Archival Report

Biological Psychiatry

Exogenous Testosterone Rapidly Increases Aggressive Behavior in Dominant and Impulsive Men

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ABSTRACT

BACKGROUND: Although traditional wisdom suggests that baseline levels of testosterone (T) promote aggressive behavior, decades of research have produced findings that have been largely weak and inconsistent. However, more recent experimental work suggests that exogenous administration of T rapidly potentiates amygdala and hypothalamus responses to angry facial expressions. Notably, these brain regions are rich in androgen receptors and play a key role in modulating aggressive behavior in animal models.

METHODS: The present experiment extends this work by examining whether acutely increasing T potentiates aggressive behavior in men. In a double-blind, placebo-controlled, between-subject design, healthy adult men (n = 121) were administered either T or placebo, and subsequently engaged in a well-validated decision-making game that measures aggressive behavior in response to social provocation. In light of prior correlational research, we also assessed the extent to which T's effects on aggressive behavior would depend on variability in trait dominance and/or trait self-control.

RESULTS: Exogenous T on its own did not modulate aggressive behavior. However, T's effects on aggression were strongly influenced by variation in trait dominance and trait self-control. Specifically, T caused an increase in aggressive behavior, but only among men scoring relatively high in trait dominance or low in trait self-control.

CONCLUSIONS: These findings are the first to demonstrate that T can rapidly (within 60 minutes) potentiate aggressive behavior, but only among men with dominant or impulsive personality styles.

Keywords: Aggression, Competition, Hormones, Self-control, Testosterone, Trait dominance

http://dx.doi.org/10.1016/j.biopsych.2016.06.009

Research in animal models indicates that testosterone (T) plays an important role in modulating aggressive behavior (1). However, evidence for a role of T in promoting human aggression has been inconsistent (2). Importantly, T concentrations are not static, but rather fluctuate rapidly in the context of competitive interactions (3). It has been speculated that acute changes in T during competition may serve to fine-tune ongoing or future aggressive behavior (4–6). In support of this hypothesis, a rise in T after winning a competitive interaction is required to potentiate subsequent aggression in male California mice (7–9). Other research in male cichlid fish indicates that winning a competition increases one's probability of winning subsequent interactions—an effect that is eliminated when blocking the competition-induced rise in T (10). Complementing this work are studies in humans demonstrating that an acute rise in T concentrations during competition (but not baseline levels of T) predicts increased competitive motivation (11,12) and aggressive behavior (13–16). These findings are consistent with theoretical models suggesting that changes in T may serve to adaptively regulate ongoing or future dominance-related behavior (4,17). However, a major limitation of this research is that it is correlational, and thus the extent to which an acute increase in T plays a causal role in modulating competitive or aggressive behavior is not clear.

Pharmacological challenge research indicates that a single administration of T increases threat-related amygdala, hypothalamic, and periaqueductal gray reactivity to angry facial expressions in healthy men (18). These findings parallel evidence in women in which a single administration of T increases amygdala and hypothalamic reactivity to angry facial expressions (19–21). Notably, these subcortical brain structures are rich in both androgen and estrogen receptors (22–24) and play a key role in potentiating reactive aggression in animal models (1,25). More recently, a single application of T increased men's perception of their own physical dominance (26), suggesting that T may increase men's perception of their own formidability. Collectively, this research suggests that acutely increasing T concentrations rapidly modulates neural and psychological processes relevant to human aggression.

It has been proposed that social-contextual or individual difference factors may moderate the effect of T on human aggression (3,27). In particular, correlational and experimental

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ISSN: 0006-3223

work suggests that trait dominance may play a role in moderating relationships between T and human dominance behavior. People with dominant personality styles tend to behave in assertive, forceful, and self-assured ways (28) to achieve or maintain high social status. In one study, a rise in T after winning a competition predicted increased aggressive behavior in a subsequent task, but only among men scoring high in trait dominance (13). Also, baseline T concentrations were positively correlated with men's dominance behavior during a mate competition, but only for men scoring high in trait dominance (29). Finally, a single administration of T to women increased their competitive motivation after a victory, but only for those scoring high on trait dominance (30).

An individual's ability to exert self-control under affectively charged situations might also mitigate the effect of T on aggression. Some research indicates that individuals scoring high on trait-based measures of self-control are more efficient at inhibiting aggressive impulses during social provocation (31). Other research indicates that tasks designed to bolster self-control decreased participants' subsequent aggression, whereas those designed to disrupt or temporarily reduce self-control increased participants' subsequent aggression (32,33). According to one theoretical model of aggression (34), instigating triggers, such as provocation, and impelling forces, such as T, may promote aggressive impulses, but these impulses may not manifest behaviorally among individuals high in trait self-control because these individuals are better equipped to override such impulses. Thus, T's effects on aggression may be reduced among those high in self-control but pronounced among those low in self-control.

In this experiment, we employed a double-blind, placebo-controlled, between-subjects design to investigate the causal role of T in promoting aggression in healthy young men. We predicted that T would increase aggressive behavior. Also, in light of previous correlational and experimental work (13,29,30), we predicted that T's effects on aggressive behavior would be most robust among men scoring relatively high on trait dominance. Also, we predicted that exogenous T would have no effect on aggressive behavior for people with strong impulse control (i.e., elevated trait self-control), Instead, T would increase aggressive behavior among men with weak impulse control. Collectively, such findings would suggest that individual differences in trait dominance or trait self-control may confer differential sensitivity to the acute effects of T on men's aggressive behavior.

METHODS AND MATERIALS

Participants

Our sample consisted of 121 healthy men between the ages of 18 and 35 (mean age = 25.27 years, SD = 4.98 years). Subjects were recruited from advertising on local media sites, through medical research participant databases, and through local colleges and universities. Prior to enrollment in the study, each prospective participant was interviewed to determine his eligibility. Exclusion criteria for participants included the following: currently receiving prescription medication affecting hormone concentrations (e.g., glucocorticoids, androgens), current diagnosis of a psychiatric disorder, diagnosed heart condition, drug or alcohol dependency, and membership on a sports team or organization where T is a banned substance. Participants who qualified for the protocol consented to providing blood samples for hormonal assay, as well as to having their T levels temporarily manipulated. The study was approved by the Nipissing University Research Ethics Board. Participant ethnicities were self-reported as follows: 77.5% Caucasian, 13.1% First Nations, 4.1% Asian, 1.7% Latin American, and 3.3% other.

Procedure

Testing occurred in a single session (see Figure 1). Participants reported to the laboratory at one of two times, 10 AM or 1 PM. Upon arrival, participants completed informed consent. Next, participants completed a battery of online self-report questionnaires assessing basic demographic information and individual differences in personality (see later). After the completion of the online questionnaires, a phlebotomist drew 10 mL of participants' blood to assess hormone concentrations (see the Supplement for details on the assay). Participants were then randomly assigned to either the drug or the control group. Drug condition (AndroGel [AbbVie Inc.,

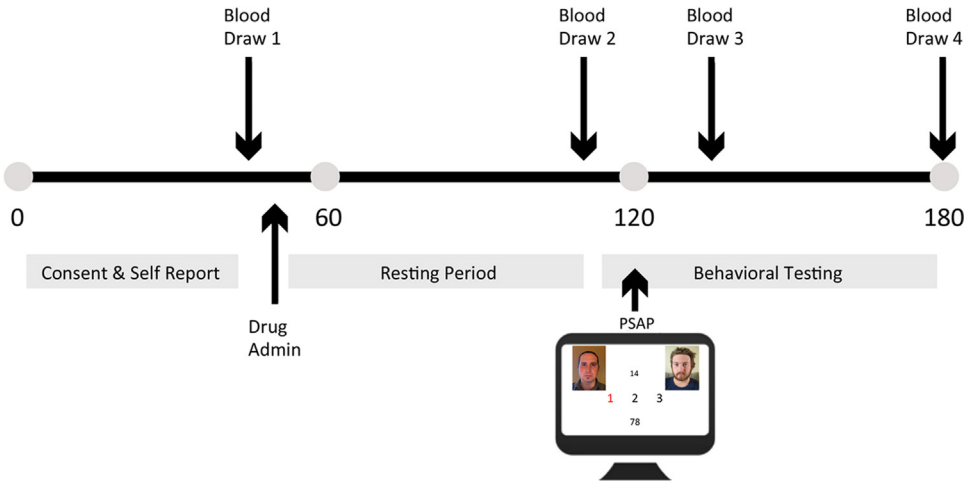

Figure 1. Experimental timeline for the entire protocol. PSAP, Point Subtraction Aggression Paradigm.

Chicago, IL] or placebo) was fully randomized across participants and was performed in a double-blind fashion. Regardless of drug condition, a male research assistant, blinded to the experimental condition, applied topical gel to the upper arm and shoulder area. One hour after drug administration, the phlebotomist drew a second blood draw. Although effects of T on aggressive behavior may be secondary to mood effects, previous studies have failed to document effects of acute T supplementation on subjective mood ratings (18,20); thus, participants did not complete mood measures after drug administration. Participants then completed a 10-minute session of the Point Subtraction Aggression Paradigm (PSAP; see later), which was used to assay aggressiveness; completed a post-PSAP questionnaire; and provided a third blood sample. Next, participants completed other behavioral tasks unrelated to the current hypotheses (risk taking, risk preferences, face perception). Prior to being debriefed, participants provided a final blood sample and were asked to guess the drug condition to which they were assigned.

Trait Dominance

Trait dominance was assessed using two separate measures: the International Personality Item Pool–Dominance Scale (IPIP-DS) (35) and the Dominance-Prestige Scale (DPS) (36). The IPIP-DS consisted of 11 items. Participants were asked to rate the extent to which each statement accurately described them on a five-point Likert-type scale ranging from 1 (very inaccurate) to 5 (very accurate). The dominance subscale of the DPS consisted of eight items. Participants were asked to rate the extent to which each item accurately described them on a seven-point Likert-type scale ranging from 1 (not at all) to 7 (very much). Cronbach's alphas for the IPIP-DS and DPS were .82 and .73, respectively. The scales were highly correlated ($r = .55$, $p < .001$) and thus were combined into a single composite measure of trait dominance. We combined both measures by standardizing (z score) each scale and then summing the standardized scores to create a composite measure of trait dominance.

Trait Self-Control

Trait self-control was assessed using two measures: the Brief Self-Control Scale (BSC) (37) and the Barratt Impulsiveness Scale (BIS) (38). There is evidence that subjective (i.e., self-report) measures of self-control positively correlate with more objective (i.e., behavioral) measures of self-control (39–41). The BSC consists of 13 items. Participants were asked to rate how well each statement reflected how they typically are on a five-point Likert-type scale ranging from 1 (not at all) to 5 (very much). The BIS consists of 30 items. Participants were asked to rate the extent to which each statement was true of them on a 4-point Likert-type scale ranging from 1 (rarely/never) to 4 (almost always/always). Cronbach's alphas for the BSC and BIS were .81 and .80, respectively. The BSC and BIS measures were highly correlated ($r = -.70$, $p < .001$), and thus were combined into a single composite measure of self-control. Prior to combining the scales, we first reverse-coded the BIS measure, so that low scores indicated higher impulsivity. Next, we standardized each scale and then summed the standardized scores to create a composite measure of trait self-control.

Point Subtraction Aggression Paradigm

There is evidence that T's relationship to human aggression is somewhat stronger when behavioral measures of aggression are used instead of self-report measures (2). Therefore, in the current study, participants performed the PSAP, a well-validated behavioral measure of reactive aggression (42,43). For this task, participants were told that hitting option 1 a hundred consecutive times would cause their point counter to enlarge and flash several times with positive signs around it, and that their point counter would increase by 1 point, indicating that they had gained a point. Participants were instructed that throughout the task, it may occur that their point counter turns red, flashes several times with negative signs around it, and decreases by 1 point. If this occurred, it meant that their game partner (actually the computer program) had stolen a point from them. Participants were told that these stolen points would be added to their game partner's point counter. Participants were instructed that they could also choose to select option 2 or option 3. They were told that hitting option 2 ten consecutive times would steal a point from their game partner, but despite the fact that their game partner would lose a point, they themselves had been randomly assigned to the experimental condition in which they did not get to keep the points that they stole. Because participants did not gain any financial reward from stealing, it can be inferred that stealing points served to punish one's game partner and as such represents the primary measure of aggressive behavior. Aggressive responding on the PSAP is consistent with the widely used operational definition of aggression as being "any form of behavior directed toward the goal of harming or injuring another living being who is motivated to avoid such treatment" (44). Importantly, the harm or injury does not need to be physical, but simply needs to be considered as an aversive stimulus by the receiver. In addition to offering participants the opportunity to select option 2 (aggressive responses), participants were also told that they could select option 3 (protective responses). Pressing option 3 ten consecutive times would protect their counter from point subtractions for a variable amount of time, thus providing a nonaggressive option. The PSAP task was programmed using E-Prime (Sharpsburg, PA). Point subtractions were delivered to participants every 6–45 seconds in the absence of any option 2 or option 3 selections. If participants completed 10 presses on option 2 or option 3, this would initiate a provocation-free interval (PFI). Participants were made aware that option 3 (protection) initiated a PFI but were not explicitly told that option 2 (aggression) would also initiate a PFI. When a PFI was initiated, the computer program did not provoke participants for a minimum of 45 seconds and a maximum of 90 seconds, after which the random point subtractions would continue to occur during the task. Another important parameter of the task was that once participants selected one of the three options, they were committed to this option until they completed the fixed ratio of button presses for the corresponding option. For example, if participants first selected option 1 (reward responses), they had to complete the 100 presses prior to selecting another option. Similarly, if participants selected option 2 (aggression) or 3 (protection), they had to complete the 10 presses prior to choosing another

option. Although provocations occurred randomly through the task in both drug conditions, participants in the placebo condition received slightly more provocations (mean = 12.4, SE = 0.45) during the task compared with participants in the T condition (mean = 11.4, SE = 0.26), $t_{112} = 1.89$, $p = .06$. To account for differences in the number of provocations received during the PSAP, aggressive behavior was computed by dividing the frequency of aggressive responses during the task by the number of provocations received during the task (i.e., total aggression/total provocation) (15). After performing the PSAP, participants completed a posttask questionnaire assessing the extent to which they enjoyed the task, the extent to which they would play the game again, and the extent to which they or their game partner played fair (–2 = not at all to +2 = very much so). Next, participants provided a third blood sample that was used to track changes in T concentrations that may have occurred in conjunction with performing the PSAP. At the conclusion of the experiment, participants were asked to guess which drug condition they were assigned to. Results indicated that 50% of participants correctly guessed that they received T, suggesting that participants were no better than chance at guessing which drug condition they were assigned to.

Statistical Analyses

A repeated measures analysis of variance was performed on T concentrations to confirm that our pharmacological challenge approach influenced T concentrations. For this analysis, time (sample 1 vs. sample 2 vs. sample 3 vs. sample 4) was a within-subject factor and drug condition (T vs. placebo) was a between-subject factor. An independent-samples *t* test was performed to examine the effect of drug condition on aggressive behavior. To test our hypotheses relating to trait dominance and trait self-control as moderators of the association between drug condition and aggression, we conducted moderated regression analyses using the SPSS macro PROCESS (SPSS Inc., Chicago, IL) (45). Predictor variables were mean centered prior to computing the interaction terms. Two participants did not complete the PSAP as they dropped out of the study prior to performing the task. Also, one participant refused to play the game (did not press buttons during the task). Finally, four participants (two placebo, two T) had aggression scores more than 3 SDs above the mean, and were thus removed prior to performing the analyses. Upon further examination of the outliers, we found that the two most extreme outliers (one T participant, one placebo participant) did not earn a single point during the PSAP, suggesting that they did not understand the task (earn as many points as possible) despite extensive instructions provided by the research assistants. Therefore, all analyses were based on 114 participants (57 received placebo, 57 received T). For all analyses, a *p* value of .05 or less (two-tailed) was considered statistically significant.

RESULTS

We first investigated the efficacy of the drug by comparing T concentrations between the drug (AndroGel) and the placebo group. A repeated-measures analysis of variance on serum T concentrations revealed main effects of time ($F_{3,342} = 32.55$, $p < .001$), drug condition ($F_{1,114} = 20.13$, $p < .001$), and a time by drug condition interaction ($F_{3,342} = 24.81$, $p < .001$). Post hoc analyses indicated that serum T concentrations were elevated in the T group relative to the placebo group within 60 minutes of drug application—an effect that was sustained throughout the experimental procedure (see Figure 2). There were no differences in serum T concentrations between the T and placebo groups prior to drug application ($p = .49$). See the Supplement for data on serum cortisol.

We then investigated whether drug condition influenced aggressive behavior on the PSAP. An independent-samples *t* test revealed no significant differences in aggressive behavior between participants who received T (mean = 16.39, SE = 1.64) versus those who received placebo (mean = 12.90, SE = 1.42; $t_{112} = 1.61$, $p = .11$, Cohen's $d = 0.30$).

Next, we examined whether individual differences in trait dominance would moderate the effect of T on aggressive behavior. Regression analysis revealed a significant trait dominance by drug condition interaction ($R^2_{change} = 5.6\%$, $F_{1,110} = 6.98$, $p = .009$). For those scoring relatively high in trait dominance (1 SD above the mean), T caused an increase in aggressive behavior ($t_{110} = 2.83$, $p = .006$). For men scoring relatively low in trait dominance (1 SD below the mean), T had no effect on aggressive behavior ($t_{110} = -0.91$, $p = .36$; see Figure 3). Next, we examined whether individual differences in trait self-control would moderate the effect of T on aggressive behavior. Results revealed a significant trait self-control by drug condition interaction ($R^2_{change} = 5.2\%$, $F_{1,110} = 6.16$, $p = .015$). For men scoring relatively low in trait self-control (1 SD below the mean), T caused an increase in aggressive behavior ($t_{110} = 3.00$, $p = .003$). For men scoring relatively high in trait self-control (1 SD above the mean), T had no effect on aggressive behavior ($t_{110} = -0.64$, $p = .52$) (see Figure 4). In light of these two significant interactions, we further examined the extent to which each interaction uniquely explained variance in aggressive behavior. Collectively, the trait dominance by drug condition and trait self-control by drug condition interactions accounted for 8.8% of the variance in aggressive behavior ($F_{2,108} = 5.64$, $p = .005$). The trait dominance by drug condition interaction emerged as a

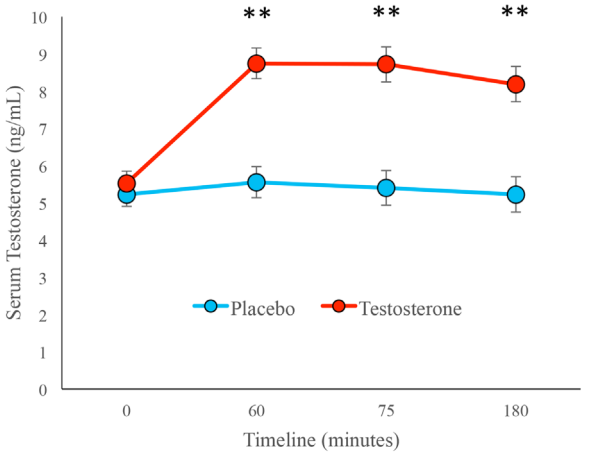

Figure 2. Serum testosterone concentrations as a function of drug condition and time. Error bars represent SEM. **$p < .001$.

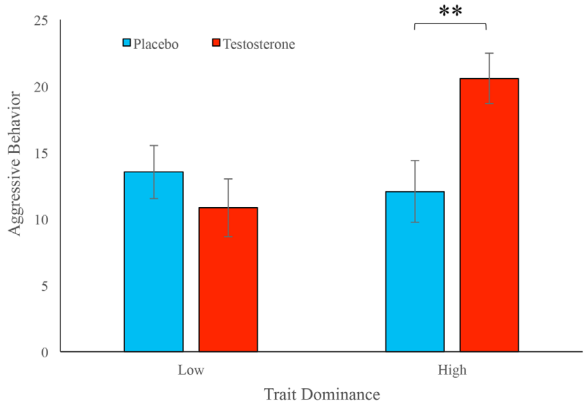

Figure 3. The effects of testosterone or placebo on aggressive responses, at high and low levels of trait dominance (±1 SD of the mean). Error bars represent SEM. $^{**}p < .01$.

significant unique predictor of aggressive behavior (R^2 = 3.7%, $F_{1,108}$ = 4.67, p = .03). Moreover, the trait self-control by drug condition interaction also emerged as a significant unique predictor of aggressive behavior (R^2 = 3.3%, $F_{1,108}$ = 4.23, p = .04). Simple slopes analyses indicated that T increased aggressive behavior for men scoring high (1 SD above the mean) on trait dominance and low (1 SD below the mean) on trait self-control (t_{108} = 3.52, p = .0006). There were no effects of T on aggressive behavior for men scoring high on trait dominance and high on trait self-control (t_{108} = 0.71, p = .48), men scoring low on trait dominance and high on trait self-control (t_{108} = –1.82, p = .07), or men scoring low on trait dominance and low on trait self-control (t_{108} = 0.71, p = .48). See the Supplement for additional exploratory analyses.

DISCUSSION

Our results indicate that exogenous administration of T on its own does not potentiate aggressive behavior. Instead, T's effects on aggressive behavior depend on variability in trait dominance and trait self-control. Specifically, T increased aggressive behavior, but only among dominant men or men scoring low in trait self-control. For men scoring low in trait dominance or high in trait self-control, there was no effect of T on aggressive behavior. These findings are the first to demonstrate that exogenous T on its own does not promote aggressive behavior in men, and they highlight the critical role that individual difference factors play in mitigating the effect of T on aggression.

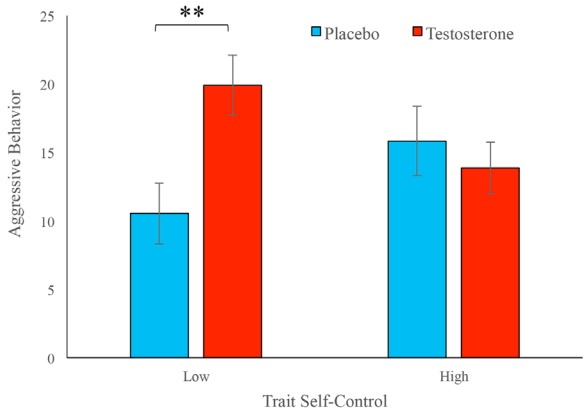

Figure 4. The effects of testosterone or placebo on aggressive responses, at high and low levels of trait self-control (±1 SD of the mean). Error bars represent SEM. $^{**}p < .01$.

Although the relationship between T and aggression has been well established in animal models (46), there is only weak evidence for a link between individual differences in baseline T concentrations and human aggression (2). However, a growing body of work indicates that acute changes in T concentrations within the context of social provocation or competition are positively correlated with aggressive and antagonistic behavior in men (13–16). Our results build on correlational and experimental work suggesting that individual differences in trait dominance influence the extent to which T modulates human dominance behavior. Specifically, T has a strong potentiating effect on aggressive behavior, but only among dominant men. Notably, we also found that individual differences in trait self-control moderated the effects of T on aggressive behavior. Here, T rapidly increased aggressive behavior, but only for men scoring relatively low in trait self-control.

What are the neural mechanisms through which T potentiates aggressive behavior in men scoring high in trait dominance or low in trait self-control? The finding that trait dominance and self-control both interacted with drug condition and explained unique variance in aggressive behavior suggests that distinct neural mechanisms may underlie the aggression-potentiating effects of T. It has been hypothesized that heightened amygdala reactivity to social signals of threat or social provocation may mediate the link between T and human aggression (3,27,47,48). Consistent with this idea, experimental work indicates that exogenous T potentiates amygdala reactivity to angry faces (18–21) and promotes prolonged eye gaze toward masked angry facial expressions (49), and that heightened amygdala reactivity to social provocation positively predicts aggressive behavior (50). Notably, people scoring high on measures that tap into the construct of trait dominance (e.g., behavioral activation system; interpersonal or affective dimensions of psychopathy) also demonstrate heightened amygdala reactivity to angry facial expressions (51,52) and demonstrate prolonged eye gaze toward masked angry faces (53). Collectively, this research leads us to speculate that T may potentiate aggressive behavior in dominant men through increasing amygdala reactivity to social cues of threat (e.g., angry faces) or through social provocation and modulating downstream limbic structures (e.g., hypothalamus, periaqueductal gray) involved in the expression of reactively aggressive behavior (25). On the other hand, T's potentiation of aggressive behavior in men scoring low in self-control may involve modulation of top-down regulatory control of limbic function. According to the prefrontal-subcortical balance model of self-regulation (54), the failure to exert self-control and override impulses results from an imbalance between prefrontal brain regions (e.g., orbitofrontal cortex [OFC]), which regulate top-down control, and subcortical brain regions, which potentiate bottom-up impulses. Consistent with this model, decreased OFC function or decreased amygdala-OFC functional coupling is commonly observed in clinical groups prone to impulsive aggression

(e.g., intermittent explosive disorder, borderline personality disorder, antisocial personality disorder, conduct disorder) (55–57). Notably, exogenous T decreases amygdala-OFC functional coupling (58), and decreased OFC reactivity to social provocation mediates the relationship between endogenous T and aggressive behavior (59). Finally, decreased OFC reactivity to angry facial expressions predicts increased aggressive behavior in young men (60). Together, these findings suggest that heightened amygdala reactivity to social threat or social provocation or decreased amygdala-OFC coupling may underlie the aggression potentiating effect of T among dominant and impulsive men. These putative neural mechanisms are not mutually exclusive, and there may be other mechanisms that may in part explain the effects observed in the current study (e.g., heightened reward-related neural function) (61).

Although our findings contribute to a greater understanding of the causal role of T in potentiating human aggression, there are some limitations that should be noted. First, our experiment included only men, and thus the extent to which similar effects would be found in women is not clear. Neuroimaging work indicates similar effects of exogenous T on threat-related brain function in men and women (18,19). Moreover, exogenous T impairs empathic processes in both men and women exposed to high prenatal androgen (as indexed by 2D:4D hand ratio) (62,63). Nevertheless, our previous correlational work suggests that acute changes in endogenous T concentrations map onto subsequent aggressive behavior in men, but not women (13,14). Future work will be needed to determine whether similar effects of T (and interactions with personality traits) potentiate aggressive behavior in women. The pharmacological challenge approach used in the current study successfully increased T concentrations to within the high-normal range within 60 minutes. However, endogenous T concentrations rise much more rapidly (within 10-15 minutes) during competitive interactions. Future research may benefit by using T preparations that more rapidly increase serum T concentrations (e.g., sublingual, intranasal) and thus represent a more ecologically valid simulation of T responses that occur within the context of human competition.

Although previous research has established that longer-term administration (6 weeks) of supraphysiologic doses of T to adult men increased aggressive behavior on the PSAP (64), the current study is the first to suggest that a single dose of T, which increases levels to within the mid-to-high-normal physiological range (65,66) can increase aggressive behavior in men scoring high on trait dominance or low in trait self-control. The speed with which the effects were observed suggest that T may increase aggressive behavior through a rapid, non-genomic mechanism (67). Future research will be needed to detail the neural mechanisms through which T rapidly modulates aggressive behavior in dominant and impulsive men and to determine whether similar mechanisms are found in women.

ACKNOWLEDGMENTS AND DISCLOSURES

This experiment was funded by a Natural Sciences and Engineering Research Council of Canada Discovery Grant (No. RGPIN-2014-06676) and a Northern Ontario Heritage Fund Corporation Grant to JMC.

We thank Erika Ruddick and Zach Root for their assistance with data collection. We also thank Medicor Research Inc. (in particular, Barb Ward) for providing testing space and subject recruitment and Algonquin Pharmasave for preparing the Androgel and placebo gels.

The authors report no biomedical financial interests or potential conflicts of interest.

ARTICLE INFORMATION

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Received April 7, 2016; revised May 31, 2016, accepted June 1, 2016.

Supplementary material cited in this article is available online at http://dx.doi.org/10.1016/j.biopsych.2016.06.009.

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