings can help us infer how distracting or engaging the memories likely were during recall. For instance, if positive memories were much more engaging than neutral memories, we would expect participants in the positive group to have spent significantly longer thinking about them than individuals in the neutral group. Yet, individuals chose to recall positive memories for the same amount of time as they chose to recall neutral memories, which was replicated across both studies (Study 1 - Behavioral: $M_{Stress\text{-}Positive} = 4.45$ sec, $SD = 2.40$ sec; $M_{Stress\text{-}Neutral} = 4.68$ sec, $SD = 3.21$ sec; $t_{64} = -0.33$, $p = .743$; $M_{Control\text{-}Positive} = 4.94$

sec, SD = 3.46 sec; $M_{Control\text{-}Neutral}$ = 4.14 sec, SD = 2.37 sec; t_{64} = 1.10, p = .274; Study 2 - fMRI: $M_{Stress\text{-}Positive}$ = 5.75 sec, SD = 2.46 sec; $M_{Stress\text{-}Neutral}$ = 5.44 sec, SD = 2.45 sec; t_{41} = 0.42, p = .678).

With respect to relation to cortisol, we also conducted the following analysis with recall duration. We compared memories that were recalled longer and therefore could be more engaging or even more distracting, with memories that were recalled for a shorter duration of time, and therefore deemed less engaging perhaps or less distracting. We found no differences in cortisol responses within the Stress-Neutral group (Study 1 - Behavioral: $AUCI_{Long\text{-}Recall}$ = 0.76, SD = 3.35, N = 16; $AUCI_{Short\text{-}Recall}$ = 3.59, SD = 8.01, N = 17; t(31) = -1.31, p = .201; Study 2 - fMRI: $AUCI_{Long\text{-}Recall}$ = 7.88, SD = 6.05, N = 10; $AUCI_{Short\text{-}Recall}$ = 5.61, SD = 8.08, N = 11; t(19) = 0.72, p = .478) or within the Stress-Positive group (Study 1 - Behavioral: $AUCI_{Long\text{-}Recall}$ = -0.76, SD = 3.99, N = 17; $AUCI_{Short\text{-}Recall}$ = -0.57, SD = 5.49, N = 16; t(31) = -0.11, p = .912; Study 2 - fMRI: $AUCI_{Long\text{-}Recall}$ = 3.75, SD = 6.83, N = 11; $AUCI_{Short\text{-}Recall}$ = 0.70, SD = 5.49, N = 11; t(20) = 1.15, p = .262).

Vividness ratings could also be an indicator of the level of engagement, interest, or distraction during memory recall. In terms of vividness of memories recollected in the fMRI study, there was no difference in vividness ratings between Stress-Positive and Stress-Neutral individuals ($M_{Stress\text{-}Positive}$ = 3.43, SD = 0.47; $M_{Stress\text{-}Neutral}$ = 3.18, SD = 0.76; t_{41} = 1.28, p = .207), suggesting that positive memories were not necessarily more engaging or interesting than neutral memories.

To examine the impact of vividness on cortisol responses, we tested whether highly interesting but neutral events might also lead to a dampening of cortisol. To address this, we first performed a median split based on vividness ratings to select individuals who reported highly engaging memories in both groups of our fMRI study. It is important to note that vividness ratings were matched across groups in these selected high vividness samples ($M_{Stress\text{-}Positive}$ = 3.77, SD =

0.34, N = 11; $M_{Stress\text{-}Neutral}$ = 3.75, SD = 0.38, N = 11; t_{20} = 0.12, p = .903). We then tested whether there were differences in cortisol response for individuals who recalled highly interesting but neutral events (i.e., Stress-Neutral high vividness group) as compared to highly interesting but positive events (i.e., Stress-Positive high vividness group). This is deemed exploratory given the small sample size; however, the analysis supports the key finding that recalling positive memories dampens the stress response, even if compared with highly vivid but neutral memories ($AUCI_{Stress\text{-}Positive}$ = 1.26, SD = 5.32; $AUCI_{Stress\text{-}Neutral}$ = 5.87, SD = 5.32; t_{20} = -2.04, p = .055).

To provide converging evidence that the degree of engagement or interest during memory recall was not the primary driver of cortisol responses, we also explored within each group (positive, neutral) comparing cortisol responses across high and low vividness memories. In line with our prediction, there were no differences in cortisol response between individuals with high vivid and low vivid memories within the Stress-Neutral group ($AUCI_{High\text{-}Vivid}$ = 5.87, SD = 5.32, N = 11; $AUCI_{Low\text{-}Vivid}$ = 7.59, SD = 8.89, N = 10; t_{19} = -0.54, p = .594) or within the Stress-Positive group ($AUCI_{High\text{-}Vivid}$ = 1.26, SD = 5.32, N = 11; $AUCI_{Low\text{-}Vivid}$ = 3.20, SD = 7.18, N = 11; t_{20} = -0.72, p = .480).

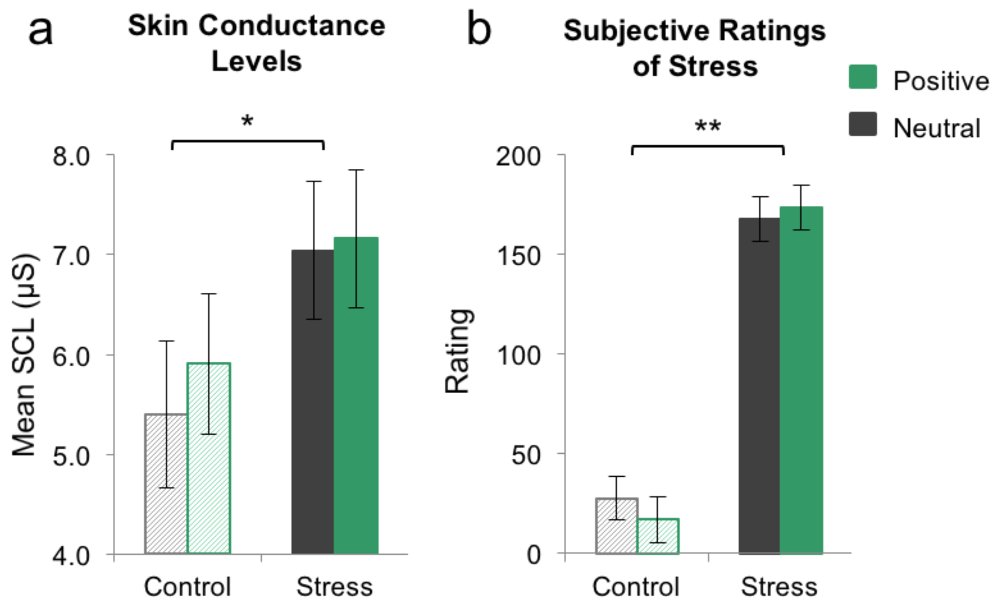
These additional analyses have provided evidence of a few key points. First, positive memories were not necessarily more engaging, interesting, or distracting than neutral memories in our study, based on similar recall duration and vividness ratings. Second, we found that memories rated as being more vivid or those which were recalled longer did not lead to a greater dampening in cortisol response after stress for neutral memories or for positive memories. Together, what these data suggest is that the degree of interest, engagement, or distraction during memory recall was not necessarily the primary driver of our cortisol results.

Supplementary Results: Feeling Rating Distributions

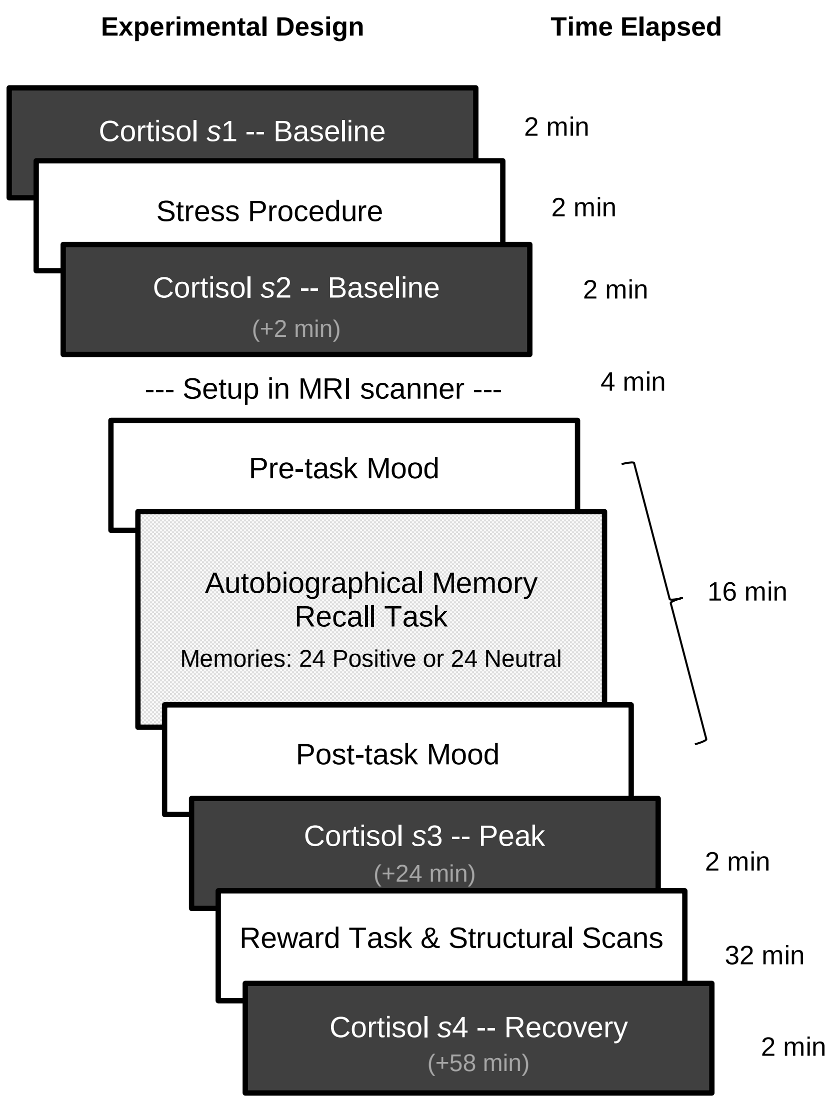
Feeling rating distributions were normal for both the Stress-Positive (M = 2.90, SD = 0.33; Shapiro-Wilk test: $W_{22} = 0.93$, $p = .100$) and Stress-Neutral groups (M = 2.06, SD = 0.53; Shapiro-Wilk test: $W_{21} = 0.95$, $p = .403$).

Supplementary Discussion: Hippocampus and Memory Retrieval

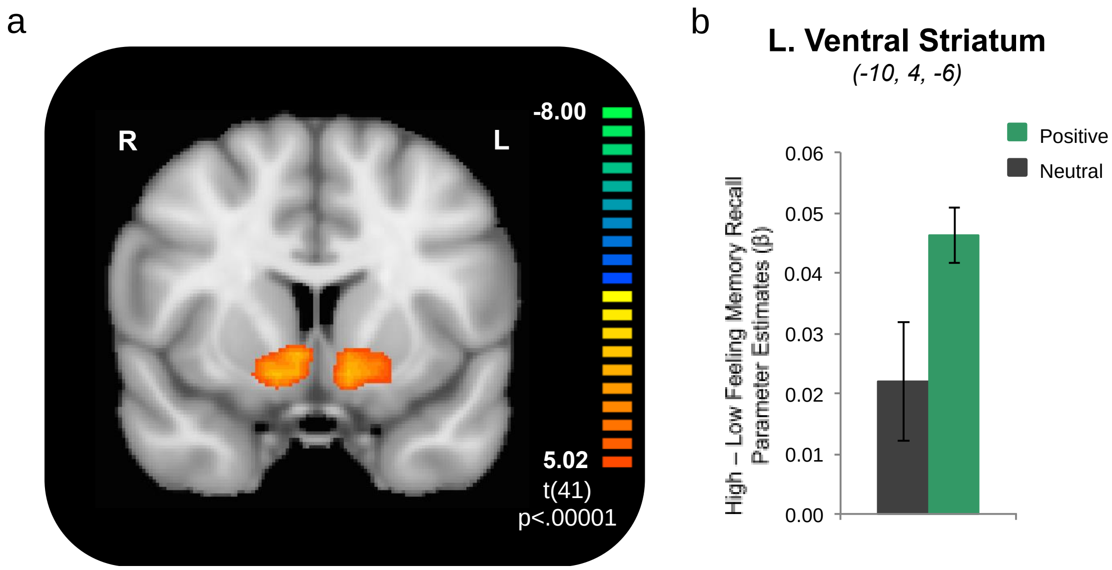
We did not observe activation in the hippocampus that survived correction. This could be for a number of reasons. First, our fMRI group analyses focused on comparing two memory processes that differed in valence (positive vs neutral retrieval), rather than memory vs baseline. Second, it could also be because the hippocampus often seems to be involved more during encoding rather than retrieval[5,6]. In the context of retrieval, it has been further linked to more recent episodic memories (e.g., lists of items recently encoded/learned) than remote ones[7,8]. Importantly, autobiographical memory retrieval engages a core network of regions that go beyond the hippocampus, for instance, other regions in the medial and lateral temporal cortices, temporoparietal junction, medial PFC, ventrolateral PFC, posterior cingulate cortex, and cerebellum, along with less consistently activated regions like the thalamus, amygdala, basal ganglia, dorsolateral PFC, medial OFC, and anterior cingulate among others[9,10]. In our study, although we did not observe hippocampal activation, we did observe activity in a number of core regions associated with autobiographical memory retrieval (e.g., MPFC, VLPFC).



Supplementary Figure 1. Physiological and Subjective Responses to Acute Stress in the Behavioral Study. a) Individuals exposed to acute stress had larger mean SCL during the SECPT/control procedure and b) greater subjective ratings of stress after the SECPT/control procedure than control participants. *p < .05; **p < .001; error bars denote SEM.



Supplementary Figure 2. Schematic of Experimental Procedure and Timeline of Neuroendocrine Assessments for Day 2 (Stress Manipulation) for the fMRI study. Salivary samples were collected immediately before the stress procedure (*s*1, baseline), immediately after the stress procedure (*s*2, +2 min), after memory recollection when cortisol was expected to peak (*s*3, peak, +24 min), and at the conclusion of the experiment when cortisol was expected to recover (*s*4, recovery, +58 min).



Supplementary Figure 3. Voxels in a Ventral Striatum Monetary Reward ROI Show Greater Differential Activity between High and Low Feeling Positive Memories as Compared to Neutral Memories. a) A contrast of gain vs. loss outcomes in a card-guessing task revealed activity in the bilateral ventral striatum. $p < 0.01$; corrected. b) Mean parameter estimates from the right ventral striatum are displayed showing greater differential activity for high minus low feeling memories for the Stress-Positive compared to the Stress-Neutral group. Error bars denote SEM.

Supplementary Table 1. Regions activated in a whole-brain parametric modulation of subjective feeling ratings during memory recollection for Stress-Positive individuals. P < 0.01, corrected.

			Talairach coordinates				
Region	BA	Laterality	x	y	z	Cluster Extent (mm^3)	t statistic
VLPFC	47	L	-31	13	-12	341	5.00
Middle Temporal Gyrus	21	L	-64	-17	-12	1997	6.55
Middle Temporal Gyrus	21	L	-52	-32	-6	1234	5.16
VLPFC	47	R	35	22	-3	757	6.00
NAcc/Caudate	48	R	14	19	-3	313	5.36
MPFC	9,10,11, 25,32		-4	46	-3	8874	7.28
PCC	23		5	-53	15	460	5.59
Angular Gyrus	39	R	38	-68	33	347	5.30
Precuneus	7		-4	-62	39	357	4.71
Angular Gyrus	39	L	-43	-71	39	4476	7.73
DMPFC	8,9		-4	46	45	1389	6.03

BA = Brodmann Area; L = left side; R = right side

Supplementary Table 2. Regions activated in a whole-brain parametric modulation of subjective feeling ratings during memory recollection for Stress-Positive > Stress-Neutral. P < 0.01, corrected.

Region	BA	Laterality	Talairach coordinates x	y	z	Cluster Extent (mm^3)	t statistic
VLPFC	47	R	35	22	-3	251	5.38
Angular Gyrus	39	R	35	-71	33	274	5.20
DLPFC	8,9	L	-52	22	33	415	5.79
Angular Gyrus	39	L	-43	-71	39	2610	7.92

BA = Brodmann Area; L = left side; R = right side

Supplementary Table 3. Regions showing positive psychophysiological interaction with right VLPFC as a function of increasing positive feeling ratings during memory recall for Stress-Positive individuals. P < 0.01, corrected.

Region	BA	Laterality	Talairach coordinates x	y	z	Cluster Extent (mm^3)	t statistic
Seed: VLPFC	47	R	35	22	-3	757	
PPI Feeling							
DLPFC	9	L	-46	22	18	319	5.64

BA = Brodmann Area; L = left side; R = right side

Supplementary Table 4. Regions activated in a whole-brain contrast of gain and loss trials in the monetary reward task. P < 0.01, corrected.

			Talairach coordinates				
Region	BA	Laterality	x	y	z	Cluster Extent (mm^3)	t statistic
Gain > Loss							
NAcc/Ventral striatum		R	14	4	-6	965	6.34
NAcc/Ventral striatum		L	-10	4	-6	716	6.27

BA = Brodmann Area; L = left side; R = right side

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