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Short communication

Single dose testosterone administration reduces loss chasing in healthy females

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reduction in punishment sensitivity, and/or an increase in reward sensitivity (van Honk et al., 2004). A trial of the aromatase inhibitor letrozole in healthy men showed that raised testosterone levels were associated with increased risk-taking under ambiguity (i.e., unknown probabilities) but not under conditions with known probabilities (Goudriaan et al., 2010).

The aim of the present study was to investigate the effects of a single dose of testosterone on loss chasing in women. We used a double-blind, placebo-controlled crossover design. Participants played a gambling task where they were asked to choose one of the two cards, displaying the numerals 5 and 25. Each card could win or lose the displayed amount with a probability of 0.5. Thus, the two options both have expected values of zero, but the 5 option is operationally "safe" (low outcome variance) and the 25 option is risky. We tested for an overall effect of testosterone administration to increase risk-taking on the task, and we hypothesized that ignoring prior outcome, testosterone would increase risk-raking. We also tested an effect on loss-chasing, manifested in how participants adjusted their choice towards the risky option following losses compared to wins (Gehring and Willoughby, 2002). We predicted that testosterone would influence loss-chasing given its effect upon reward/punishment sensitivity (van Honk et al., 2004). Second-digit-to-fourth digit (2D:4D) ratios were measured, in light of earlier findings that the effect of testosterone administration can be moderated by this proxy for prenatal testosterone exposure in both women (van Honk et al., 2011) and men (Carré et al., 2015).

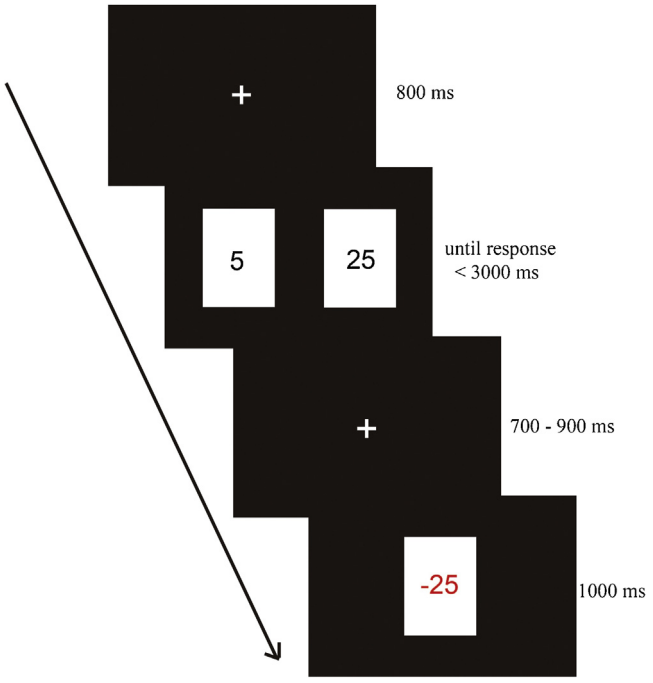

Fig. 1. Sequence of events in a single trial. This trial displays a loss outcome, on which the participant has lost 25 on the chosen card (For interpretation of the references to color in the figure, the reader is referred to the web version of the article).

2. Methods

2.1. Participants

Twenty-six healthy females (mean age = 21.5 years, *SD* = 1.96; age range = 18–25) were recruited through university advertisements. All the contacted persons were screened in a telephone interview to exclude individuals (5 in total) taking psychotropic medications, or having any psychiatric or neurological disorders. We only recruited females as the dosing and pharmacokinetics associated with single sublingual administration of testosterone are only established for women, and are unclear in men (Tuiten et al., 2000). Participants were instructed to abstain from alcohol, caffeine intake and smoking for 24 h before the testing session. They were tested within 10 days after the beginning of the menstrual cycle (interval of two testing days, *M* = 25.96 days, *SD* = 6.32, range = 11–36), when endogenous levels of sex hormones tend to be low and stable. Each participant received a single dose of testosterone and placebo in a crossover, double-blind, placebo-controlled, within-participant design. The study was conducted in accordance with the Declaration of Helsinki and was approved by the Ethics Committee of the Department of Psychology, Peking University. Written informed consent was obtained from all participants. Participants were paid 240Chinese Yuan (~$36.84) as a show-up fee. Then they were endowed with 20 Yuan to play the gambling task. The points that were gained or lost on the task were added or subtracted from this endowment, which was a bonus payment.

2.2. Testosterone administration

The testosterone preparation contained 0.5 mg of testosterone base, 5 mg of cyclodextrin (as a carrier), 5 mg of ethanol, and 5 mL of water. The placebo contained no testosterone but was otherwise identical. Testosterone and placebo were administrated sublingually. All sessions started at 13:00 and lasted approximately 5 h. Due to the established time lag of 4 h for behavioral effects to appear after sublingual application of 0.5 mg testosterone in healthy young women (Tuiten et al., 2000), the gambling task commenced 4 h post-dosing. The participants also completed two further tasks of social cognition, not reported here. During the waiting period, participants rested in the laboratory and were provided with newspapers and magazines that were not related to the study.

2.3. Gambling task

Participants completed 480 experimental trials on a computerized gambling task modified from Gehring and Willoughby (2002); see Fig. 1), and programmed using Presentation software (Neurobehavioral System Inc.). On each trial, participants were presented with two cards, displaying the numerals 5 and 25 that corresponded to the possible gain or loss outcomes with a probability of 0.5. Participants were informed that each point corresponded to 0.1 Chinese Yuan they could earn or lose. But they were not informed of the gain or loss probability, although the outcomes were pseudo-randomized to ensure the effective expected value was zero. They were asked to choose one of them by pressing the corresponding button within 3000 ms. After a jittered blank screen, the outcome on the selected card was presented for 1000 ms. The + or − symbols on the card indicated the amounts the participant won or lost. The next trial started after a 800 ms intertrial interval.

2.4. Digit ratio measurement

Digit ratio was measured from an image scan of the right-hand by measuring the length of the index (2D) and ring (4D) finger from the ventral proximal crease to the tip of the finger using Adobe Photoshop. Two experienced raters (blind to the purpose of the study) measured the 2D:4D ratio on three occasions, and the mean value was used for analysis. Inter-rater reliability was high, $r = 0.96$, $p < 0.001$.

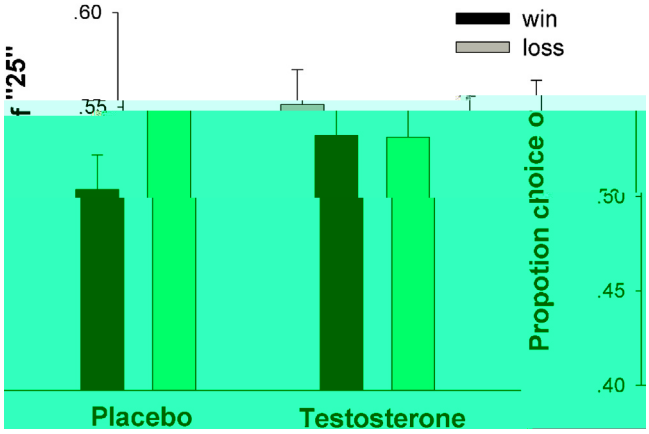

Fig. 2. Proportion of risky choices as a function of prior outcome.

2.5. Mood measurement

The shortened version of the Profile of Mood States was used to control for possible effects of testosterone on anger, anxiety, fatigue, vigor, and depression.

2.6. Statistical analysis

We first compared the proportion choice of the high risk (25) option between the testosterone and placebo conditions. We then looked at the proportion of risky choices as a function of prior outcome. Testing order (testosterone first vs. placebo first) was entered in preliminary models and did not exert a significant main effect or interact with testosterone condition, both $ps > 0.1$, thus it was omitted in the following analysis.

3. Results

On average, participants' net earnings on the gambling task were −14.23 points ($SD = 47.68$) in the placebo condition, and −0.38 ($SD = 58.68$) in the testosterone condition. The outcomes did not differ between conditions, $t(25) = -0.97$, $p = 0.33$. Moreover, these final scores did not differ from zero in either condition, placebo: $t(25) = -1.52$, $p = 0.14$ and testosterone: $t(25) = 0.97$, $p = 0.97$, such that performance did not deviate from the neutral expectation in practice.

A comparison of the proportion of risky (25) choices between the testosterone and placebo conditions revealed no significant difference (testosterone: $M = 52.85\%$, $SD = 12.22\%$; placebo: $M = 52.55\%$, $SD = 8.39\%$), $t(25) = -0.16$, $p = 0.88$. Thus, sublingual testosterone administration had no overall influence upon risk-taking behavior in our female participants.

When we examined choice behavior as a function of prior outcome, using a 2 (Treatment: placebo vs. testosterone) × 2 (Prior Outcome: win vs. loss) × 2 (Magnitude: 25 vs. 5) within-participant ANOVA, a significant interaction was observed between Treatment and Prior Outcome, $F(1, 25) = 6.36$, $p = 0.018$, $\eta_p^2 = 0.20$. Analysis of simple main effects was conducted for the choice behavior in the placebo and testosterone conditions respectively (see Fig. 2). For the placebo condition, prior losses ($M = 55.13\%$, $SD = 9.46\%$) increased the probability of risky choice in the next trial relative to prior wins ($M = 50.63\%$, $SD = 9.39\%$), $F(1, 25) = 5.49$, $p = 0.027$, $\eta_p^2 = 0.18$. For the testosterone condition, risk choice did not differ on trials following losses ($M = 53.41\%$, $SD = 15.33\%$) compared to trials following wins ($M = 53.50\%$, $SD = 10.52\%$), $F(1, 25) = 0.002$, $p = 0.97$. When the two-way interaction was decomposed from the other direction, risky choice did not differ between testosterone and placebo conditions on trials following losses, $F(1, 25) = 0.55$, $p = 0.47$, nor on trials following gains, $F(1, 25) = 2.45$, $p = 0.13$. The proportion of risky choices was significantly above chance (50%) after losses in the placebo condition, one-sample t test $t(25) = 2.77$, $p = 0.01$, whereas for the other conditions, all $ps > 0.1$. The other main effects and interactions were not significant: Treatment, $F(1, 25) = 0.09$, $p = 0.76$; Prior Outcome, $F(1, 25) = 1.35$, $p = 0.26$; Magnitude, $F(1, 25) = 0.13$, $p = 0.72$; Treatment × Magnitude, $F(1, 25) = 0.06$, $p = 0.81$; Prior Outcome × Magnitude, $F(1, 25) = 0.06$, $p = 0.81$; Treatment × Prior Outcome × Magnitude, $F(1, 25) = 0.001$, $p = 0.97$.

For each participant, we derived a change score to represent the difference in loss chasing (proportion of risky choices following losses minus wins) in the testosterone condition relative to the placebo condition. For example, if the proportion of risky choices following losses and wins were 60% and 51% in the placebo condition, and 53% and 52% in the testosterone condition, then the change score was +8% (i.e., (60%–51%) − (53%–52%)). This index was not correlated with 2D:4D ratio measurement, $r = -0.02$, $p > 0.1$. Paired t tests on the POMS mood state subscales showed no significant relationships with the loss chasing change score, all $ps > 0.1$.

4. Discussion

The present study investigated the effect of testosterone on choice behavior and loss chasing in a gambling task. Exogenous testosterone did not influence the proportion of risky choices in our female sample, consistent with previous observations that testosterone administration has little effect on basic risk preferences (Boksem et al., 2013; Zethraeus et al., 2009).

Under placebo, participants showed a clear loss chasing effect such that they selected more often the risky alternative following losses than following gains (Gehring and Willoughby, 2002). This is consistent with a broad definition of the gambler's fallacy that people do not expect runs of consecutive identical outcomes in a random sequence. Accordingly, people strategically increase their bets following losses, giving perceived increased

dopaminergic transmission on the effects of testosterone as well as neural mechanisms by which these systems modulate loss chasing.

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Contributors

Y.W., J.L. and X.Z. developed the concepts for the study. J.L. and L.Q. collected the data. Y.W. and L.Q. analyzed the data. All authors contributed to the manuscript and approved the final version of the manuscript for submission.

Conflict of interest

The authors declare that there are no conflicts of interest.

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