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Digit ratio (2D:4D) and psychopathic traits moderate the effect of exogenous testosterone on socio-cognitive processes in men

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ABSTRACT

Recent evidence suggests that testosterone is negatively correlated with empathic processes in both men and women. Also, administration of testosterone to young women impairs socio-cognitive performance as assessed using the "Reading the Mind in the Eyes Task", especially among those exposed to elevated testosterone concentrations prenatally. However, the extent to which testosterone plays a similar causal role in socio-cognitive abilities in men is currently unknown. Here, using a crossover, double-blind, placebo-controlled, within-subject design, we investigated the extent to which a single administration of testosterone to healthy young men ($N = 30$) would impair socio-cognitive abilities assessed using the "Reading the Mind in the Eyes Task" (RMET). Also, we investigated whether individual differences in 2D:4D ratio and psychopathic traits would moderate the effect of testosterone on task performance. Results indicated that testosterone administration on its own did not impair RMET performance. However, variability in both 2D:4D ratio and psychopathic traits moderated the effect of testosterone on task performance. Specifically, testosterone impaired RMET performance among individuals with relatively low (i.e., masculinized) 2D:4D ratio and among individuals scoring relatively low on the interpersonal/affective facet (i.e., Factor 1) of psychopathy. Our findings highlight the importance of considering theoretically- and empirically-based individual difference factors when attempting to characterize the neuroendocrine mechanisms underlying socio-cognitive processes.

1. Introduction

A number of cognitive/affective processes are thought to be important for empathizing with others (Bird and Viding, 2014), including the ability to take another's perspective and compute their likely emotional state. This ability to compute the emotional states of others without necessarily experiencing these emotional states is sometimes referred to as 'cognitive empathy' (de Vignemont and Singer, 2006). Another critical process important for empathy involves sharing of the other person's emotional states (i.e., emotional resonance; Davis, 1983), sometimes referred to as 'affective empathy'. Although the ability to empathize is an important capacity enabling people to successfully navigate through their social environments, there exists substantial variability in empathic abilities. Below, we briefly review how sex differences, variability in testosterone, and psychopathic traits may give rise to individual differences in one's empathic capacity.

A large body of evidence indicates that empathy is a sexually dimorphic trait, with women outperforming men on numerous self-report measures of empathy (see Eisenberg and Lennon, 1983 for meta-analysis). Recent studies employing the "Reading the Eyes in the Mind Task" (RMET; Baron-Cohen et al., 2001), a task that is believed to tap into one's ability to gain a perspective on another person's thoughts and emotions based upon the expression of their eyes, also find reliable sex differences favoring women (Kirkland et al., 2013). This task is thought to index both mentalizing/perspective taking and affect recognition—both processes that play a role in empathic capacities of an individual. Given the robust sex differences in empathic abilities, researchers have also begun to investigate the extent to which testosterone, a steroid

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hormone produced in much large quantities in men (Dabbs, 1990) contributes to variability in socio-cognitive abilities.

In one study, Ronay and Carney (2013) reported that endogenous testosterone concentrations were negatively correlated with participants' accuracy in estimating their conversation partner's thoughts and feelings. Specifically, individuals with relatively elevated endogenous testosterone concentrations were impaired in their ability to accurately detect the thoughts and feelings of their conversation partner. In other work, there was a negative (albeit marginally significant) correlation between testosterone and a self-report measure of empathy in women (but not men), but no relationship between testosterone and RMET performance in either men or women (Zilioli et al., in press). Going beyond correlational studies, other work has examined whether a single administration of testosterone to women modulates performance on measures that index processes thought to be involved in empathizing with others. Specifically, a single administration of testosterone decreases facial mimicry (Hermans et al., 2006), emotion recognition accuracy (van Honk and Schutter, 2007) and RMET performance (van Honk et al., 2011). The latter study found that the effect of testosterone on RMET performance depended on variability in the 2D:4D ratio, a putative measure of the balance between fetal testosterone and fetal estrogen exposure, whereby low 2D:4D ratio is suggestive of high fetal testosterone and low fetal estrogen exposure (see Manning et al., 2014 for review). Specifically, testosterone administration impaired RMET performance, but only among women with relatively low (i.e., masculinized) 2D:4D ratios (van Honk et al., 2011). These findings suggest that both organizational and activational effects of testosterone must be considered when examining links between neuroendocrine function and individual differences in socio-cognitive processes.

In addition to examining the role of testosterone, researchers have investigated socio- cognitive deficits in populations characterized by a lack of empathy—namely, individuals with psychopathy and/or individuals scoring relatively high on self-report measures of psychopathic traits. Typically, researchers have characterized psychopathy/psychopathic traits as varying along two distinct dimensions (Hare and Neumann, 2008). Factor 1 is characterized by interpersonal/affective features of psychopathy and involves lack of guilt and empathy, shallow affect, and pathological lying, whereas Factor 2 involves characteristics such as impulsivity, antisocial behavior, and sensation-seeking (Hare and Neumann, 2008). Although clear impairments in the ability to resonate with others' emotions (i.e., 'affective empathy') have been identified in clinical psychopaths (Blair et al., 1997; Shamay-Tsoory et al., 2010) and among community individuals scoring relatively high on psychopathic traits (e.g. Lockwood et al., 2013; Seara-Cardoso et al., 2012, 2013), there have been mixed findings regarding impairments using some socio-cognitive measures that are thought to index processes relevant for empathy (Richell et al., 2003; Dolan and Fullam, 2004; Brook and Kosson, 2013; Ali and Chamorro-Premuzic, 2010). One possible reason for the inconsistent findings may be that different measures have been used to assess socio-cognitive processes—some of which require identification of other people's feelings, rather than just their thoughts. Thus, negative associations between psychopathic traits and socio-cognitive performance on tasks that draw on both affective processes, as well as perspective taking, may be related to more basic problems with affective processing, rather than with cognitive empathy/perspective-taking (Lockwood et al., 2013).

In the current study, we build upon the existing literature and examine the impact of testosterone administration on socio-cognitive task performance (as measured by RMET) in males and whether this would be modulated by digit ratio or psychopathic traits. Based on previous work in women (van Honk et al., 2011), we predicted that testosterone administration would impair task performance in men, and that this effect would be most robust among men with relatively low (i.e., masculinized) 2D:4D ratios. In addition, we investigated the extent to which psychopathic traits would be associated with RMET performance. Given that Factor 1 of psychopathy (i.e., interpersonal and affective facets) is characterized by deficits in socio-cognitive processes (including empathic abilities and emotion recognition), we predicted that variability in Factor 1 scores would be negatively correlated with RMET performance. We also investigated whether Factor 1 or Factor 2 scores might moderate the association between testosterone administration and RMET performance. To our knowledge, only one study has examined the extent to which psychopathic traits moderate the relationship between testosterone and human social behavior. Geniole et al. (2013) reported that self-reported psychopathic traits and changes in testosterone during a competitive interaction positively predicted antagonist behavior. However, psychopathic traits did not interact with changes in testosterone to predict antagonistic behavior (Geniole et al., 2013). Nevertheless, there is evidence indicating that psychopathic traits can moderate the relationship between psychosocial variables (e.g., parenting, peer delinquency) and externalizing behavior (e.g., aggression, antisocial behavior; Oxford et al., 2003; Kerr et al., 2012; Yeh et al., 2011). We were interested in investigating whether testosterone had a similar effect on task performance regardless of the level of the interpersonal/affective psychopathic traits (which in particular index lack of empathy) or whether RMET task performance would be either particularly affected in individuals scoring relatively low on interpersonal/affective facets of psychopathy (i.e., those with greater empathic capacity) or especially detrimental to those who lacked empathic capacities in the first place (i.e., those scoring high on interpersonal/affective facets of psychopathy).

2. Methods

Thirty male undergraduate students between the ages of 18 and 28 (M_{age} = 21.21, SD = 2.19; n = 28 Caucasian/White, n = 1Hispanic, n = 1 First Nations/Aboriginal) were recruited from Nipissing University / Canadore College. Participants were interviewed prior to their enrollment in the study to determine eligibility. Exclusion criteria for the study included the following: participants must be free of medications affecting hormone concentrations, have no history or diagnosis of a psychiatric illness or drug dependency, and not be members of athletic teams or organizations for which testosterone is a banned substance. All procedures were approved by the Nipissing University Research Ethics Board.

Experimental procedures occurred on 3 separate days. On the first day of testing, participants were familiarized with the experimental procedures, provided informed consent, and provided anthropological measures (e.g., height, weight, 2D:4D ratio). Moreover, participants completed several self-report questionnaires, including the Self-Report Psychopathy Scale-Short Form (SRP-SF; see below). On the second day of testing, participants arrived at the Urology Clinic where all medical procedures took place. Upon arrival, a blood sample (10 mL) was drawn from each participant in order to measure baseline testosterone concentrations. In a counter-balanced, double-blind design participants then received 150 mg of testosterone (Androgel®) or placebo. Androgel® is a topical gel most commonly used for the treatment of male hypogonadism (a condition whereby men experience low concentrations of testosterone). In both instances, a male research assistant blind to the drug condition applied the gel to the participants' upper arms and shoulders. Additional blood samples were collected at 60 and 120 min post-gel administration to assess changes in testosterone concentrations in response to the experimental manipulation. All blood samples were allowed to clot, after

which they were centrifuged at 3000 rpm and serum samples were extracted and stored at −60 °C until assayed. Next, participants were transported to Nipissing University where they completed a number of computer-based tasks as part of a larger protocol assessing social perception, cognition, attention, and decision-making abilities. Participants performed the RMET approximately 3 h and 50 min after gel application (M = 229.39 min, SD = 12.11 min). Previous testosterone administration research using the same dose of Androgel® found that serum testosterone concentrations begin rising within 2 h of administration, reaching peak levels within 3 h (Eisenegger et al., 2013). Moreover, effects of testosterone on threat-related brain function have been detected within 40–90 min of drug application (van Wingen et al., 2008; Goetz et al., 2014). Thus, although the time-course for the effects of testosterone on social, cognitive, and behavioral processes in men is not known, our choice of a 4 h delay between drug administration and assessment of empathic abilities is reasonable in light of the pharmacokinetic data (Eisenegger et al., 2013) and neuroimaging work (van Wingen et al., 2008; Goetz et al., 2014). The third day of testing took place 2 weeks later and mirrored the second day as described above, with the exception that participants received whichever drug they did not receive on the second day of testing. At the conclusion of day 3 of testing, participants were asked whether they believed they received testosterone on the 2nd or 3rd day of testing. A binomial test indicated that participants were no better than chance at guessing which day they received testosterone (p = .20)

2.1. Serum testosterone concentrations

Serum samples were stored at −60 °C until assayed using commercially available enzyme immunoassay kits (DRG International, NJ). All samples were assayed in duplicate, and the average of the duplicates was used for all statistical analyses. Average intra- and inter-assay coefficients of variation were below 6%.

2.2. Digit ratio measure

2D:4D ratios were measured by two research assistants from a scan of the left and right hands of participants. Lengths of the second and fourth digits were computed by measuring the distance between the ventral proximal creases of the digits to the fingertips using ImageJ software. The intraclass correlation coefficients (ICC) was used to determine the repeatability of measurements across the two raters. Repeatability was high for left 2D:4D ratio, ICC = .91, F = 10.51, p < .001, and right 2D:4D ratio, ICC = .95, F = 18.81, p < .001.

2.3. Self- Report Psychopathy scale

The Self-Report Psychopathy-Short Form (SRP-SF; Paulhus et al., 2015) was used to assess variability in psychopathic traits. The SRP-SF is a self-report measure consisting of 29 items assessing the Interpersonal, Affective, Lifestyle, and Antisocial facets of psychopathy. Participants were asked to respond on the extent to which they agree with each statement using a 5-point Likert scale (1 = disagree strongly, 5 = agree strongly). The interpersonal facet consists of items such as "I have pretended to be someone else in order to get something," "I would get a kick out of scamming someone," and "Sometimes you have to pretend you like people to get something out of them". The affective facet consists of items such as "People sometimes say that I'm cold-hearted," "I never feel guilty over hurting others," and "I sometimes dump friends that I don't need anymore". The lifestyle facet includes items such as "I'm a rebellious person," "I've often done something dangerous just for the thrill of it," and "I admit that I often mouth off without thinking." The antisocial facet includes items such as "I have broken into a building or vehicle in order to steal something or vandalize," "Every now and then I carry a weapon (knife or gun) for protection," and "I was convicted of a serious crime." Scale reliabilities as assessed using Cronbach's alpha ranged from .60 to .88 (Interpersonal = .88, Affective = .73, Lifestyle = .70, Antisocial = .60). Similar to the Psychopathy Checklist-Revised (Hare and Neumann, 2008; Seara-Cardoso et al., 2012, 2013), the 4 facets can be modeled using the traditional two-factor model of psychopathy. Specifically, interpersonal and affective items were summed to create "Factor 1" scores, whereas the lifestyle and antisocial items were summed to create "Factor 2" scores. The SRP and SRP-SF both have good basic psychometrics, as demonstrated by the theoretically sound and mathematically strong latent structures (Carré et al., 2013; Neumann and Pardini, 2012; Sera-Cardoso et al., 2013). The SRP is strongly positively correlated with the PCL-R (Neumann et al., in press), the Youth Psychopathic Traits Inventory (Neumann and Pardini, 2012), and a psychopathy self-report based on the five-factor model of personality (Lynam et al., 2011; Miller et al. (2015)). Across a wide diversity of samples, the SRP traits are associated in the expected theoretical directions with relevant external correlates, such as criminal offenses and externalizing psychopathology (Fite et al., 2010; Nathanson et al., 2006; Neumann and Pardini, 2012), moral reasoning (Seara-Cardoso et al., 2012, 2013), amygdala activation to fearful faces (Carré et al., 2012), and amygdala reactivity to emotional cues (Seara-Cardoso et al., in press).

2.4. Reading the Mind in the Eyes task (RMET)

The Reading the Mind in the Eyes (RMET) was designed to measure variability in one's ability to infer other people's affective mental states from the eye region of the face. The task includes 36 photos of the eye regions of both male and female faces and a forced choice is required from four alternative words representing a feeling or thought that the person depicted in the picture is experiencing. Participants were given an unlimited amount of time to complete the task. Also, a glossary of terms used in the task was provided to participants in case they did not recognize/understand any of the words presented during the task. Higher scores on this task indicate better overall accuracy.

2.5. Statistical analyses

A paired sample t-test was performed to examine differences in task performance as a function of drug condition. Also, Pearson correlations were computed to investigate bivariate correlations between psychopathic traits, 2D:4D ratio, and RMET performance. Finally, mixed factor ANCOVAs were performed to examine whether digit ratio and/or psychopathic traits moderated the effect of drug condition on task performance. For these analyses, drug condition was treated as the within-subject factor and the moderators (mean-centered) were treated as covariates. All analyses were performed using alpha = .05 (two-tailed).

3. Results

3.1. Serum testosterone concentrations

A 3 (Time; baseline vs. 60-min vs. 120-min) X 2 (Drug Condition; Androgel® vs. Placebo) repeated measures ANOVA was performed on serum testosterone concentrations. Results revealed a significant main effect of drug condition ($F_{1,29}$ = 31.68, p < .001), with the Androgel® condition yielding significantly higher testosterone concentrations compared to the placebo condition ($M_{\text{Androgel®}}$ = 5.85 ng/mL, M_{placebo} = 4.51 ng/mL). There was also a significant main effect of time ($F_{2,58}$ = 53.83, p < .001) and a significant time × drug condition interaction [$F_{2,58}$ = 46.05, p < .001], demonstrating that testosterone concentrations were significantly

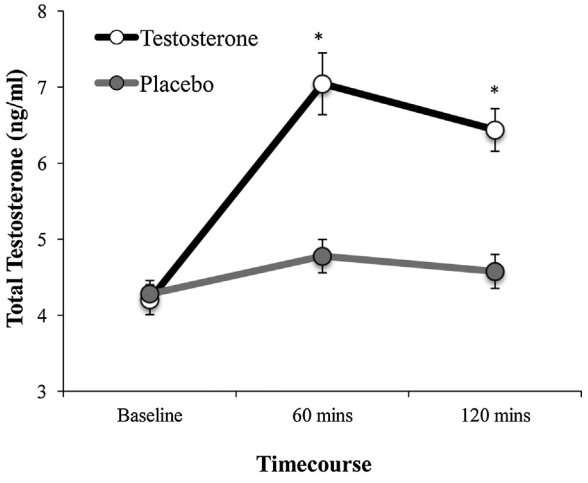

Fig. 1. Serum testosterone concentrations as a function of drug condition. Note: *$p < .001$

higher at 60 min and 120 min post Androgel® administration, but not at baseline (see Fig. 1).

3.2. Does testosterone administration modulate RMET performance?

Although performance on the RMET was lower after testosterone relative to placebo, a paired sample *t*-test revealed that this difference was not statistically significant (testosterone; $M_{accuracy} = 70.38\%$, SD = 8.30%, placebo; $M_{accuracy} = 72.23\%$, SD = 9.66%, $t_{29} = 1.19$, $p = 0.245$).

3.3. Does 2D:4D ratio predict RMET performance and/or moderate the effect of testosterone on RMET performance?

Bivariate correlations indicated that left hand 2D:4D ratio was negatively correlated with RMET performance after placebo ($r = -.52$, $p = .003$) but not after testosterone administration ($r = -.24$, $p = .21$; see Table 1). There were no bivariate correlations between right hand 2D:4D ratio and RMET performance on either placebo or testosterone days (all $ps > .40$).

To examine the extent to which 2D:4D ratio moderates the effect of testosterone on RMET performance, separate mixed factor ANCOVAs were performed on RMET scores with drug condition as a within-subject factor and 2D:4D ratio (left and right; mean centered) as covariates. Results revealed a marginally significant left hand 2D:4D ratio × drug condition interaction ($F_{1,28} = 4.15$, $p = .051$, $\eta_p^2 = .13$). Simple slopes analyses indicated that testosterone impaired RMET performance among men with relatively low left hand 2D:4D ratio ($M = -4.93\%$, $t_{29} = -2.34$, $p = .027$), but not high left hand 2D:4D ratio ($M = 1.22\%$, $t_{29} = .58$, $p = .57$). See Fig. 2.

In contrast, there was no right hand 2D:4D ratio × drug condition interaction ($F_{1,28} = .24$, $p = .63$, $\eta_p^2 = .008$).

3.4. Do interpersonal/affective traits of psychopathy (Factor 1) predict RMET performance and/or moderate the effect of testosterone on RMET performance?

Bivariate correlations indicated that Factor 1 scores were negatively (though marginally) associated with RMET performance after placebo ($r = -.35$, $p = .058$) but not after testosterone administration ($r = .09$, $p = .65$). A mixed factor ANCOVA was performed to examine the role of Factor 1 in moderating the effect of testosterone administration on RMET performance. Results revealed a significant Factor 1 × drug condition interaction ($F_{1,28} = 8.35$, $p = .007$, $\eta_p^2 = .23$), Simple slopes analyses indicated that testosterone impaired RMET performance among men scoring relatively low on Factor 1 ($M = -5.71\%$, $t_{29} = 2.96$, $p = .006$), but not high on Factor 1 ($M = 2.33\%$, $t_{29} = 1.16$, $p = .26$). See Fig. 3.

3.5. Do lifestyle/antisocial traits of psychopathy (Factor 2) predict RMET performance and/or moderate the effect of testosterone on RMET performance?

Bivariate correlations revealed no correlations between Factor 2 scores and RMET performance after placebo or testosterone (all $ps > .27$; see Table 1). A mixed factor ANCOVA was performed to examine the role of Factor 2 in moderating the effect of testosterone administration on RMET performance. Results revealed no Factor 2 × drug condition interaction ($F_{1,28} = .05$, $p = .83$, $\eta_p^2 = .002$).

4. Discussion

Our findings indicate that testosterone administration impairs socio-cognitive abilities in young men, but this effect is not universal. Results of the current study indicate that individual differences in 2D:4D ratio and psychopathic traits moderate the effect of testosterone administration on socio-cognitive processes believed to index empathic abilities. Specifically, testosterone caused a decrease in RMET task performance, but only among men with relatively low (i.e., masculinized) 2D:4D ratios and among men who scored relatively low on psychopathic traits (in particular, those scoring low on the interpersonal/affective facets, i.e., Factor 1).

The current study is the first to examine the potential causal role of testosterone in modulating socio-cognitive processing in healthy young men. This is surprising in light of the wealth of research examining the effects of a single administration of testosterone on a variety of socio-cognitive processes in women (e.g., empathic processing, emotion recognition, ratings of trust; see Bos et al., 2012 for review). However, investigators have recently started to develop pharmacological challenge probes for use in men. For instance, some research indicates that a single administration of testosterone modulates economic (Zak et al., 2009) and

Table 1
Correlations and descriptive statistics ($N = 30$).

Variables	1	2	3	4	5	6	7	Mean	SD
1. Left 2D:4D	–							.956	.03
2. Right 2D:4D	.71*	–						.964	.03
3. SRP Factor 1	.21	.14	–					35.52	10.00
4. SRP Factor 2	−.28	−.24	.63*	–				26.59	5.93
5. RMET, Placebo	−.52*	−.16	−.35†	.14	–			72.23	9.66
6. RMET, Androgel	−.24	−.09	.09	.20	.56*	–		70.38	8.30
7. RMET, A − P	.36#	.09	.48*	.04	−.59*	.34‡	–	−1.85	8.55

Note: SRP—self-report psychopathy, RMET—Reading the Eyes in the Mind, A − P—androgel minus placebo.
* $p < .01$.
# $p = .051$.

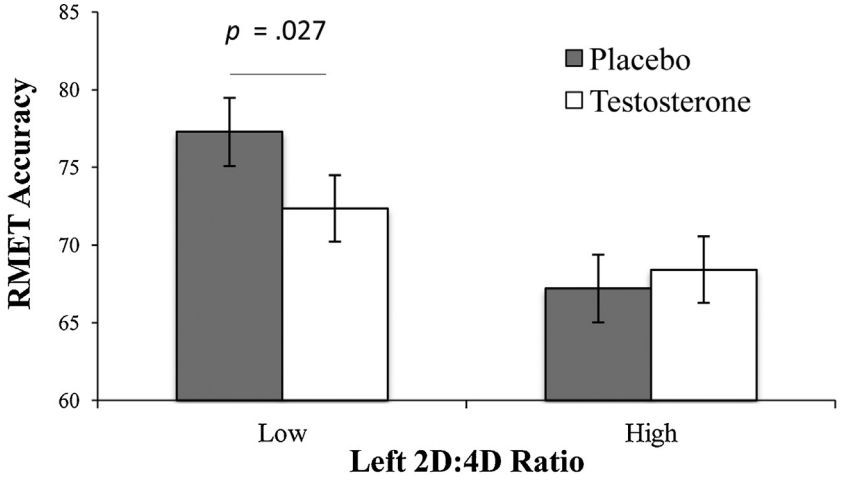

Fig. 2. Left digit ratio (2D:4D) moderates the effect of testosterone on cognitive empathy performance. Note: low and high 2D:4D ratio are displayed at −/+1 SD from the mean for display purposes. Statistical analyses were based on the entire range of 2D:4D scores.

ethical decision-making (Wibral et al., 2012) in men. The latter studies used a significant time lag (18–24 h) between testosterone administration and the assessment of behavioral outcomes on the basis of pharmacokinetic research in hypogonadal men demonstrating testosterone peaks about 16–22 h after administration (Swerdloff et al., 2000). However, similar pharmacokinetic data in healthy eugonadal men indicates that testosterone concentrations begin to rise within 2 h after administration, and reach peak levels at 3 h post administration (Eisenegger et al., 2013). Moreover, pharmacological-fMRI studies indicate that testosterone administration to men and women rapidly (within 40–90 min) influence threat-related neural function (Goetz et al., 2014; van Wingen et al., 2008). Finally, there is correlational evidence that acute fluctuations in testosterone during competition may rapidly modulate social cognition (Carré et al., 2014) and aggressive behavior in young men (see Carré and Olmstead, 2015). Collectively, this body of work suggests that acute fluctuations in testosterone (either exogenous or endogenous) have the potential to rapidly modulate socio-cognitive processes.

Consistent with previous work in women (van Honk et al., 2011), testosterone caused a significant reduction in RMET performance, but only among men exposed to relatively high testosterone concentrations early in development (as indexed by left hand 2D:4D ratio). It is noteworthy that the moderation effect observed in the current study was found in the left hand, but not right hand. Previous testosterone administration work in women found that the effect of testosterone administration on RMET performance and moral decision making was moderated by right hand 2D:4D ratio (van Honk et al., 2011; Montoya et al., 2013). The latter studies looked exclusively at right hand 2D:4D ratio, and thus, the extent to which there was a laterality effect in this work is unclear. Although previous work has typically found that relationships between digit ratio and psychological/behavioral traits have been stronger for right hand 2D:4D ratio (see Manning, 2002), other work finds that associations between 2D:4D ratio and behavioral outcomes are similar for left hand and right hand (e.g., sport performance; Honekopp and Schuster, 2010). Despite these inconsistencies, our findings indicate that indirect measurements of prenatal testosterone exposure must be considered when studying how social cognition and behavior is affected by fluctuations in testosterone levels (experimentally induced or natural). This is important if we want to fully characterize the neuroendocrine mechanisms underlying individual differences in human social cognition and behavior. Our findings are in line with a recent correlational study which indicates that acute fluctuations in testosterone in response to viewing an aggressive video prime are positively correlated with subsequent aggressive behavior, but only among men with relatively low (i.e., masculinized) left hand 2D:4D ratios (Kilduff et al., 2013). To the extent that 2D:4D ratio represents a valid marker of prenatal testosterone exposure (Zheng and Cohn, 2011; see

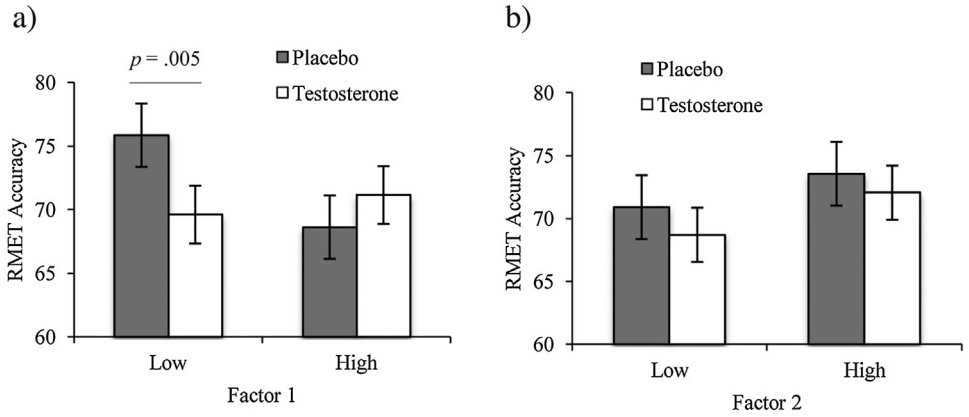

Fig. 3. (a) Factor 1 moderates the effect of testosterone on RMET performance. (b) Factor 2 does not moderate the effect of testosterone on RMET performance. Note: low and high Factor 1/Factor 2 scores are displayed at −/+1 SD from the mean for display purposes. Statistical analyses were based on the entire range of Factor 1 and Factor 2 scores.

Manning et al., 2014 for review), the above findings are consistent with the organizational-activational hypothesis (Phoenix et al., 1959) whereby exposure to testosterone during critical periods of development (e.g., prenatally and/or during adolescence) masculinizes neural circuitry, ultimately programming behavioral and physiological responses to the activational effects of testosterone in adulthood (see Sisk and Zehr, 2005; McCormick and Mathews, 2007).

One unexpected finding from the current study was the negative correlation between left hand 2D:4D ratio and RMET performance. Specifically, we found that men with relatively low 2D:4D ratios (i.e., masculinized) performed better on the RMET relative to men with high 2D:4D ratios. This finding contrasts with some work suggesting that elevated prenatal testosterone concentrations (indexed by amniotic testosterone concentrations) are associated with impairments in RMET performance (Chapman et al., 2006). However, other work using different indices of prenatal testosterone exposure have found mixed evidence for the link between early androgen exposure and empathic/socio-cognitive abilities. For instance, although some studies have found that low 2D:4D ratio was associated with decreased empathic/socio-cognitive abilities in men (Manning et al., 2010), others have found that low 2D:4D ratio was associated with better empathic/socio-cognitive abilities (Honekopp, 2012), and yet others have found no link between these variables (Voracek and Dressler, 2006; Sapienza et al., 2009). Moreover, males with congenital adrenal hyperplasia—a genetic condition characterized by elevated androgen exposure early in development (White and Speiser, 2000), demonstrate better performance on tasks that tap into empathic processes, whereas females with CAH demonstrate decreased performance on similar tasks (Mathews et al., 2009). Collectively, these findings indicate that links between early androgen exposure and empathic abilities are mixed, and thus, more work in this area is clearly needed.

We observed a marginally significant negative correlation between Factor 1 scores (which assesses the callous, unemotional, manipulative and deceitful facets of psychopathic traits) and RMET performance on the placebo day (see Table 1), which replicates previous work reporting negative associations between this factor and empathic processes (Seara-Cardoso et al., 2012, 2013). In addition, our results indicate that a single administration of testosterone most strongly affected men who scored low on Factor 1 (who performed relatively well on the RMET while on placebo), rendering their performance essentially equivalent to men scoring high on Factor 1, who performed relatively poorly on the RMET across placebo and testosterone conditions. The moderating effect of psychopathic traits highlights the importance of considering individual difference factors when examining the role of testosterone in modulating socio-cognitive processes. The moderation effects observed in the current study are consistent with a growing body of research examining the role of oxytocin (OXT) administration on social cognition and behavior. Specifically, effects of OXT on social cognition and behavior are typically moderated by contextual and/or psychological factors (see Bartz et al., 2011 for review). Thus, given that testosterone administration work in men is in its infancy, it will be critical to consider theoretically- and empirically-based individual difference factors that may moderate effects of testosterone on social, cognitive and behavioral processes.

Although the current investigation revealed novel findings, there are some limitations that should be noted. First, despite finding no significant main effect of testosterone on RMET performance, we cannot rule out the possibility that such an effect may exist had we used a different time lag between testosterone administration and the measurement of RMET performance. The time lag used in the current study was based on pharmacokinetic research indicating that testosterone concentrations begin to rise within 2 h of drug administration and reach peak concentrations after 3 h (Eisenegger et al., 2013). However, in the current study, we found that significant increases in testosterone (+60%) occurred within just 1 h after drug administration. Thus, we cannot exclude the possibility that main effects of testosterone on RMET performance may have been detected if we assessed RMET performance earlier (e.g., 1-h after administration). On the other hand, it may be that we assessed RMET performance too early. A 3.5–4.5 h time lag between testosterone administration and assessment of social, cognitive, and behavioral outcomes is common practice in single administration research conducted in women (see Bos et al., 2012 for review). This time lag is based on a landmark study in which a single administration of sublingual testosterone was administered to healthy young women while vaginal pulse responses to sexual stimuli were assessed continually over several hours (Tuiten et al., 2000). Although testosterone concentrations peaked within 15 min of receiving the drug, effects on physiological and psychological processes were not observed until 3 to 4.5 h after drug administration. The authors argued that such effects were consistent with a genomic mode of steroid action (Tuiten et al., 2000). We assessed RMET performance approximately 2 h and 45 min after peak testosterone concentrations, and thus, it is possible that main effects of testosterone on RMET performance would be observable had we assessed RMET performance later (i.e., 3.5–4.5 h after peak levels of testosterone were observed). However, it is important to note that testosterone may exert more rapid (perhaps non-genomic) effects through interacting with extranuclear androgen and estrogen receptors in the hippocampus, amygdala, hypothalamus, and cortex (DonCarlos et al., 2003; Tabori et al., 2005; Blaustein et al., 1992; McEwen, 2001). These extra-nuclear androgen and estrogen receptors are well positioned to modulate neuronal signaling (Sarkey et al., 2008), thus facilitating modulation of social behavior through non-genomic mechanisms (Trainor et al., 2007; Oliveira et al., 2009). Thus, given the paucity of research on the time- course of the physiological/behavioral effects of exogenous testosterone in men (see Zak et al., 2009; Goetz et al., 2014), it will be important for future experiments to examine both rapid and delayed effects of steroid hormone administration on subsequent physiological and behavioral processes.

Another limitation of the current study is that the RMET is only one index of empathic processing. The RMET was designed to measure an individual's ability to infer the mental states from the eye region of the face (Baron-Cohen et al., 2001). Performing this task requires both affect processing and perspective taking. As such any difficulties in performing this task may stem from either of these processes and it is not possible, using this task, to differentiate what precisely drives deteriorating task performance in those individuals whose accuracy drops after testosterone administration.

In summary, results from the current experiment indicate that testosterone impairs socio-cognitive processing as assessed using the RMET, but this effect critically depends on variability in 2D:4D ratio and psychopathic traits. These findings highlight the importance of considering theoretically- and empirically- based individual difference factors when examining the causal role of testosterone in shaping variability in human social cognition.

Conflict of interest

None.

Contributors

JMC, TLO, BL, and BJPM designed and conceived the study.
TLO, BL, and BJPM collected the data.
BJPM performed hormone assays.

JMC analyzed the data.
BG supervised the drug administration component.
JMC, EV and CSN wrote the paper.
All authors approved the final draft.

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