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Alleviating social avoidance: Effects of single dose testosterone administration on approach–avoidance action

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ABSTRACT

Testosterone is an important regulator of social–motivational behavior and is known for its dominance-enhancing and social-anxiolytic properties. However, to date no studies have systematically investigated the causal effect of testosterone on actual social approach–avoidance behavior in humans. The present study sets out to test the effects of testosterone administration in healthy female volunteers using an objective implicit measure of social motivational behavior: the social Approach–Avoidance Task, a reaction time task requiring participants to approach or avoid visually presented emotional (happy, angry, and neutral) faces. Participants showed significantly diminished avoidance tendencies to angry faces after testosterone administration. Testosterone did not affect approach–avoidance tendencies to social affiliation (happy) faces. Thus, a single dose testosterone administration reduces automatic avoidance of social threat and promotes relative increase of threat approach tendencies in healthy females. These findings further the understanding of the neuroendocrine regulation of social motivational behavior and may have direct treatment implications for social anxiety, characterized by persistent social avoidance.

Introduction

The Hypothalamus–Pituitary–Gonadal (HPG) axis with its end product testosterone plays an important role in the regulation of social motivational behavior. Testosterone is associated with social dominance and approach behavior, and has socially anxiolytic effects (Eisenegger et al., 2011; Maner et al., 2008; Mazur and Booth, 1998; Mehta and Josephs, 2010; van Honk et al., 1999). According to the challenge hypothesis testosterone levels rise in preparation to a challenging encounter in which social status might be threatened, thereby initiating approach motivation and simultaneously reducing fear (Archer, 2006; Bos et al., 2012).

In the past decade, several studies of testosterone administration to healthy female participants confirmed the causal relationship between testosterone and its dominance-enhancing and social-anxiolytic properties. Concerning the latter, testosterone administration has been shown to reduce fear-potentiated startle reflexes in highly anxious participants, attentional bias to fearful facial expressions, and conscious recognition of threat-related facial expressions (Hermans et al., 2006, 2007; van Honk and Schutter, 2007; van Honk et al., 2005). Enhancement of social dominance was indicated by increased heart rate acceleration, slower gaze aversion, and by an increase of activity in a social approach related brain circuit when viewing angry faces (Hermans et al., 2008; Terburg et al., 2012; van Honk et al., 2001).

Together, these findings indicate that testosterone administration reduces fear and sensitivity to threat, and enhances social dominance related behavior. However, so far evidence is constrained to processing of emotion and gaze behavior. No studies have systematically tested effects on actual social approach–avoidance actions. Elucidating the effects of testosterone on actual approach behavior would not only advance our theoretical understanding of steroid involvement in social emotional behavior, but also have great implications for the treatment of social avoidance related disorders associated with reduced testosterone levels such as social phobia and depression (Gerra et al., 2000; Giltay et al., 2012).

This study sets out to test whether testosterone administration diminishes threat avoidance and promotes threat approach, using an objective implicit measure of social motivational behavior: the Approach–Avoidance Task (AAT). The AAT is a valid and reliable measure of social approach–avoidance action tendencies (Heuer et al., 2007; Roelofs et al., 2009a, 2009b, 2010; Volman et al., 2011a, 2011b). This reaction time (RT) task involves participants to approach and avoid socially aversive and appetitive visually presented stimuli (angry and happy faces, respectively) by pulling a joystick towards

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themselves (approach) or pushing the joystick away from themselves (avoidance). Angry faces with direct gaze constitute a potent threat stimulus potentially signaling impending aggression, and elicit increased avoidance tendencies in high socially anxious individuals in particular (Adams et al., 2003; Öhman, 1986; Roelofs et al., 2010).

Based on the role of testosterone in social dominance and in enhancement of action motivation, we predict that administration of testosterone would reduce threat avoidance and increase threat approach tendencies to angry faces on the AAT.

Method

Participants

Twenty-four healthy females with a mean age of 29 years (SD = 8.4, range 20–50), served as participants for partial fulfillment of course credit or financial compensation. Only female participants were included, because there are as yet no known parameters (e.g., dose and time course) for inducing neurophysiological effects in men after administration of a single dose of testosterone (Tuiten et al., 2000). The sample was recruited via advertisement in the Leiden metropolitan area (The Netherlands). Exclusion criteria were age <18 and >50, use of medication, somatic illnesses, neurological conditions, recent or past psychiatric problems, history of head injury, left-handedness, peri- or postmenopause, and pregnancy or breast feeding. Fourteen women were using single-phase contraceptives, whereas ten women were normally cycling and evenly distributed over menstrual cycle phases.[1] All participants had normal or corrected-to-normal vision, were unaware of the aim of the study and provided written informed consent. The study was approved by the Medical Ethics Committee of the Leiden University Medical Center, and was in accordance with the declaration of Helsinki.

Testosterone administration

In a double-blind, randomized, placebo-controlled, crossover design participants received a single dose of 0.5 mg testosterone suspended in a clear solution (0.5 ml) with 0.5 mg hydroxypropyl-beta-cyclodextrin, 0.005 ml ethanol 96%, and distilled water. The matched placebo contained the same ingredients, except testosterone. Participants were asked to hold the liquid under their tongue for 60 s. During sublingual administration of 0.5 mg testosterone cyclodextrine, testosterone is directly absorbed into the bloodstream. In females, such a dose yields a sharp increase of 20–25 nmol/l in plasma testosterone levels within 15 min, which declines to baseline levels within the next 90 min. Subsequently, pharmacodynamic effects are measurable approximately 4 to 6 h after testosterone intake (Tuiten et al., 2000).

Approach–Avoidance Task (AAT)

During this reaction time (RT) task, participants responded to emotional face pictures presented on a computer screen, by pulling a joystick either towards their body (approach movement) or pushing it away from their body (avoidance movement) (task adapted from Heuer et al., 2007). Pulling or pushing the joystick increased or decreased the size of the picture respectively, giving the impression of moving towards or moving away from the participant. The speed of the size change was proportional to the amplitude of the joystick movement. As soon as the joystick reached its target position (i.e., the required direction; full movement involved a 30° rotation from the upright position) the picture disappeared from the screen. The time between the onset of the stimulus and its disappearance from the screen was recorded with <1 ms accuracy. After each completed trial the participant moved the joystick back to its central position and initiated a new trial by pressing the fire button near the top of the joystick. Face stimuli were selected from the Karolinska Directed Emotional Faces database based on quality of emotional expression (Goeleven et al., 2008; Lundqvist et al., 1998). Happy, Angry, and Neutral facial expressions were taken from the same model (five male and five female models in all) and each picture was presented either with a yellowish or a grayish filter. In addition, checkerboards (10 yellow, 10 gray) were included as non-facial control stimuli.[2] This resulted in a total of 80 different stimuli, which were presented in random order. All participants were instructed to push on yellow stimuli and to pull on gray stimuli, and to respond as fast and as accurately as possible. Usually, response latencies are shorter for affect-congruent (e.g., happy-approach; angry-avoid) as compared to affect incongruent response conditions (e.g., angry-approach; happy-avoid). Before the real test started, participants were presented with eighteen practice trials, which were similar to the test trials except for the fact that the pictures showed different models.

Social Phobia and Anxiety Inventory

The Social Phobia and Anxiety Inventory (SPAI; Turner et al., 1989; validated Dutch version: Bögels and Reith, 1999) has good reliability ($\alpha = .99$), and was used to assess the severity of social anxiety on a separate day prior to participation. It features 45 items in total, of which 32 items assess social phobia, and 10 items measure agoraphobia. Following van Peer et al. (2009), only the social phobia score ($\alpha = .99$; mean ± SD: 49.6 (25.3)) was added to the statistical analysis of the RTs.

Procedure

Participants were tested individually at two identical testing sessions with two days in between. Testing sessions started at either 930 h or 1330 h, and participants were tested on the same time of day on both sessions. Four and a half hours after administration of testosterone or placebo participants performed the AAT in a dimly lit and sound attenuated room. There was no significant difference between the early and late testing sessions for the AAT effect scores, $F(1, 22) = 0.37$, $p = .549$, nor SPAI-SP scores, $t(22) = 0.67$, $p = .511$, nor was there an influence of testing order, $F(2, 42) = 0.82$, $p = .449$. After completion of the two sessions participants had to indicate in which session they thought to have had testosterone or placebo. Thirteen of the 24 participants were correct, which is at chance-level, Binomial $P(X = 13) = 0.149$, confirming that participants were unaware of the condition.

Statistical analyses

RT outliers were filtered using a <150 and a >1500 ms cut-off. A cut-off of three standard deviations from the mean was used for defining outliers in the remaining RTs. Error rates were calculated after removal of outliers. For each participant, the median of the remaining RTs (97%) for the correct responses was calculated per cell (defined by: Emotion and Movement). AAT effect scores were computed for each participant and for each emotion separately by subtracting median pull RTs from corresponding median push RTs (e.g., RT angry push–RT angry pull; RT happy push–RT happy pull; RT neutral push–RT neutral pull). As a

[1] Of the fourteen women using contraceptives, nine were using single-phase estrogen/progestogen contraceptives, two were using a progestogen-only intra-uterine device, and three were using an estrogen/cyproterone acetate contraceptive. Of the other ten – normally cycling – women, three were likely in the menstrual phase, two in the follicular phase, two in the ovulatory phase and three in the luteal phase during testing. Phase was defined by cycle day (Colzato et al., 2010).

[2] Checkerboard stimuli yielded significantly slower reaction times ($p \leq .009$; RTs (ms ± SEM) for placebo condition: push 569 (22) and pull 542 (19); testosterone condition: push 548 (21) and pull 520 (16)). It is likely that this slowing is caused by an oddball effect as they were outnumbered by the facial stimuli (i.e., 20 checkerboards to 60 emotional faces). Therefore the checkerboard stimuli have not been included in the main analyses.