Cognitive Control and Cortisol Response to Stress in Generalized Anxiety Disorder: A Study of Working Memory Capacity with Negative and Neutral Distractors

Supplemental Material

Manipulation Check

In order to ensure the effectiveness of the stress induction, we conducted a group (GAD, CTL) by time (Anxiety1-Anxiety6) repeated-measures analysis of variance (ANOVA) on self-reported anxiety ratings (see Table 1 in the manuscript). As expected, this analysis yielded a significant main effect of time, $F(5, 245) = 36.74$, $p < .001$, $\eta^2 = .43$. Participants' anxiety significantly increased from baseline (Anxiety1) to stressor (Anxiety2), Mean Difference = 2.68, $SE = .32$, $p < .001$; it then significantly decreased from immediately post stressor (Anxiety3) to 10-minutes post stressor (Anxiety4), Mean Difference = -2.05, $SE = .34$, $p < .001$. The interaction of group and time was not significant, $F(5, 245) = 1.75$, $p = .125$, $\eta^2 = .03$, suggesting that the effectiveness of the stress induction did not differ between the GAD and CTL groups. As expected, however, there was a significant main effect of group, $F(1, 49) = 21.381$, $p < .001$, $\eta^2 = .30$, reflecting higher anxiety scores in the GAD versus CTL group throughout the session.

Bivariate Correlations

We examined the correlation of subjective anxiety with RSpan-Negative, RSpan-Neutral, and salivary cortisol (see Supplemental Table 1). The only significant correlation was between self-reported anxiety at baseline (Anxiety 1) and salivary cortisol level at time 3 (Cortisol 3), $r(52)=.30$, $p=.031$, suggesting that higher levels of self-reported anxiety at baseline were associated with higher levels of cortisol at peak. Including baseline anxiety as a covariate in the main analyses did not change the findings, and baseline anxiety was not significantly associated with baseline cortisol, cortisol reactivity, or cortisol recovery.

Preliminary Cortisol Analyses

Prior to building our baseline HLM model, we visually inspected the cortisol data and conducted a repeated-measures analysis of variance (ANOVA) with time (Cortisol 1 through Cortisol 5) as the within-subject factor and group as the between-subject factor. This analysis yielded a main effect of time, $F(4, 196) = 5.29$, $p < .001$, $\eta^2 = .097$. In contrast, the main effect of group, $F(1, 49) = 0.02$, $p = .892$, $\eta^2 = 0.00$, and the time by group interaction, $F(4, 196) = 0.84$, $p = .501$, $\eta^2 = 0.02$, were not significant. To follow-up on the main effect of time, paired-samples *t*-tests were conducted. Cortisol levels significantly increased from Cortisol 1 to Cortisol 2, $t_{paired}(51) = -2.09$, $p = .042$, and then increased slightly from Cortisol 2 to Cortisol 3, $t_{paired}(51) = -0.71$, $p = .476$. Cortisol levels then significantly declined from Cortisol 3 to Cortisol 4, $t_{paired}(51) = 2.95$, $p = .005$, and declined again from Cortisol 4 to Cortisol 5, $t_{paired}(51) = 4.29$, $p < .001$. Moreover, by Cortisol 5, cortisol levels did not differ significantly from cortisol levels at baseline (Cortisol 1), $t_{paired}(51) = 1.01$, $p = .316$. Thus, in our sample, cortisol levels peaked at sample 3 (provided 23 minutes after stressor exposure) and did not differ significantly from baseline by sample 5 (taken 30 minutes after stressor offset).

Final Level 1 and Level 2 Model

We specified the following model at Level 1:

$$\text{Cortisol} = \pi_{0j} + \pi_{1j}(\text{stress reactivity}) + \pi_{2j}(\text{stress recovery}) + e_{ij}$$

The intercept, π_{0j}, represents cortisol levels immediately before the stressor onset (baseline), π_{1j} represents the slope of cortisol reactivity to stress, and π_{2j} represents the slope of cortisol recovery from stress for participant *j*.

We specified the following models at Level 2:

$$\text{Baseline Cortisol: } \pi_{0j} = \beta_{00} + \beta_{01}(\text{Group}) + \beta_{02}(\text{RSpan-Negative}) + \beta_{03}(\text{RSpan-Neutral}) + \beta_{04}(\text{Group x RSpan-Negative}) + \beta_{05}(\text{Group x RSpan-Neutral}) + r_0$$

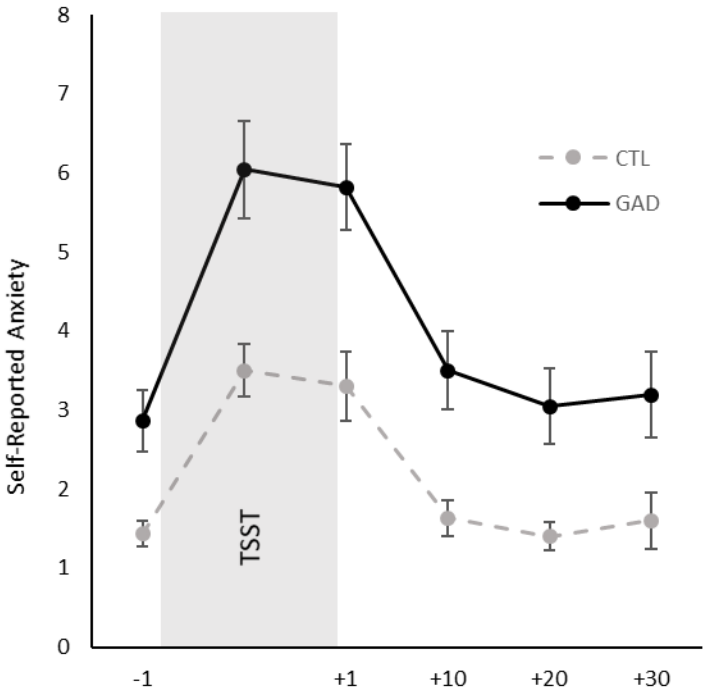
Stress Reactivity: $\pi_{1j} = \beta_{10} + \beta_{11}(\text{Group}) + \beta_{12}(\text{RSpan-Negative}) + \beta_{13}(\text{RSpan-Neutral}) +$

$\beta_{14}(\text{Group x RSpan-Negative}) + \beta_{15}(\text{Group x RSpan-Neutral}) + r_1$

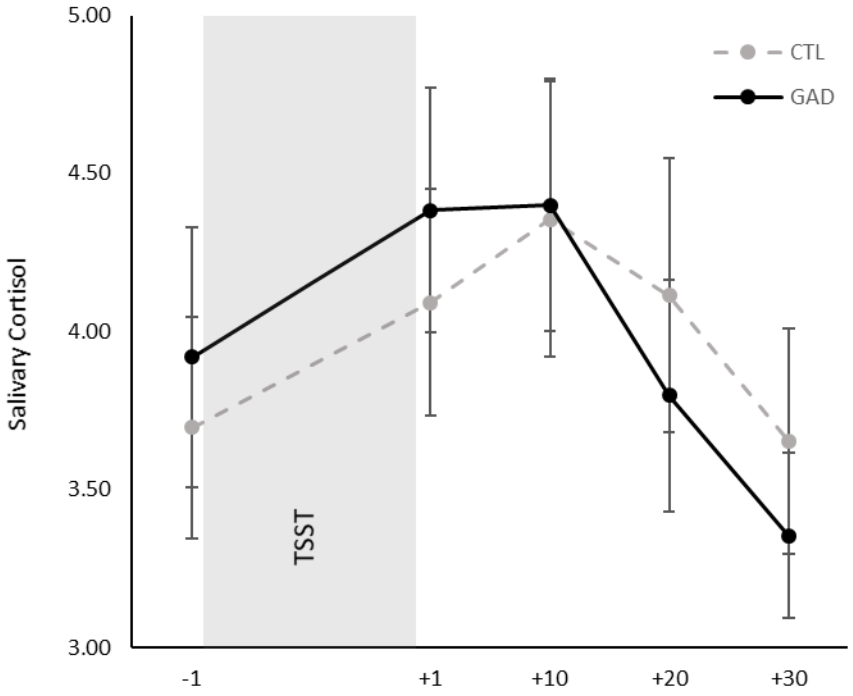
Stress Recovery: $\pi_{2j} = \beta_{20} + \beta_{21}(\text{Group}) + \beta_{22}(\text{RSpan-Negative}) + \beta_{23}(\text{RSpan-Neutral}) +$

$\beta_{24}(\text{Group x RSpan-Negative}) + \beta_{25}(\text{Group x RSpan-Neutral}) + r_2$

Supplemental Figure 1. Self-reported anxiety in response to the TSST in the GAD and CTL groups.



Supplemental Figure 2. Salivary cortisol in response to the TSST in the GAD and CTL groups.



Supplemental Table 1

Correlation of self-reported anxiety with Rspan-Negative, Rspan-Neutral, and salivary cortisol

Measure	RSpan-Negative	RSpan-Neutral	Cortisol1	Cortisol2	Cortisol3	Cortisol4	Cortisol5
Anxiety1	-.06	-.06	.12	.18	.30*	.17	.18
Anxiety2	-.15	.06	.04	-.10	-.07	-.16	-.14
Anxiety3	.02	.04	.15	-.04	-.07	-.17	-.16
Anxiety4	-.07	-.10	.00	.00	.13	.02	.07
Anxiety5	-.13	-.13	.04	.07	.22	.11	.13
Anxiety6	-.09	.05	-.10	-.10	.11	.01	.04

RSpan = Reading Span Score

Anxiety levels were reported at six time points: immediately before the stressor (Anxiety 1), after the speech (Anxiety 2), and at 0 (Anxiety 3), 10 (Anxiety 4), 20 (Anxiety 5), and 30 minutes (Anxiety 6) after stressor offset.

Cortisol samples were provided at five time points: immediately before the stressor onset (Cortisol 1), and at 0 (Cortisol 2), 10 (Cortisol 3), 20 (Cortisol 4), and 30 minutes (Cortisol 5) after stressor offset.

* $p = .031$

Supplemental Table 2

Predicting Cortisol Response to Stress

	Coeff	SE	*p*
Baseline	-0.126	0.145	0.391
Group	0.071	0.145	0.627
RSpan-Negative	0.033	0.165	0.841
RSpan-Neutral	0.017	0.168	0.919
Group x RSpan-Negative	-0.014	0.165	0.936
Group x RSpan-Neutral	0.272	0.168	0.111
Stress Reactivity	0.012	0.006	**0.040**
Group	-0.001	0.006	0.864
RSpan-Negative	0.001	0.005	0.858
RSpan-Neutral	-0.005	0.006	0.432
Group x RSpan-Negative	0.010	0.005	0.073
Group x RSpan-Neutral	-0.013	0.006	**0.024**
Stress Recovery	-0.026	0.003	**< .001**
Group	-0.007	0.003	0.051
RSpan-Negative	-0.002	0.005	0.702
RSpan-Neutral	-0.001	0.005	0.916
Group x RSpan-Negative	-0.013	0.005	**0.008**
Group x RSpan-Neutral	0.011	0.005	**0.027**

Note: Coeff = Coefficient; SE = Standard Error; Group = Diagnostic Group; RSpan = Reading Span Score

Significant *p*-values are presented in bold