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Testosterone abolishes implicit subordination in social anxiety

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ABSTRACT

Neuro-evolutionary theories describe social anxiety as habitual subordinate tendencies acquired through a recursive cycle of social defeat and submissive reactions. If so, the steroid hormone testosterone might be of therapeutic value, as testosterone is a main force behind implicit dominance drive in many species including humans. We combined these two theories to investigate whether the tendency to submit to the dominance of others is an implicit mechanism in social anxiety (*Study-1*), and whether this can be relieved through testosterone administration (*Study-2*). Using interactive eye-tracking we demonstrate that socially anxious humans more rapidly avert gaze from subliminal angry eye contact (*Study-1*). We replicate this effect of implicit subordination in social anxiety in an independent sample, which is subsequently completely abolished after a single placebo-controlled sublingual testosterone administration (*Study-2*). These findings provide crucial evidence for hormonal and behavioral treatment strategies that specifically target mechanisms of dominance and subordination in social anxiety.

1. Introduction

Humans are extremely social creatures and similar to other social species our social cohesion depends on hierarchical relationships. The formation and maintenance of such social hierarchies are generally recursive processes in which repeated defeat promotes subordinate behavior, and repeated victory promotes dominance behavior (Mazur and Booth, 1998; Öhman, 1986). For our complex society this basic mechanism has its flaws as those who act dominantly in each and every situation are often regarded as aggressive, and those who always submit to the dominance of others are perceived as anxious. Social anxiety can therefore be conceptualized as a habitual manifestation of subordination (Capps, 2010; Öhman, 1986; Trower and Gilbert, 1989). This theory finds support in evidence that individuals with social anxiety have relatively high self-reported levels of subordination (Walters and Inderbitzen, 1998), and show less dominance behavior (Walters and Hope, 1998), and more submissive gestures (Weeks et al., 2011), during role-playing. Observations of implicit gestures of subordination and appeasement in social anxiety, like blushing and gaze aversion, combined with increases in ritualized behavior in relation to anxiety (Lang et al., 2015), have further fed this idea and lead to the neuro-evolutionary theory that social anxiety may be directly linked to implicit subordination (Bateson et al., 2011; Öhman, 1986; Stein and Bouwer, 1997a; Stein and Bouwer, 1997b).

The present study has two goals. First, we test the hypothesis that social anxiety is indeed characterized by implicit subordination. Next, we seek to reduce this implicit behavior in social anxiety by means of a single administration of the steroid hormone testosterone. Testosterone is often regarded as the endocrine agent of dominance behavior (Archer, 2006; Eisenegger et al., 2011; Mazur and Booth, 1998; Terburg and van Honk, 2013; van Honk et al., 2014), and the recursive properties of dominance behavior, as described above, can certainly be attributed to testosterone. Testosterone recursively promotes competition for status and dominance in many species (Archer, 2006; Mazur and Booth, 1998; Wingfield et al., 1990), including humans (Eisenegger et al., 2011; Terburg and van Honk, 2013), as winning a status competition boosts testosterone which in turn promotes dominance behavior. Likewise, repeated defeat decreases testosterone levels, subsequently decreasing dominance drive (Archer, 2006). As social

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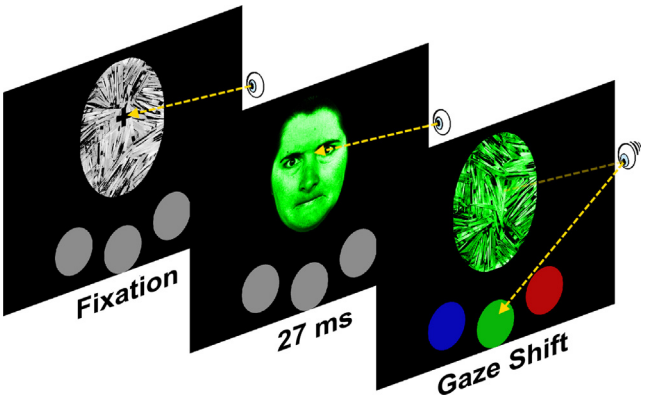

Fig. 1. Example of the stimulus sequence in the Social Dominance Task (SDT). Fixation is presented for 1000–1500 ms and the trial only commences when gaze is indeed fixated on the cross. Face stimulus is presented for 27 ms after which a colorized mask stimulus is presented and the dots randomly change color to blue, green and red in random. Mask stimulus remains on screen until gaze shift to the dot with the same color as the mask. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

anxiety has been linked to lower endogenous testosterone levels (Giltay et al., 2012), and as testosterone administration has been shown to increase implicit dominance behavior in healthy individuals (Terburg et al., 2012b), it can be hypothesized that, if social anxiety is indeed associated with implicit subordination, this might be reduced after testosterone administration.

To test these hypotheses, we applied a validated paradigm that taps directly into dominance/submission reactions. Among primates, including humans, a fundamental mechanism to assert dominance is maintaining angry eye contact until the opponent averts gaze (Mazur and Booth, 1998). Gaze aversion is thus an act of subordination that prevents direct confrontation and physical violence. Using interactive eye-tracking methodology in a social dominance task (SDT), we have recently shown that the latency of gaze aversion in such face-to-face dominance challenges is indeed a marker for dominance drive in humans (Hortensius et al., 2014; Terburg et al., 2011). In the SDT (see Fig. 1) participants actively avert their gaze from eye contact with angry, happy and neutral faces. Crucially, these expressions are presented subliminally, using forward- and backward-masking, rendering the SDT suitable to measure implicit and unconscious modulation of gaze aversion behavior. Slower gaze aversion from angry compared to happy eye contact in the SDT predicts dominance drive (Terburg et al., 2011), and similar results were obtained using aggressive and joyful body postures (Hortensius et al., 2014). Interestingly, in line with a neuro-evolutionary model of dominance behavior, this type of dominance reactions have been linked to subcortical processing (Hofman et al., 2013) and can be enhanced by testosterone administration in healthy individuals (Terburg et al., 2012b).

Finally, following evidence that prenatal testosterone exposure, as indexed by second-to-fourth digit ratio (2D:4D), drives the effect of testosterone on conscious but not reactive behavior later in life (Terburg and van Honk, 2013), we also included this metric to our administration study as well as the profile of mood states 2nd edition (POMS-II) (Heuchert and McNair, 2012) to assess baseline mood differences due to drug administration.

2. Methods and materials

2.1. Participants and procedure: study-1

This study was approved by the Human Research Ethics Committee of the Faculty of Health Sciences at the University of Cape Town, and complied with ethical guidelines established in the Declaration of Helsinki. Participants were selected from a pool of healthy volunteers (University of Cape Town students, $N > 100$) who were recruited to fill out the Liebowitz Social Anxiety Scale Self Report (LSAS-SR) questionnaire (Rytwinski et al., 2009) and were unaware of the study rationale. Those whose scores fell within the high (>70) or normal (<36) range were selected to participate. The high range was chosen to ensure these participants scored within the clinical range of social anxiety. The low range was partly driven by participant availability and is slightly higher than the optimal cutoff score of 30 (Rytwinski et al., 2009). For this reason we refer to this group as 'normal' instead of 'low social anxiety' throughout this report. Other exclusion criteria were: Score of >30 on Beck's Depression Inventory (BDI-II) to exclude comorbidity with depression; self-reported current or former presence of psychiatric diagnosis; self-reported use of psychiatric or hormonal medication; self-reported color-blindness (three potential participants were excluded based on these criteria). Participants were instructed to refrain from alcohol or drug consumption at least 24 h before participation.

Upon invitation the participants came to the lab, were informed on the test-procedure, provided written informed consent, filled-in the LSAS-SR for a second time (Cronbach's alpha = 0.97) and completed the SDT and an expression awareness test (EAT). Thirty-eight participants performed in the experiment and were awarded either course-credit or payment, but due to equipment failure three participants could not complete the SDT, resulting in a final sample of $N = 35$ (see Table 1). Lastly, due to time constraints two participants did not complete the EAT.

2.2. Participants and procedure: study-2

This study was approved by the Human Research Ethics Committee of the Faculty of Health Sciences at the University of Cape Town, and complied with ethical guidelines established in the Declaration of Helsinki. Participants were selected from a pool of healthy volunteers (University of Cape Town students) who were recruited to fill out the LSAS-SR and were unaware of the study rationale. Those whose scores fell within the high (>70) range were selected to participate. Exclusion criteria were similar to *Study-1* with the addition that only women were included, and to minimize effects of endogenous hormone fluctuations we selected only women that did not use hormonal contraception and were able to participate during the first ten days of their menstrual cycle (i.e. follicular phase).

Before invitation to the lab the participants were informed on the test and hormone-administration procedure, and provided written informed consent. Drug administration was done in double-blind cross-over design. The two sessions were separated by at least two days to provide for a washout period of exogenous testosterone and its behavioral effects (Tuiten et al., 2000). Drug administration was always done in the morning (9–12 A.M.) and to avoid unwanted effects of diurnal variation in endogenous testosterone levels this time was kept similar within-subjects. After drug administration we incorporated a waiting period of 4 h (see below) before testing during which the participants were asked to refrain from arousing activities. Experimental sessions were thus always performed in the afternoon and in both sessions the participants performed the SDT. The EAT was only completed in the second session. Twenty women participated in the study for payment, but five had incomplete data sets due to; equipment failure (3), starting to take oral contraceptives between the sessions (1), and no-show on session 2 (1). Thus, our final sample included 15 participants (see Table 1). For one of these participants the mood measurements and digit ratio were not recorded, leaving 14 participants for these control measures.