

Background

- **Emotional Memory Tradeoff:** The emotional tradeoff effect refers to the fact that memory for emotionally salient information is often preserved or enhanced at the expense of less salient information^{1, 2}
- **Cortisol and Testosterone:** Stress-related hormones (e.g., cortisol) have been shown to modulate emotional memory effects. Critically, cortisol may interact with other hormones, such as testosterone, to affect behavior (See *Dual-Hormone Hypothesis, DHH*) and memory³ by modulating activity in emotional-memory relevant neuroanatomical structures including the prefrontal cortex^{4, 5}, amygdala^{6, 7}, and hippocampus^{8, 9}
- **Dual-Hormone Hypothesis:** DHH refers to the fact that testosterone is associated with status relevant behavior (e.g., aggression and dominance) in humans, but only when cortisol is low^{10, 11}.
- **Approach/Avoid Behavior:** Evidence suggests increases in testosterone can impair identification of threat related cues (e.g., angry faces)¹², and provoke greater approach behavior toward threatening stimuli, but only when concurrent cortisol levels are low¹³.
- Given that concurrent high testosterone/low cortisol concentrations can lead to changes in approach/avoidance behavior via modulation of the PFC and amygdala⁶ it is likely these factors also affect the processing and consolidation of emotionally salient stimuli^{2, 4}.
- To date, there are no studies that have investigated the relation between testosterone and cortisol, approach/avoidance behavior, and its influence on emotional memory.

Fig. 1; Hypothalamic-Pituitary-Gonadal (HPG) Axis

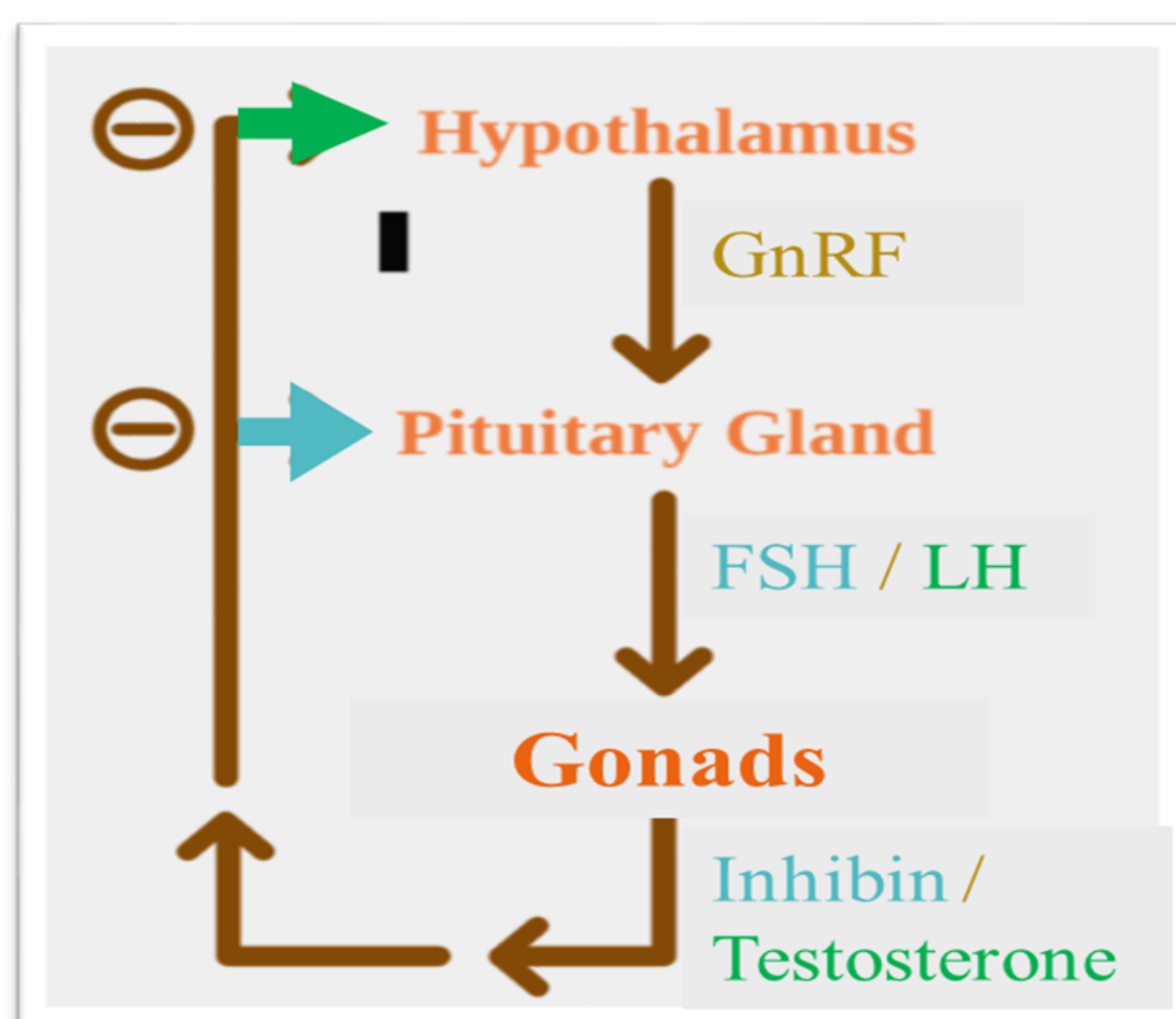
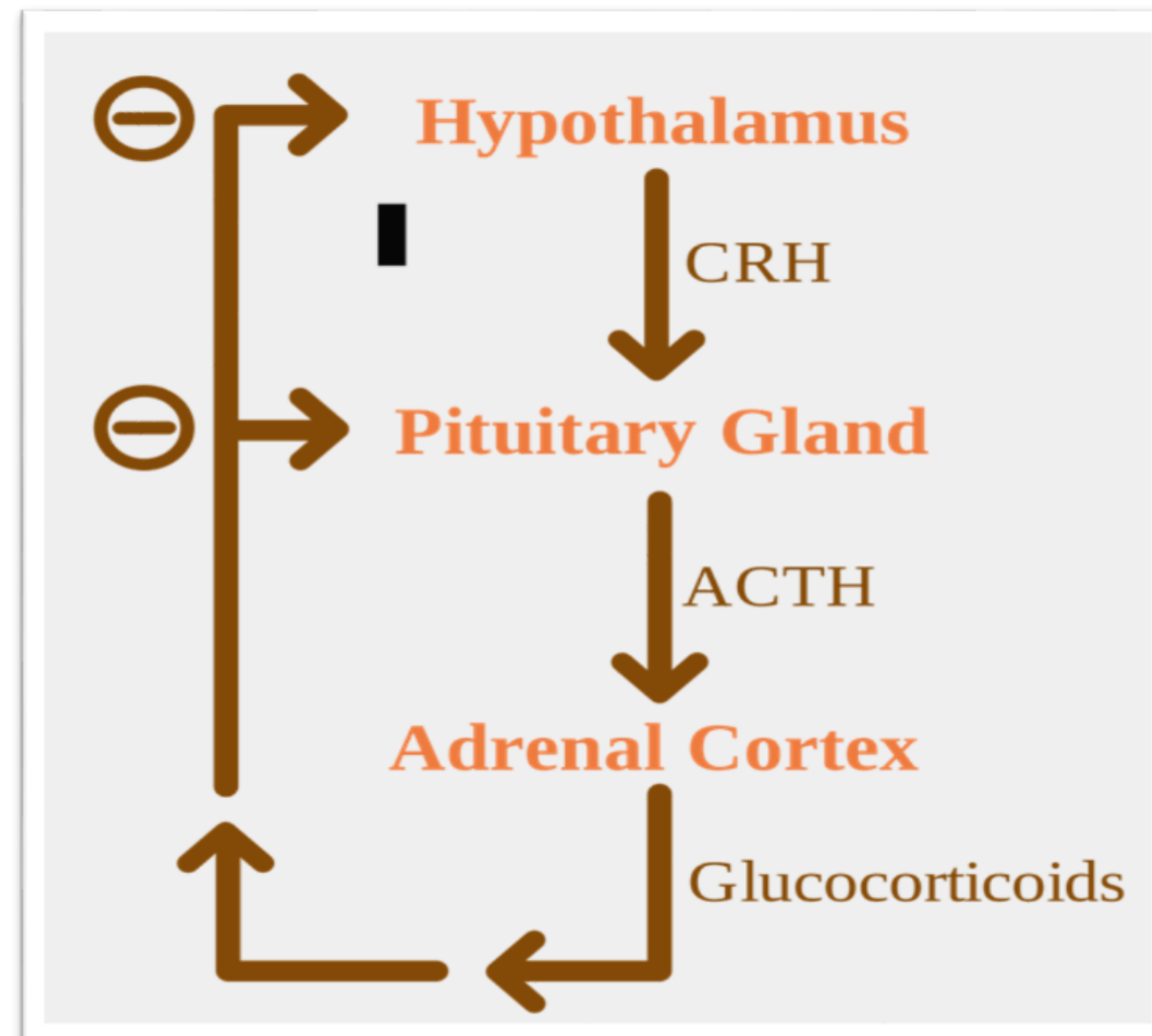


Fig. 2; Hypothalamic-Pituitary-Adrenal (HPA) Axis



Hypotheses

- Testosterone will be positively associated with approach behavior to negatively valenced stimuli, but only when cortisol levels are low.
- Higher approach behavior to negative stimuli in the context of high testosterone/low cortisol will be negatively associated with retention of emotionally salient over neutral information, due to impaired identification of negative/threatening stimuli. i.e. negative stimuli being more “approachable” suggests they are perceived as less negatively salient and are thus processed more like the neutral stimuli, which should result in a decreased emotional memory tradeoff effect.
- Greater testosterone concentrations will thus be negatively associated with the emotional tradeoff effect, but only when cortisol levels are low.
- Conversely, greater cortisol concentrations will be positively associated with the emotional tradeoff, but only at low levels of testosterone.

Methodology

Participants

Participants (N = 143; women = 89, control = 68) consisted of University of Notre Dame students 18-30 years of age. Participants reporting a history of or ongoing substance use disorder or a developmental or cognitive disorder at the time of study were excluded from participation.

Emotional Memory Tradeoff Task

The emotional memory tradeoff task depicts scenes consisting of negative or neutral objects placed on neutral backgrounds.^{14, 15} The objects and backgrounds were normed on dimensions of valence and arousal. Approach or avoidance behaviors were measured using a Likert scale (1 – 7) where higher scores reflected the participant’s likelihood of backing away should they come across the scene in real life.



Fig. 3; Images from the Negative Trade-off Task

Procedure

Participants arrived at ~4 pm, completed a set of questionnaires, and provided a baseline saliva sample. They viewed 64 scenes (32 neutral and 32 negative) which were displayed for 5 sec. Participants were then randomly assigned to a stress (Trier Social Stress Test) or a matched control condition.¹³ Immediately after the stress manipulation, participants gave a second saliva sample and then three more at 15 minute intervals (5 samples total). The next morning, participants completed a recognition task where they indicated whether a component of a scene (object or background) had been previously viewed or was new. Saliva samples were measured for testosterone and cortisol via ELISA and 125-I radioimmunoassay protocols, respectively.

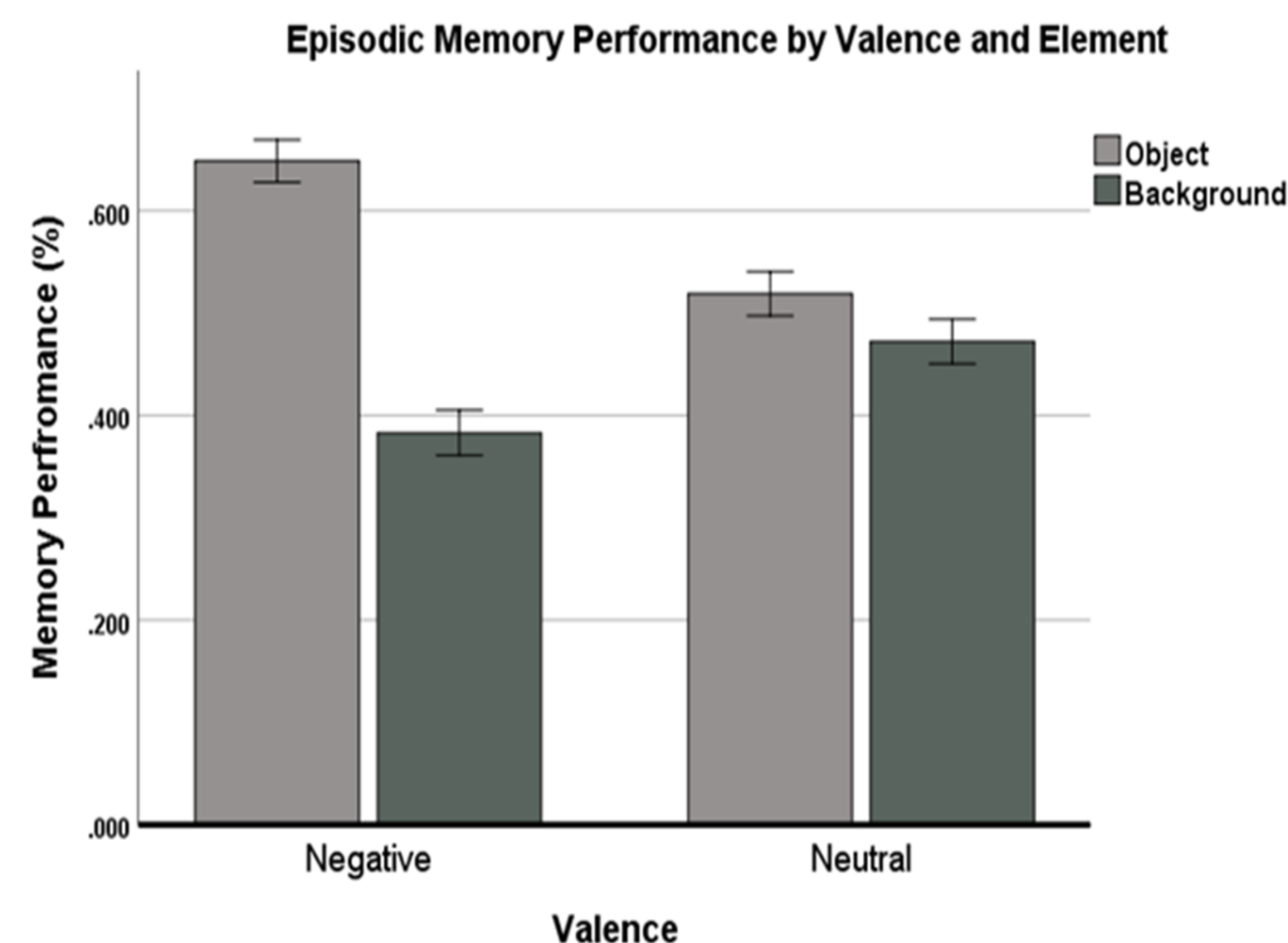


Fig. 4; Emotional Tradeoff: Memory Performance by Valence and Scene Element

Results

Raw hormone data were transformed and standardized across sex according to procedures described in Panizzon et al. (2018). Emotional tradeoff scores were created according to Payne et al. (2015, see Fig 4). Hierarchical regression was used to test the relation between approach/avoid behaviors and cortisol-testosterone interactions. A simple slope analysis was used to further assess the relation of the interaction (hypothesis 1). A correlation was used to test the association between approach/avoid behaviors and the magnitude of the emotional tradeoff (hypothesis 2). Another hierarchical regression tested the association between cortisol-testosterone interaction and emotional tradeoff (hypotheses 3 & 4).

- Hypothesis 1: The cortisol-testosterone interaction significantly predicted approach/avoidance ratings ($\beta_z = 0.272$, $t = 3.163$, $p = 0.002$). Follow-up simple slope analysis indicated testosterone significantly predicted approach behavior toward negative stimuli ($\beta_z = -0.360$, $t = -2.635$, $p = 0.009$, but only when cortisol was low (fig. 5).
- Hypothesis 2: Approach behavior toward negative stimuli was significantly negatively associated with emotional tradeoff ($r = 0.207$, $p = 0.013$; fig. 6)
- Hypothesis 3 & 4: There was no significant relation between cortisol-testosterone interaction and emotional tradeoff ($\beta_z = -0.058$, $t = -0.635$, $p = 0.527$).

Fig. 5; Approach/Avoid Ratings by High/Low levels of Testosterone and Cortisol

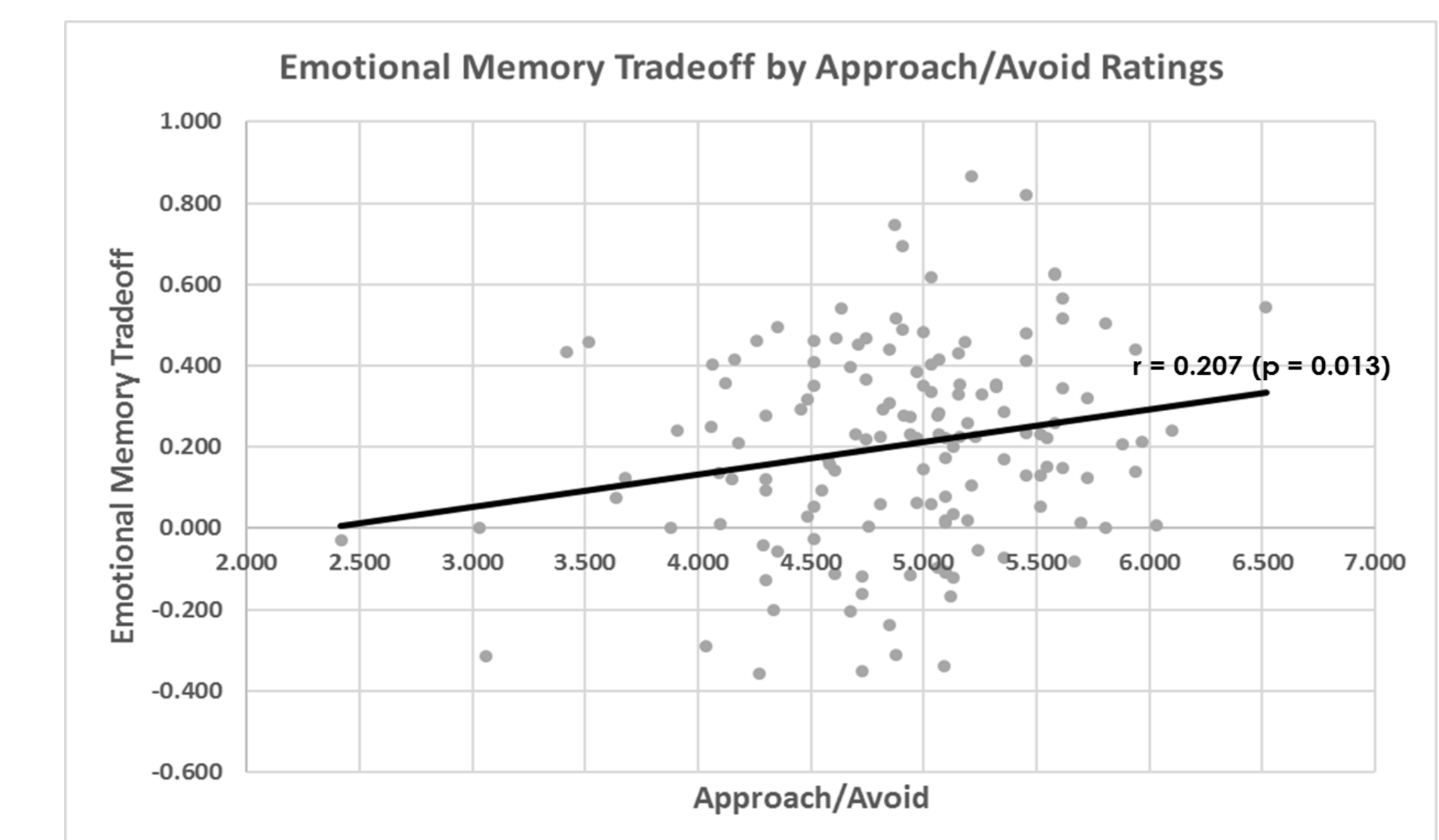
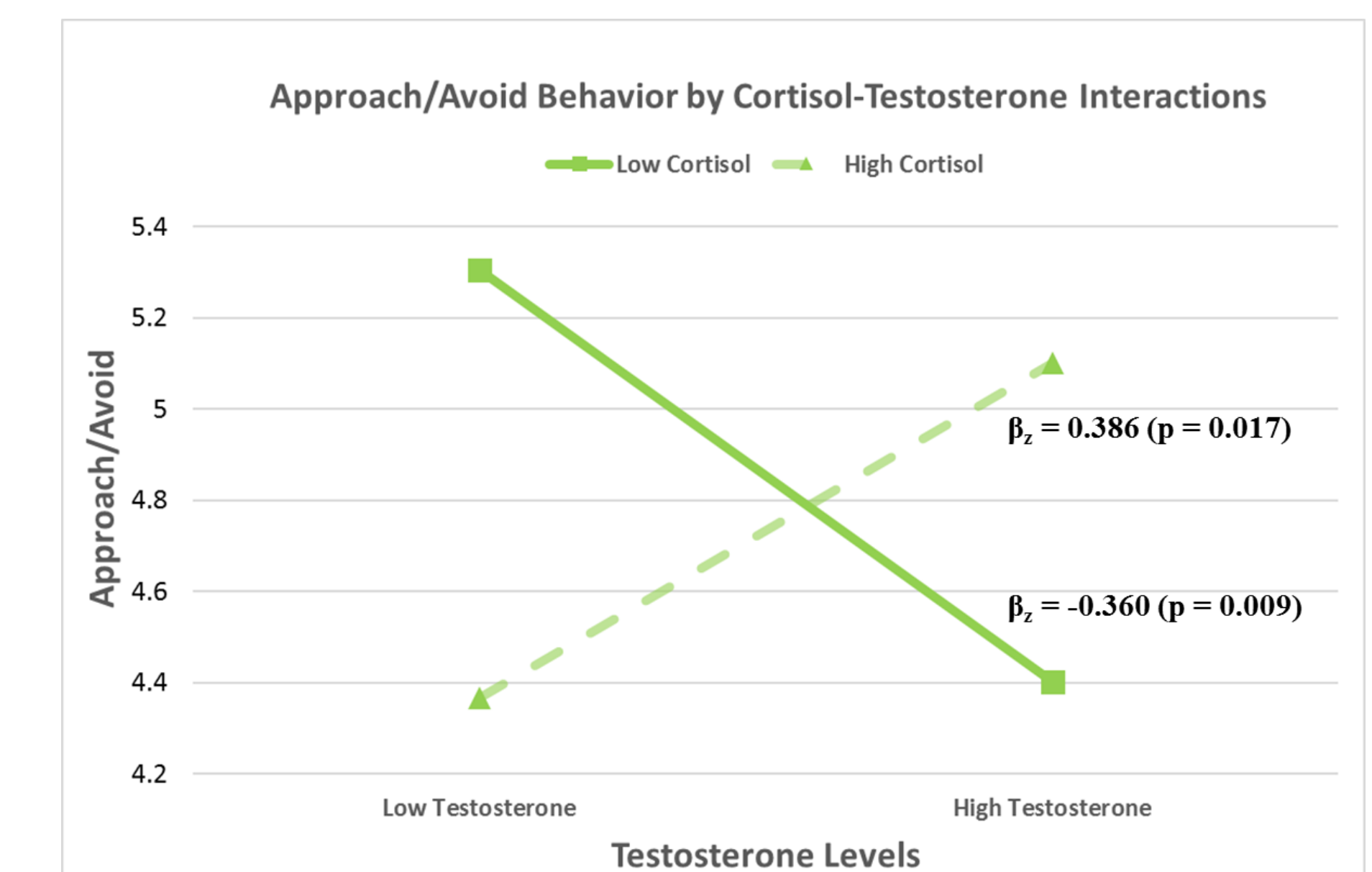


Fig. 6; Emotional Memory Tradeoff by Approach/Avoid Rating

Conclusion

Testosterone may reduce the perception of threat towards negative stimuli and thus increase approach behaviors, but only when cortisol is low. Additionally, by reducing the perceived threat of negative stimuli, as evidenced by increased approach behavior, the emotional salience of the negative stimuli is also reduced, resulting in a reduced emotional tradeoff. There was no direct relation between cortisol-testosterone interactions and emotional tradeoff; however an indirect association via approach/avoidance behavior may be present and future studies will explore this possibility. This experiment provides preliminary evidence that threat perception as measured by approach/avoidance behavior, modulated by cortisol-testosterone interactions, may influence the consolidation of emotional memory. **References available upon request.**