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The Relationship of Testosterone and 5-HT to Aggressive, Self-Aggressive, and Antisocial Behavior in Men

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THE RELATIONSHIP OF TESTOSTERONE AND 5-HT TO AGGRESSIVE, SELF-AGGRESSIVE, AND ANTISOCIAL BEHAVIOR IN MEN

by

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ABSTRACT

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Studies of humans show an inconsistent relationship between aggression and T, as well as between T and antisocial and self-aggressive behavior. Other biological variables, including cortisol and brain serotonin, have been implicated as having an effect on the regulation of antisocial and self-aggressive behavior. Researchers have suggested that inconsistencies in the T-aggression relation may be due to the presence of moderating variables. One theory posits that serotonin moderates the relation between T and aggression. The purpose of this study was to examine the relationship between T (as well as cortisol and 5-HT) and aggression-related constructs. A second purpose was to determine if 5-HT functioning moderates the relation between T and aggression and related constructs. Participants for the current study were derived from two archival datasets. Participants (N = 98) who completed the Life History of Aggression semi-structured interview were also administered placebo or paroxetine. Cortisol, free and total testosterone, and 5-HT activity were measured by assaying serum samples via venipuncture at four time points. Results showed that cortisol was negatively correlated with antisocial behavior and that blunted cortisol response (i.e., decreased 5-HT activity) predicted increased aggressive behavior, both of which were consistent with expectations.

However, results also showed that increased aggressive and antisocial behavior predicted lower total testosterone levels, which was contrary to hypotheses. No moderating effects for 5-HT were found. The implications and limitations of the current study are discussed. Suggestions for future research are also noted.

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CHAPTER I

INTRODUCTION AND REVIEW OF RELATED LITERATURE

Aggressive, self-aggressive, and antisocial behaviors are associated with a wide range of negative consequences, including incarceration, interference with interpersonal relationships, and harm to oneself or others (Bradshaw, Rodgers, Ghandour, & Garborino, 2009; Gradinger, Strohmeier, & Spiel, 2009; Horwitz, Santiago, Pearson, & Larussa-Trott, 2009; McAndrew, 2009). However, the biological underpinnings of these behaviors are both complex and poorly understood. Among the variables implicated in aggression and related behaviors, testosterone (T) has played a prominent role, though the empirical findings for this relationship have been mixed. The purpose of this study is to examine the role of T in human aggression and related behaviors, and to examine the potential moderating effects of another biological variable (brain serotonin) that has been implicated in human aggression.

Animal Models of Testosterone and Aggression

The relationship between testosterone and aggression has long been of interest to researchers and clinicians. One of the leading biological theories suggests that testosterone, a type of androgen and sex steroid, is positively correlated with aggression (for a review, see Archer, Graham-Kevan, & Davies, 2005). Experimental studies using lower animal species have provided strong evidence for a link between T and aggression in non-humans. For example, Farrell and McGinnis (2003) examined the relationship between testosterone and aggression in peripubertal male rats that were injected with anabolic androgen steroid (AAS; a testosterone derivative) by observing the number of attacks, threats, mounts, and dominance postures that were displayed toward opponent

rats. Peripubertal rats injected with AAS showed a significantly elevated level of aggression relative to controls, but only when rats were placed in an opponent's cage (Farrell & McGinnis, 2003).

Salas-Ramirez, Montalto, and Sisk (2008) conducted a similar study that examined the relationship between testosterone and aggressive/dominant behaviors in adolescent and adult male Syrian hamsters. Aggressive/dominance behaviors were defined as the sum of flank marking (i.e., rubbing the flank gland against the wall of his home cage, which serves to communicate dominance status), total contact time with an opponent (e.g., length of time the subject approached the intruder and showed interest by sniffing), as well as total attacks, bites, and offensive posturing (Salas-Ramirez et al., 2008). In this study, AAS-injected adolescents showed significantly higher levels of aggressive behaviors relative to controls, especially in the form of attacking opponents (Salas-Ramirez et al., 2008). By contrast, AAS-injected adults did not display significantly higher levels of aggression (Salas-Ramirez et al., 2008). According to their results, the elevated levels of aggression observed in the AAS-injected adolescents are perhaps indicative of either "hyper-responsivity to steroids" or of a "relative lack of inhibition of the underlying neural circuits at this stage of development" (Salas-Ramirez et al., 2008, p. 383). Thus, adolescent male hamsters may be less able to inhibit socially aggressive behavior compared to adult male hamsters, particularly after testosterone exposure (Salas-Ramirez et al., 2008). A third study, which also used a sample of male Syrian hamsters, replicated these findings (Salas-Ramirez, Montalto, & Sisk, 2010). Specifically, Salas-Ramirez et al. (2010) compared the effects of AAS exposure during adolescence and adulthood. Aggressive behaviors were again defined by flank marking,

total contact time, attacks, bites, and offensive posturing (Salas-Ramirez et al., 2010). Results indicated that AAS treatment significantly increased the number of attacks and number of bites against opponent hamsters in both adolescent and adult hamsters (Salas-Ramirez et al., 2010). Furthermore, males exposed to AAS during adolescence displayed significantly more attacks and bites relative to males exposed to AAS during adulthood (Salas-Ramirez et al., 2010). Taken together, these animal studies support the notion that adolescence is a hormonally sensitive period of development, and exposure to AAS during this stage of life can have differential effects on male aggressive behaviors during social interactions (Salas-Ramirez et al., 2008; Salas-Ramirez et al., 2010; Farrell & McGinnis, 2003).

Testosterone, Aggression, and Potential Moderators

Animal models of the relationship between testosterone and aggression have helped researchers and clinicians understand this relationship in humans. Accordingly, it has been shown that human males also experience a hormonally sensitive period during adolescence (for a review, see Lumia & McGinnis, 2010; Sato, Schulz, Sisk, & Wood, 2008). For example, young men who expose themselves to AAS (to gain body mass and strength and/or to enhance physical appearance) during adolescence are at risk of disrupting brain development that involves the learning of socially appropriate behaviors during social interactions, comparable to the disruptive effects of AAS shown in non-human animals (Lumia & McGinnis, 2010).

Although a positive relationship between testosterone and aggression has been well-established in non-human animals, studies using human samples have been relatively inconsistent (e.g., Archer et al., 2005; Book, Starzyk, & Quinsey, 2001). For

example, a meta-analysis conducted by Book et al. (2001), which included samples of both clinical and nonclinical human males, found a weak positive relationship between testosterone and aggression. More specifically, Book et al. (2001) concluded that the association between testosterone and aggression was highest among males aged 13-21, which they contributed to the increased mating efforts during puberty. By contrast, Archer et al. (2005) reanalyzed Book et al.'s findings but did not report the same results. Specifically, Archer et al. (2005) found a weaker positive relationship between testosterone and aggression, albeit still significant. Moreover, Archer et al.'s reanalysis did not show a significantly higher correlation between testosterone and aggression in males aged 13-21. Instead, their findings showed that the correlation between testosterone and aggression was higher in the 22-35 age category relative to the 13-21 and over-35 age categories (Archer et al., 2005). Thus, Archer et al.'s reanalysis did not support the link between a rise in testosterone during puberty and aggression in men. Other studies (e.g., Inoff-Germaine, Arnold, Nottelmann, Susman, Cutler, & Chrousos, 1988) have found no relationship between testosterone and aggression in adolescent males.

Results from studies linking testosterone and aggression in clinical male samples have also been inconsistent (Brooks & Reddon, 1996; Coccaro, Beresford, Minar, Kaskow, & Gerocioti, 2007; Popma et al., 2007). Popma et al. (2007) hypothesized that this inconsistency in human subjects may be in part due to moderating factors such as cortisol, which is the steroid hormone hydrocortisone that is commonly referred to as the stress hormone, as it is secreted during anxiety-provoking situations (e.g., Hanson & Chen, 2010). Therefore, Popma et al. (2007) examined cortisol as a potential moderator

to the relationship between testosterone, which was assessed using saliva samples, and two subtypes of aggression (overt/covert) in delinquent male adolescents. In this study, overt aggression, which was defined as "feeling angry and displaying verbal and/or physical aggression," and covert aggression, which was defined as "feeling angry without expressing it openly" were assessed (Popma et al., 2007, p. 407). According to their results, there was no relationship between testosterone and aggression (Popma et al., 2007). However, their results indicated a significant interaction between cortisol and testosterone as it relates to overt aggression, with a significant positive relationship between testosterone and overt aggression in subjects with low cortisol levels (Popma et al., 2007). Their results suggest that other moderating factors not taken into account in previous studies may contribute to the inconsistent results in the current literature (Popma et al., 2007).

Along with certain hormones, personality variables may also moderate the relationship between testosterone and aggression (Berman, Gladue, & Taylor, 1993). To illustrate, Berman et al. (1993) used a male sample to examine whether there was a significant relationship between testosterone and overt aggressive behavior. Furthermore, they were interested in whether Type A behavior pattern (TABP) had a moderating effect on the relationship between testosterone and overt aggression (Berman et al., 1993). In this study, aggression was assessed using a behavioral measure of overt aggression. Specifically, aggression was defined as the level of shock the subject was willing to set for a fictitious opponent during a competitive reaction-time task (Berman et al., 1993). Their results provided strong evidence that a positive relationship between testosterone and aggression exists in men. Furthermore, their results provided some support for a

moderating effect of TABP on the relationship between testosterone and aggression (Berman et al., 1993).

Other studies have examined how biological variables, such as neurotransmitters, affect the relationship between testosterone and aggression. For example, one theory suggests the neurotransmitter serotonin (5-HT) has a moderating effect on the relationship between testosterone and aggression (e.g., Berman, McCloskey, Fanning, Schumaker, & Coccaro, 2009; Keleta, Lumia, Anderson, & McGinnis, 2007). It is well-established that serotonin plays an important role in the regulation of impulsivity and inhibitory responses (Witte et al., 2009). Thus, researchers believe that serotonin may have a significant impact on the ability of humans and nonhuman animals to inhibit aggressive behavior, especially when exposed to increased levels of testosterone (Witte et al., 2009). Animal studies examining serotonin as it relates to testosterone and aggression have provided evidence supporting this theory (Higley, Mehlman, Poland, & Taub, 1996; Keleta et al., 2007). To illustrate, Higley et al. (1996) used adolescent male rhesus macaques to examine serotonin as a moderator to the testosterone-aggression relationship. Their findings showed that macaques with low serotonin levels exhibited high rates of aggression (Higley et al., 1996). Furthermore, macaques that possessed both low serotonin levels and high testosterone levels showed significantly higher rates and intensity of aggression relative to macaques with (a) low serotonin levels and normal testosterone levels, or (b) normal serotonin levels and high testosterone levels (Higley et al., 1996). This study provides evidence that serotonin acts a moderator to the testosterone-aggression relationship (Higley et al., 1996).

Another animal study conducted by Keleta et al. (2007) explored the behavioral effects of low serotonin in male rats. In this study, rats were assigned to one of three treatment conditions: (a) parachlorophylalanine (PCPA) treatment (a drug used to deplete serotonin in the brain), (b) testosterone treatment, or (c) PCPA + testosterone treatment (Keleta et al., 2007). Their findings provided further evidence that serotonin moderates the relationship between testosterone and aggression in non-human animals (Keleta et al., 2007). Specifically, their results showed that PCPA was not positively correlated with aggression; however, rats in the testosterone condition displayed more aggression than rats in the PCPA condition (Keleta et al., 2007). Most relevantly, their results indicated that rats in the PCPA + testosterone condition displayed a significant increase in aggression (particularly in response to physical provocation) relative to the other treatment conditions (Keleta et al., 2007). This finding suggests that the interaction between increased testosterone and decreased serotonin has significant effects on other-directed aggression (i.e., overt aggressive behavior that is not directed at the self), especially when provoked by a competitor (Keleta et al., 2007).

To explore the theory that serotonin moderates aggression in humans, Berman et al. (2009) recruited aggressive (+AG) and non-aggressive (-AG) individuals who were randomly assigned to receive either an inert placebo (lactose) or 40 mg of paroxetine (Paxil®), a selective serotonin reuptake inhibitor (SSRI) that acutely increases 5-HT activity. Aggressive individuals were grouped according to their score on the Aggression Scale (AG) of the Life History of Aggression inventory (LHA; Coccaro, Berman, & Kouvassi, 1997). In this study, participants were intentionally provoked by a fictitious opponent during a competitive reaction-time task (i.e., Taylor Aggression Paradigm;

TAP; Taylor, 1967). According to their results, +AG individuals who received placebo displayed significantly higher levels of aggression towards their opponent relative to +AG individuals who received paroxetine. Moreover, +AG individuals in the paroxetine condition showed similar levels of aggression towards their opponent as –AG individuals in the paroxetine condition. Thus, +AG showed a reduced response to provocation during the TAP if they received paroxetine (Berman et al., 2009). Berman et al.'s (2009) findings suggest that acutely increasing 5-HT activity results in a significant reduction in other-directed aggression following provocation (Berman et al., 2009). These results were essentially replicated in another study by McCloskey and colleagues, which was designed to study the separate and interactive effects of alcohol and serotonin augmentation on aggression (McCloskey, Berman, Echevarria, & Coccaro, 2009a). In McCloskey et al. (2009a), 20 mg of paroxetine seemed to reduce aggression in men, and alcohol increased aggression. However, these effects appeared to be independent of each other. Although not directly tested, the findings are not inconsistent with the notion that 5-HT may serve as a potential biological moderator in the relationship between testosterone and aggression (McCloskey et al., 2009a). As part of both studies, testosterone levels were measured by assaying serum samples via venipuncture. However, these T data were not reported in the study but will serve as part of the dataset in the current investigation.

Antisocial Behavior

As mentioned previously, cortisol is believed to play a role in aggressive behavior in humans (Popma et al., 2007). Specifically, cortisol appears to be negatively associated with aggression (Popma et al., 2007). This relationship has been especially implicated in

men (Poustka et al., 2010). Despite the growing literature involving the relation between cortisol and aggression, other research findings suggest that cortisol may be an underlying biological mechanism in the display of antisocial (Haltigan, Roisman, Susman, Barnett-Walker, & Monahan, 2011) and delinquent (Poustka et al., 2010) behavior, particularly in adolescent men. For example, Haltigan et al.'s (2011) findings suggest that plasma cortisol levels are significantly negatively correlated with antisocial behavior in adolescent men. Interestingly, though, Poustka et al. (2010) reported that callous, unemotional personality traits, which are typically associated with antisocial behavior (American Psychiatric Association, 2000), were not related to cortisol levels in adolescent men. Instead, they found that general externalizing problems (e.g., overt aggressive and delinquent behavior) and impulsivity were significantly negatively correlated with plasma cortisol levels. These findings suggest that the callous, unemotional traits that are often associated with antisocial behavior may not influence the relationship between antisocial behavior and cortisol levels. Externalizing behaviors caused by impulsive traits may instead play a significant role in this relationship (Poustka et al., 2010).

Along with cortisol, a growing body of research has implicated testosterone as having a role in the development of antisocial behavior. Specifically, there is some evidence that elevated testosterone levels predispose individuals to the display of antisocial behavior (van Honk & Schutter, 2007). It has been shown, for example, that the rise in testosterone during pubertal development is related to increased antisocial behaviors, particularly nonaggressive behaviors (i.e., not involving physical aggression), and social dominance in peer groups (Rowe, Maughan, Worthman, Costello, & Angold,

2004). One theory posits that testosterone reduces the ability to recognize and process specific social cues (van Honk & Schutter, 2007). According to van Honk and Shutter (2007), when individuals with lower testosterone levels view fearful or angry facial expressions, empathic feelings are elicited in the viewer, thereby decreasing the likelihood that the viewer will violate the rights of the displayer. However, they found that individuals with high testosterone levels have reduced ability to consciously recognize these types of facial expressions, thus bypassing the elicitation of empathic feelings and thereby increasing the likelihood of violating the rights of the displayers (van Honk & Schutter, 2007).

As noted previously, serotonin is believed to play a role in the ability to inhibit aggressive impulses (Witte et al., 2009). Given that aggressive behavior often overlaps with antisocial behavior (e.g., frequent physical fighting with others; American Psychiatric Association, 2000), it follows that serotonin is believed to also play a role in the ability to inhibit antisocial behavior (LeMarquand et al., 1997). Behavioral disinhibition, or the lack of behavioral inhibition, often results in a disregard for social norms as well as the consequences involved with certain behaviors (e.g., theft), leading to increased recklessness, impulsivity, and aggression (American Psychiatric Association, 2000; LeMarquand et al., 1997). Behavioral disinhibition is one of the primary descriptors for individuals with antisocial personality features (American Psychiatric Association, 2000; LeMarquand et al., 1997). It follows, then, that decreased serotonin levels may contribute to the expression of behavioral disinhibition during displays of antisocial behavior (LeMarquand et al., 1997). Indeed, it has been shown that serotonin depletion results in increased antisocial behavior in men (e.g., LeMarquand et al., 1997).

To demonstrate, LeMarquand et al. (1997) examined the effects of the depletion of the amino acid tryptophan, which is a precursor in the synthesization of serotonin (i.e., tryptophan must be present for serotonin to be produced in the central nervous system), in a sample of adolescent and young adult men. Behavioral disinhibition was assessed using a behavioral task (go/no-go task) approximately 6 hours following consumption of a tryptophan-depleting acid mixture (LeMarquand et al., 1997). Their results supported the hypothesis that decreased serotonergic functioning leads to an increase in behavioral disinhibition (LeMarquand et al., 1997), which is consistent with the notion that decreased serotonin contributes to an increase in antisocial behavior.

Self-Aggressive Behavior

Despite the growing literature dedicated to examining cortisol as it relates to aggression and antisocial behavior there are relatively few studies investigating cortisol as it relates to self-injurious behavior, the definitions of which vary among the literature. For the purpose of this study, self-injurious behavior is defined as intentional and direct injury to oneself that produces tissue damage (ranging from minor to severe) that may or may not involve suicidal intent (Bornovalova, Tull, Gratz, Levy, & Lejuez, 2011; Coccaro et al., 1997). One study (Mcardle, 2004) examined cortisol as a potential underlying mechanism in adolescent men and women who self-injure. Specifically, cortisol response to an interpersonal stressor was examined to determine hypothalamic-pituitary adrenal (HPA) axis reactivity to stress and its relation to self-aggressive behavior (Mcardle, 2004). According to Mcardle's (2004) findings, women showed a positive relation between self-injurious behavior and cortisol, but men did not show such a relation. This is perhaps because self-injurious behavior in men is related to different

underlying processes (Mcardle, 2004). Because of the limited studies examining cortisol and self-injurious behavior in men, more studies are needed to clarify these processes.

Although a relatively large body of literature exists regarding the neurobiology of antisocial and aggressive behavior in men, there are currently no known studies examining the contribution of testosterone or serotonin to predicting self-aggressive behavior specifically in men. However, a relatively limited body of research suggests that decreased levels of serotonin enhance self-aggressive behavior in studies examining both men and women (McCloskey, Ben-Zeev, Lee, Berman, & Coccaro, 2009b). For example, McCloskey et al. (2009b) reported that serotonin depletion enhances self-injurious behavior in both healthy adults and adults with a diagnosis of intermittent explosive disorder (IED; American Psychiatric Association, 2000). This finding follows the notion that decreased serotonin levels are associated with decreased ability to inhibit impulsive aggressive urges (Witte et al., 2009). However, given that self-aggressive behavior in men appears to involve different biological processes than self-aggressive behavior in women (Mcardle, 2004), more research is needed to fully understand the neurobiological underpinnings of self-aggression in men.

Aggression, Antisocial Behavior, and Self-Aggression

Aggression, antisocial behavior, and self-aggression are defined differently throughout the extant literature. However, they appear to be related constructs. For example, the construct of self-aggressive behavior is subsumed under the construct of aggressive behavior, as self-aggression involves acting aggressively (Bornovalova et al., 2011). Moreover, antisocial behavior consists of both other-directed aggressive (e.g., frequent physical assaults) and nonaggressive (e.g., manipulating or deceiving others

frequently) behavior (American Psychiatric Association, 2000). Unfortunately, the relation between antisocial behavior and self-aggressive behavior is less clear. One study used an adolescent sample to examine the relation between exposure to violence (i.e., aggressive antisocial behavior) during childhood and adolescence and self-aggressive and suicidal behavior (Vermeiren, Ruchkin, Leckman, Deboutte, & Schwab-Stone, 2002). Their results indicated that exposure to violence is positively associated with self-aggressive behavior and suicide risk (Vermeiren et al., 2002). Furthermore, they found that the display of aggressive antisocial behavior (e.g., vandalism, assault) predicts the relation between exposure to violence and self-aggressive behavior in boys but not girls. Specifically, the display of aggressive antisocial behavior predicts a positive association between rates of exposure to violence and rates of self-aggressive acts (Vermeiren et al., 2002). Taken together, the research suggests that aggressive, antisocial, and self-aggressive behaviors are related constructs.

Rationale for the Current Investigation

The first purpose of this study was to attempt to reduce current inconsistencies in the literature regarding the relationship between T and aggression by examining both free and total testosterone and several constructs related to aggression (other-directed aggression, self-aggression, and antisocial behavior) in men.

A second purpose for this study involves examining both free and total testosterone levels. Free testosterone is termed “free” because it is not bound to proteins in the bloodstream (Nazian, 1986). Free testosterone circulates in a free, or unbound, state, which allows it to be biologically active, or bioavailable (Nazian, 1986). By contrast, total testosterone is the sum of free testosterone and protein-bound (i.e.,

biologically inactive) testosterone (Nazian, 1986). Thus, total testosterone levels are generally much higher than free testosterone levels; however, free testosterone levels show more biological activity (Nazian, 1986). The current study sought to examine whether free and total testosterone have differential associations with the behavioral measures. In doing so, we could provide new information for future studies regarding the value of using free testosterone versus total testosterone when examining their effect(s) on aggressive, self-aggressive, and/or antisocial behavior. Because total testosterone levels are significantly higher (Nazian, 1986), it is expected that total testosterone will produce more positive results than free testosterone in the current study.

A final purpose of this study was to examine cortisol as it relates to aggression and related constructs. As mentioned previously, cortisol is the steroid hormone hydrocortisone that is produced by the adrenal gland and secreted during times of autonomic arousal, such as when a normal-functioning individual gives a public presentation (Popma et al., 2006). Currently, cortisol's effects on aggressive and antisocial behavior are better understood relative to its effects on self-aggression. A positive association between cortisol and self-aggressive behavior has been reported in women; however, these findings are not well-replicated in men (Mcardle, 2004). Furthermore, a negative association between cortisol and aggressive (Yang, Shin, Noh, & Stein, 2007) and antisocial (Popma et al., 2006) behavior has been reported in men, but inconsistencies in this area remain. Given that cortisol has been implicated as affecting the presentation of aggressive, self-aggressive, and antisocial behavior, the current study conducted exploratory analyses using the available cortisol data in an effort to extend the current literature.

Hypotheses

We predicted a positive correlation between: (a) both baseline free and total testosterone and life history of aggression, (b) both baseline free and total testosterone and life history of self-aggression, and (c) both baseline free and total testosterone and life history of antisocial behavior. Exploratory analyses were conducted to examine the relation between cortisol and the behavioral measures. No specific hypotheses were offered, but based on the literature reviewed, it is reasonable to expect that cortisol would be negatively correlated with life history of aggression and antisocial behavior (that is, lower stress levels would be associated with higher rates of other-directed aggressive behavior and antisocial behavior), but positively correlated with life history of self-aggression. Further exploratory analyses were conducted to examine whether life history of aggressive, self-aggressive, and antisocial behavior were related constructs. Based on the literature, we expected that the LHA subscales would be positively related to each other.

We also predicted that aggression, self-aggression, and antisocial behavior would be inversely associated with serotonin levels and positively associated with free and total T levels in a smaller sample that included cortisol response to paroxetine as a measure of 5-HT activity, but that these main effects would be limited by the interaction between T and 5-HT. Thus, it was expected that serotonin activity (as assessed by cortisol response to paroxetine) would moderate the relation between free and total testosterone and life history of aggression, self-aggression, and antisocial behavior. Exploratory analyses were conducted to examine the correlation between serotonin activity and the behavioral measures. No specific hypotheses were offered, but based on the literature reviewed, it is

reasonable to expect that serotonin activity would be negatively correlated with life history of aggression, self-aggression, and antisocial behavior.

CHAPTER II

METHODOLOGY

Participants

Participants were derived from datasets used to examine the neurobiology of aggression for which data on T have not yet been reported (Berman et al., 2009 and McCloskey et al., 2009a). Berman et al. (2009) oversampled aggressive individuals (i.e., LHA AG scores > 11) using both advertisements for "healthy volunteers" and for people with "a short fuse who sometimes feel out of control" (Berman et al., 2009, p. 715). McCloskey et al. (2009a) used community postings to recruit "healthy men aged 21 years and older for a research project being conducted to study the effects of alcohol on motor skills" (McCloskey et al., 2009a, p. 3). Although women were included in Berman et al. (2009), they were excluded from the current subject pool, as examining women was beyond the scope of the current investigation due to (a) generally low levels of serum T and lower life history of aggression scores compared to men, and (b) women represented a proportionally small number of participants across the two datasets.

Two different samples, each consisting of participants from both studies, were used for separate sets of analyses (see *Baseline Sample* and *Pharmacochallenge Sample* sections) to test the proposed hypotheses. Specifically, the data for the current study were derived from archival datasets. One study was part of a National Institutes of Health (NIH) R29 funded project on serotonin and aggression (Berman et al., 2009). This study involved the administration of either 40 mg Paxil® or placebo in 80 men and women. Individuals with elevated life histories of aggression were oversampled in this study.

Baseline biological data relevant for the current project were available for 42 male participants.

The second study was funded by the Alcoholic Beverage Medical Research Foundation (ABMRF) to study the separate and combined effects of alcohol and Paxil® (McCloskey et al., 2009a) on aggression. The ABMRF study recruited men only (*N* = 56), and self-reported aggression was assessed using the same measures as Berman et al. (2009). Individuals with elevated life histories of aggression were not oversampled in this study. This study involved the administration of 20 mg Paxil® or placebo crossed with alcohol or no alcohol. Thus, participants were in one of four possible drink-drug conditions. Because alcohol is not of interest in this study (and could affect cortisol and T levels), the cases in the ABMRF study who received alcohol (*n* = 31) were used only in the baseline T and cortisol analyses described below. For the analyses examining the role of 5-HT (using cortisol response to paroxetine as an index of 5-HT activity), only cases who received paroxetine (but not alcohol) were included (*n* = 13).

Exclusionary criteria for both studies included current major depression; life history of bipolar disorder, psychosis, or substance dependence; a medical reason not to take paroxetine; and a positive alcohol or toxicological screen (opiates, THC, methamphetamine, benzodiazepine, and cocaine) at the time of the study. Volunteers who abstained from alcohol use, were currently taking psychotropic medication, and/or had a history of hepatic, neurological, or other significant medical condition(s) were also excluded. Trained graduate-level students administered the Structured Clinical Interview for the *Diagnostic and Statistical Manual of Mental Disorders*, fourth edition, text revision (DSM-IV-TR; American Psychiatric Association, 2000) to each participant,

which was used to assign DSM-IV-TR psychiatric diagnoses (SCID; First, Gibbon, Spitzer, & Williams, 1998). Participants were required to abstain from alcohol for 48 hours before the experimental session and to refrain from taking any medication for the 7 days leading up to the session. Most participants were never married (89% in McCloskey et al.; 75.6% in Berman et al.). Median income was in the $10,000 to $12,499 range for all participants. Following is a summary of the characteristics for the subsamples.

Baseline Sample

Participants in Baseline Sample were 98 men ages 18 to 48 (M = 23.91, SD = 5.23). Racial composition of this subsample was 79.6% Caucasian, 16.3% African American, 2% Hispanic, 1% Asian, and 1% "other." Baseline Sample consisted of 42 men from Berman et al. (2009) and 56 men from McCloskey et al. (2009a).

Pharmacochallenge Sample

Participants in Pharmacochallenge Sample were 34 men ages 18 to 41 (M = 24.62, SD = 6.32). Racial composition of this subsample was 67.6% Caucasian, 26.5% African American, 2.9% Asian, and 2.9% Hispanic. Pharmacochallenge Sample consisted of 21 men from Berman et al. (2009) and 13 men from McCloskey et al. (2009a).

Written informed consent was obtained from all participants. The procedures used in both studies were reviewed by the Institutional Review Board for the Protection of Human Subjects at The University of Southern Mississippi. Participants in both studies received $10 per hour as compensation.

Aggression Measure

Life History of Aggression (LHA; Coccaro et al., 1997)

The LHA is an 11-item semi-structured interview designed to assess the frequency of aggressive, self-aggressive, and antisocial behavior since age 13. Items are rated on a five-point scale based on the number of occurrences of the behavior (0 = *no occurrences*; 1 = *one event*; 2 = *two or three events*; 3 = *four to nine events*; 4 = *10 or more events*; 5 = *more events than can be counted*). The LHA consists of three subscales: the Aggression (AG) subscale, the Self-Aggression (SA) subscale, and the Antisocial Behaviors (AB) subscale. To obtain the total LHA score, the three subscales are summed.

The AG subscale was used to assess history of other-directed aggressive behavior. The AG subscale consists of five items: (a) verbal aggression, (b) aggression toward objects or animals, (c) physical fighting, (d) physical assaults against people, and (e) temper tantrums. The Self-Aggression (SA) is a 2-item subscale that was used to assess history of self-aggressive behavior. Items on the SA subscale are: (a) self-injurious behavior, and (b) suicide attempts. The AB was used to assess history of antisocial behavior, and it consists of four items: (a) school disciplinary problems, (b) problems with vocational supervisors (e.g., firings), (c) antisocial behavior not involving the police (e.g., selling drugs, driving under the influence of drugs and/or alcohol), and (d) antisocial behavior involving the police (e.g., being arrested or convicted).

Coccaro et al. (1997) demonstrated that the AG subscale has shown good interrater agreement (intraclass correlation = .94), internal consistency ($\alpha = .87$), and test-retest reliability ($r > .80$). The AB subscale has demonstrated good interrater agreement (intraclass correlation = .88) and test-retest reliability ($r > .89$), and adequate internal

consistency (α = .74). The SA subscale has shown good interrater agreement (intraclass correlation = .84) and test-retest reliability (*r* = .97). The SA subscale has shown less than adequate internal consistency (α = .48), presumably because relatively few items comprise this subscale and the majority of non-clinical respondents do not report self-aggressive behavior (Coccaro et al., 1997).

Procedures

Paroxetine Manipulation

Participants were randomly assigned to receive either an inert placebo (lactose) or 20 mg (McCloskey et al., 2009a) or 40 mg (Berman et al., 2009) of paroxetine (Paxil®), administered in capsule form. Paroxetine, which is characterized as a selective serotonin reuptake inhibitor (SSRI), rapidly increases 5-HT concentrations in serotonergic synapses (Schatzberg & Nemeroff, 2001). In healthy individuals, administration of paroxetine stimulates the hypothalamus (via central 5-HT), which in turn elevates cortisol levels within 1 hour following administration (Kojima et al., 2003). However, it has been shown that aggressive individuals exhibit a blunted cortisol response to serotonergic agents (Berman et al., 1997; Siever, 2008). In an effort to extend these findings cortisol response to paroxetine was examined to determine the contribution of serotonin to predicting aggressive, self-aggressive, and antisocial behavior. This method of examining cortisol response to serotonin agonists has shown to be a reliable way to examine serotonin activity (Kuepper et al., 2010).

Measurement of Biological Variables

Cortisol (μg/dL), free testosterone (ng/dL), and total testosterone (ng/dL) levels were examined by assaying serum samples via venipuncture at four time points (baseline,

and 1, 3, and 5 hours following placebo or paroxetine administration) using a direct competitive chemiluminescent immunoassay procedure (Chiron Diagnostic ACS: 180, Bayer HealthCare LLC Diagnostic Division, New York, NY). Given that paroxetine affects cortisol levels within 1 hour following administration (Kojima et al., 2003), cortisol response to paroxetine was determined by subtracting the Time 2 cortisol measurement (1 hour post-paroxetine administration) from the baseline cortisol measurement (i.e., Time 1). Blunted cortisol response, as indicated by a higher total after subtracting the Time 2 cortisol measurement from the baseline cortisol measurement, indicated low serotonin levels prior to paroxetine administration. Increased cortisol response, as indicated by a lower total after subtracting the Time 2 cortisol measurement from the baseline cortisol measurement, indicated normal serotonin levels prior to paroxetine administration.

In both datasets, both cortisol and testosterone (free and total) sample collection was conducted once before, and then three times following, capsule administration. As mentioned previously, the dose of Paxil® administered in each study was different. However, we did not examine dose response for several reasons. First, the difference in cortisol response between 20 mg and 40 mg Paxil® is not significant (Kojima et al., 2003). Additionally, separating the studies to examine the differential effects of 20 mg and 40 mg Paxil® would substantially reduce the sample size used for each analysis, significantly reducing power.

Laboratory Procedure

Participants made two visits to the lab, scheduled 1 to 4 weeks apart. During the first visit, trained graduate-level diagnostic raters administered the clinical interview,

which included the SCID, LHA, and demographic information. During the second visit, participants were randomly assigned to either a paroxetine or placebo condition. Toxicological screening was followed by the capsule administration (paroxetine or placebo). Blood samples were obtained via venipuncture at baseline (just before the capsule was administered) and 1, 3, and 5 hours later.

CHAPTER III

RESULTS

Baseline Sample

Recall that pharmacological manipulations occurred after baseline, which could confound the relationship between testosterone and cortisol. Thus, for the first set of analyses we used baseline measurements of total T (ng/dL), free T (ng/dL), and cortisol (μ/dL), which allowed us to use all cases of men from the two studies (N = 98) to maximize power to examine the direct effects of these biological variables on aggression and related constructs (assessed using the three subscales of the LHA: AG, SA, and AB). Bivariate analyses revealed no significant correlations between age or race and baseline total T, baseline free T, baseline cortisol, or the LHA subscales. Descriptive statistics for this subsample are presented in Table 1.

Table 1

Baseline Sample: Descriptive Statistics

	N	Min.	Max.	Mean	Std. Dev.	Skewness (SE)		Kurtosis (SE)	
LHA AG	98	0.0	22.00	8.63	5.14	.58	.24	-.18	.48
LHA SA	98	0.0	4.00	.13	.60	4.83	.24	24.09	.48
LHA AB	98	0.0	12.00	2.70	2.81	1.15	.24	1.06	.48
Baseline Cort	98	7.10	27.60	17.48	4.52	.06	.24	-.51	.48
Baseline Total T	98	185.47	1156.26	637.51	200.96	.25	.24	-.14	.48
Baseline Free T	98	11.50	46.90	22.06	6.13	1.17	.24	2.52	.48

Note. LHA AG, LHA SA, and LHA AB represent the Aggression, Self-Aggression, and Antisocial Behaviors subscales, respectively, of the Life History of Aggression semi-structured interview. Baseline Cort (μg/dL), Baseline Total T (ng/dL), and Baseline Free T (ng/dL) represent the measurement of cortisol, total T, and free T, respectively, prior to drug or placebo administration.

Bivariate Pearson correlations were conducted to test the hypotheses that (a) free and total T would be positively correlated with life history of aggressive, self-aggressive, and antisocial behavior, (b) cortisol would be negatively correlated with life history of aggressive and life history of antisocial behavior, but positively correlated with life history of self-aggressive behavior, and (c) each of the LHA subscales would be positively related to each other. As can be seen in the top left-hand quadrant of Table 2, the LHA subscales were significantly and positively related to each other, which was consistent with expectations.

Table 2

Baseline Sample: Two-Tailed Pearson Correlations

Variables	LHA AG	LHA SA	LHA AB	Baseline Cort	Baseline Total T	Baseline Free T
LHA AG	-	.27**	.43***	-.13	-.08	-.07
LHA SA	.27**	-	.27**	-.15	-.18	-.09
LHA AB	.43***	.27**	-	-.23*	-.19	-.04
Baseline Cort	-.14	-.15	-.23*	-	.23*	.33**
Baseline Total T	-.08	-.18	-.19	.23*	-	.68***
Baseline Free T	-.07	-.09	-.04	.33**	.68***	-

Note. LHA AG, LHA SA, and LHA AB represent the Aggression, Self-Aggression, and Antisocial Behaviors subscales, respectively, of the Life History of Aggression semi-structured interview. Baseline Cort (μg/dL), Baseline Total T (ng/dL), and Baseline Free T (ng/dL) represent the measurement of cortisol, total T, and free T, respectively, prior to drug or placebo administration.

* $p < .05$. ** $p < .01$. *** $p < .001$.

Specifically, the LHA AG subscale was positively correlated with the LHA SA subscale, $r = .27$, $p < .01$, and the LHA AB subscale, $r = .43$, $p < .001$. Furthermore, the LHA SA subscale was positively correlated with the LHA AB subscale, $r = .27$, $p < .01$.

The only significant correlation that emerged between the LHA subscales and the biological measures was a negative correlation between cortisol and the LHA AB subscale, $r = -.23$, $p < .05$, indicating that life history of antisocial acts was inversely associated with cortisol levels (see Table 2).

Pharmacochallenge Sample

To test the hypotheses that serotonin activity would moderate the relation between aggression, self-aggression, and antisocial behavior, we examined serotonin functioning (as indicated by cortisol response to paroxetine), testosterone levels (free and total; ng/dL), and the separate and combine effects of T and 5-HT on scores on the LHA subscales. Given that alcohol affects testosterone and cortisol levels (Danel, Vantyghem, & Touitou, 2006; Yap, Mascord, Starmer, & Whitfield, 1993), we only used participants who received paroxetine but not alcohol ($n = 34$). Descriptive statistics for this subsample are presented in Table 3.

Table 3

Pharmacochallenge Sample: Descriptive Statistics

	N	Min.	Max.	Mean	Std. Dev.	Skewness (SE)		Kurtosis (SE)	
LHA AG	34	1.00	22.00	9.24	5.64	.54	.40	-.69	.79
LHA SA	34	.00	4.00	.12	.69	5.83	.40	34.00	.79
LHA AB	34	.00	10.00	2.85	2.75	.80	.40	-.10	.79
Baseline Free T	34	11.5	31.50	20.39	5.14	.54	.40	-.50	.79
Baseline Total T	34	232.45	1019.00	611.39	196.28	.26	.40	-.42	.79
Cortisol Resp	34	-6.50	13.70	3.01	4.82	.05	.40	-.63	.79

Note. LHA AG, LHA SA, and LHA AB represent the Aggression, Self-Aggression, and Antisocial Behaviors subscales, respectively, of the Life History of Aggression semi-structured interview. Baseline Total T (ng/dL) and Baseline Free T (ng/dL) represent the measurement of total T and free T, respectively, prior to drug or placebo administration. Cortisol Resp represents the cortisol response to paroxetine (Time 2 measurement of cortisol subtracted by Time 1 measurement of cortisol).

Note that the mean cortisol response to paroxetine for this subsample was 3.01 (*SD* = 4.82), indicating that the average cortisol response to paroxetine was blunted (i.e., decrease in cortisol following administration of paroxetine).

Bivariate analyses revealed no significant correlations between age and the LHA subscales, baseline total T, baseline free T, or cortisol response. However, race was correlated with the LHA SA subscale, $r = .65$, $p < .001$. None of the Caucasian ($n = 23$), African-American ($n = 9$), or Asian ($n = 1$) men in this subsample endorsed an item on the LHA SA subscale ($M = 0.00$; $SD = 0.00$ for each race). However, one Hispanic man scored a 4 (out of 10) on this subscale, thus contributing to the significant *R.* Note that a

positive relationship between race and LHA SA scores was not found for the larger Baseline Sample, indicating that the results for the smaller sample should be interpreted cautiously. Furthermore, race was not associated with the LHA AG subscale, the LHA AB subscale, baseline total T, baseline free T, cortisol response, or age.

For Pharmacochallenge Sample, bivariate Pearson correlations were conducted to test the hypotheses that (a) free and total T would be positively correlated with life history of aggressive, self-aggressive, and antisocial behavior, and that (b) cortisol response to paroxetine would be negatively correlated with life history of aggressive, self-aggressive, and antisocial behavior. As can be seen in the top left-hand quadrant of Table 4, the LHA subscales were significantly and positively related to each other, which was consistent with expectations. Specifically, the LHA AG subscale was positively correlated with the LHA SA subscale, $r = .40$, $p < .05$, and the LHA AB subscale, $r = .39$, $p < .05$. Furthermore, the LHA SA subscale was positively correlated with the LHA AB subscale, $r = .46$, $p < .01$.

Table 4

Pharmacochallenge Sample: Two-Tailed Pearson Correlations

Variables	LHA AG	LHA SA	LHA AB	Baseline Total T	Baseline Free T	Cortisol Response
LHA AG	-	.40*	.39*	-.33	-.29	.44**
LHA SA	.40*	-	.46**	-.25	-.06	-.09
LHA AB	.39*	.46**	-	-.44**	-.20	.08
Baseline Total T	-.33	-.25	-.44**	-	.61***	-.15

Table 4 (continued).

Variables	LHA AG	LHA SA	LHA AB	Baseline Total T	Baseline Free T	Cortisol Response
Baseline Free T	-.29	-.06	-.20	.61***	-	-.11
Cortisol Response	.44**	-.09	-.08	-.15	-.11	-

Note. LHA AG, LHA SA, and LHA AB represent the Aggression, Self-Aggression, and Antisocial Behaviors subscales, respectively, of the Life History of Aggression semi-structured interview. Baseline Total T (ng/dL) and Baseline Free T (ng/dL) represent the measurement of total T and free T, respectively, prior to drug or placebo administration. Cortisol Response represents the cortisol response to paroxetine (Time 2 measurement of cortisol subtracted by Time 1 measurement of cortisol).

* $p < .05$. ** $p < .01$. *** $p < .001$.

As shown in Table 4, cortisol response to paroxetine was positively correlated with life history of aggression scores, $r = .44$, $p < .01$, indicating that blunted cortisol response is associated with aggressive behavior. Furthermore, LHA AB scores were inversely correlated with total T, $r = -.44$, $p < .01$, indicating that antisocial behavior is associated with decreasing levels of total T. However, this finding should be viewed cautiously given the non-significant *R* in the larger Baseline Sample.

Regression Analyses

Hierarchical multiple regression analyses were used in the second set of analyses to test the hypothesis that serotonin activity would moderate the relation between each of the LHA subscales. Specifically, we examined the unique contributions of serotonin activity (as indicated by cortisol response) and T (baseline total and free T levels) as well as the interaction of 5-HT with each T index in the prediction of aggression, self-aggression, and antisocial behavior. Three separate hierarchical multiple regression

analyses were conducted using LHA AG scores, LHA SA scores, and LHA AB scores as dependent variables. Each analysis involved two blocks (Step 1 through Step 2), with all variables in each block entered simultaneously. We centered the baseline free T levels, baseline total T levels, and cortisol response totals, and we used these centered variables to create the two interaction terms (cortisol response × baseline free T and cortisol response × baseline total T). These variables were centered to avoid multicollinearity and other analytical problems (Yi, 1989).

Prediction of Other-Directed Aggressive Behavior

For the first hierarchical multiple regression analysis, the LHA AG subscale was used as the dependent variable. Cortisol response, baseline total T, and baseline free T were entered as predictors at Step 1. Examination of the beta (β) coefficients in Table 5 shows that baseline total T levels and cortisol response to paroxetine made unique contributions to the prediction of other-directed aggressive behavior at Step 1 ($\Delta R^2 = .36$, $p < .01$). There was a significant main effect for baseline total T ($\beta = -.44$, $t = -2.27$, $p < .05$) at Step 1, with lower baseline total T levels predicting higher levels of other-directed aggression. A significant main effect at Step 1 was also found for cortisol response ($\beta = .51$, $t = 3.35$, $p < .01$), with blunted cortisol responses predicting higher levels of other-directed aggression. The two interaction terms were entered at Step 2 to determine whether other-directed aggression is predicted by an interaction between cortisol response and baseline free T and/or an interaction between cortisol response and baseline total T. As shown in Table 5, Step 2 revealed no significant interactions.

Table 5

Pharmacochallenge Sample: Hierarchical Multiple Regression Analyses Predicting Other-Directed Aggression (AG) Scores

	Prediction of AG scores					
Block/Variable	β	t	p	R	R^2	ΔR^2
Step 1				.60	.36**	.36**
Baseline Total T	-.44*	-2.27	.032			
Baseline Free T	.04	.20	.84			
Cortisol Response	.51**	3.35	.002			
Step 2				.70	.49*	.13*
Baseline Total T	-.57**	-2.93	.007			
Baseline Free T	.26	1.24	.227			
Cortisol Response	.74***	4.50	.000			
Baseline Total T × Cortisol Response	.16	.90	.374			
Baseline Free T × Cortisol Response	.34	1.76	.089			

Note. AG scores are from the Aggression subscale of the Life History of Aggression semi-structured interview. Baseline Total T (ng/dL) and Baseline Free T (ng/dL) represent the measurement of total T and free T, respectively, prior to drug or placebo administration. Cortisol Response represents the cortisol response to paroxetine (Time 2 measurement of cortisol subtracted by Time 1 measurement of cortisol).

* $p < .05$. ** $p < .01$. *** $p < .001$.

However, entering the interaction terms in Step 2 improved the prediction of other-directed aggressive behavior ($\Delta R^2 = .13$, $p < .05$). Baseline total T ($\beta = -.57$,

t = -2.93, p < .01) and cortisol response (β = .74, t = 4.50, p = .000), when considered individually at Step 2, made significant unique contributions to the prediction of other-directed aggression.

Prediction of Self-Aggressive Behavior

For the second hierarchical multiple regression analysis, the LHA SA subscale was used as the dependent variable. Cortisol response, baseline total T, and baseline free T were entered as predictors at Step 1.

Table 6

Pharmacochallenge Sample: Hierarchical Multiple Regression Analyses Predicting Self-Aggressive Behavior (SA) Scores

	Prediction of SA scores					
Block/Variable	β	t	p	R	R^2	ΔR^2
Step 1				.27	.07	.07
Baseline Total T	-.32	-1.40	.173			
Baseline Free T	.13	.58	.567			
Cortisol Response	-.03	-.15	.882			
Step 2				.34	.11	.04
Baseline Total T	-.34	-1.33	.193			
Baseline Free T	.18	.63	.531			
Cortisol Response	.09	.41	.688			
Baseline Total T × Cortisol Response	.19	.83	.414			

Table 6 (continued).

	Prediction of SA scores					
Block/Variable	*β*	*t*	*p*	*R*	R^2	ΔR^2
Baseline Free T × Cortisol Response	.06	.22	.824			

Note. SA scores are from the Self-Aggression subscale of the Life History of Aggression semi-structured interview. Baseline Total T (ng/dL) and Baseline Free T (ng/dL) represent the measurement of total T and free T, respectively, prior to drug or placebo administration. Cortisol Response represents the cortisol response to paroxetine (Time 2 measurement of cortisol subtracted by Time 1 measurement of cortisol).

Examination of the beta coefficients in Table 6 shows that these variables did not contribute to the prediction of self-aggressive behavior at Step 1 ($\Delta R^2 = .07$, $p = .504$). The two interaction terms were entered at Step 2 to determine whether self-aggressive behavior is predicted by an interaction between cortisol response and baseline free T and/or an interaction between cortisol response and baseline total T. Entering the interaction terms at Step 2 did not improve the prediction of self-aggressive behavior ($\Delta R^2 = .04$, $p = .549$). Baseline total T, baseline free T, and cortisol, when considered individually at Step 2, did not make unique contributions to self-aggressive behavior.

Prediction of Antisocial Behavior

For the third hierarchical multiple regression analysis, the LHA AB subscale was used as the dependent variable. Cortisol response, baseline total T, and baseline free T were entered as predictors at Step 1. Examination of the beta coefficients in Table 7 reveals that a linear combination of these variables did not predict antisocial behavior at Step 1 ($\Delta R^2 = .20$, $p = .076$). However, there was a significant main effect for baseline

total T (β = -.52, t = -2.40, p < .05) at Step 1, with higher baseline total T levels predicting lower levels of antisocial behavior, which should be viewed cautiously given the non-significant R in the larger Baseline Sample. The two interaction terms were entered at Step 2 to examine whether antisocial behavior is predicted by an interaction between cortisol response and baseline free T and/or an interaction between cortisol response and baseline total T. As revealed in Table 7, there were no significant interactions in Step 2 and entering the interaction terms in Step 2 did not improve the prediction of antisocial behavior (ΔR^2 = .05, p = .406). However, baseline total T, when considered individually at Step 2, made a unique contribution to the prediction of antisocial behavior (β = -.55, t = -2.32, p < .05). Again, this should be viewed cautiously given the non-significant R in Baseline Sample.

Table 7

Pharmacochallenge Sample: Hierarchical Multiple Regression Analyses Predicting Antisocial Behavior (AB) Scores

	Prediction of AB scores					
Block/Variable	β	t	p	R	R^2	ΔR^2
Step 1				.45	.20	.20
Baseline Total T	-.52*	-2.40	.022			
Baseline Free T	.12	.58	.568			
Cortisol Response	.02	.11	.916			
Step 2				.50	.25	.05

Table 7 (continued).

	Prediction of AB scores					
Block/Variable	β	t	p	R	R^2	ΔR^2
Baseline Total T	-.55*	-2.32	.028			
Baseline Free T	.19	.72	.475			
Cortisol Response	.15	.76	.452			
Baseline Total T × Cortisol Response	.21	.96	.346			
Baseline Free T × Cortisol Response	.09	.37	.717			

Note. AB scores are from the Antisocial Behaviors subscale of the Life History of Aggression semi-structured interview. Baseline Total T (ng/dL) and Baseline Free T (ng/dL) represent the measurement of total T and free T, respectively, prior to drug or placebo administration. Cortisol Response represents the cortisol response to paroxetine (Time 2 measurement of cortisol subtracted by Time 1 measurement of cortisol).

CHAPTER IV

DISCUSSION

The main purpose of this study was to examine the relationship between three baseline biological measures (cortisol, total testosterone, and free testosterone) and the AG, SA, and AB subscales of the LHA. Additionally, the current study sought to examine the independent and interactive effects of serotonin activity (as assessed by cortisol response to paroxetine), baseline total testosterone, and baseline free testosterone on the AG, SA, and AB subscales of the LHA.

It was hypothesized that baseline free and baseline total testosterone would be positively correlated with life history of aggression, self-aggression, and antisocial behavior. Furthermore, it was predicted that baseline cortisol would be negatively correlated with life history of aggression and antisocial behavior, but positively correlated with life history of self-aggression. Serotonin activity was hypothesized to moderate the relation between (a) free and total testosterone and life history of aggression, (b) free and total testosterone and life history of self-aggression, and (c) free and total testosterone and life history of antisocial behavior. Specifically, it was predicted that life history of aggression, self-aggression, and antisocial behavior would each be positively associated with an interaction term consisting of decreasing serotonin levels and increasing baseline free and total testosterone levels.

Life History of Aggression

The hypothesis that baseline free and total testosterone would be positively correlated with life history of aggression was not supported. The findings in the extant research with regard to this relation have been mixed (e.g., Archer et al., 2005; Book et

al., 2001). For example, Berman et al. (1993) found a strong positive relation between aggression and testosterone using a male sample. However, Archer et al.'s (2005) reanalysis of a previous meta-analytic study using male samples (Book et al., 2001) found a weak positive relation between these variables. Such inconsistencies may be, as suggested by McAndrew (2009), due to complex interactions between cultural, evolutionary, hormonal, and social/situational variables. According to McAndrew (2009), human aggression cannot be fully understood without considering a relatively wide range of biological and environmental factors. There is a growing body of evidence that a positive correlation between testosterone and aggression in men occurs primarily in a context involving competition with other men and/or involving a challenge to social status (McAndrew, 2009). This is referred to as the "Challenge Hypothesis," which suggests that testosterone levels become elevated in response to threatening environmental cues (e.g., prior to or during an argument with another male; McAndrew, 2009, p. 331; Wingfield, 1985). Thus, elevated testosterone levels do not directly elicit aggression, but instead it is the interaction between testosterone and a challenge to social status that facilitates aggressive behavior (McAndrew, 2009). Accordingly, the relation between testosterone and aggression is much weaker in men when a challenge to achieve high status is not present within that context. The current study did not employ a competition or status challenge task, but instead assessed aggression by inquiring about the frequency of past aggressive behaviors. It is possible that we obtained unexpected results (with regard to the testosterone-aggression relation) by not considering the cultural or situational context in which past aggressive behaviors occurred.

Contrary to expectations, cortisol was not associated with life history of aggression. The former finding is not consistent with previous studies which suggest that decreased cortisol is related to an increase in aggressive behavior (Yang et al., 2007). Some evidence suggests that cortisol plays a protective role in the development of aggressive behavior because, as discussed previously, it is believed to inhibit externalizing behavior problems (Popma et al., 2006; Yang et al., 2007). However, the results of the current study do not support this theory. One explanation for this inconsistency is that moderators not taken into account in previous studies may be influencing the relationship between cortisol and aggression. Illustratively, Shoal, Giancola, and Kirillova (2003) found that low cortisol was independently associated with low self-control and increased aggressive behavior in adolescent men. However, further examination revealed that low self-control moderated the relationship between cortisol and aggression, indicating that participants with low cortisol exhibited more aggressive behavior if they also had a compromised ability to inhibit impulsive responses (i.e., low self-control; Shoal et al., 2003). It is possible, therefore, that the results of the current study found no relation between cortisol and aggression because specific moderators were not examined. It is thus important that future studies consider behavioral variables that could predict the cortisol-aggression relationship.

Contrary to hypotheses, serotonin activity did not moderate the relation between baseline testosterone (free and total) and life history of aggression. This finding is inconsistent with previous human (Kuepper et al., 2010) and non-human animal (Higley et al., 1996; Keleta et al., 2007) studies, which suggest that an interaction between increased testosterone levels and decreased serotonin levels predicts an increase in

aggressive behavior. However, a review of the interaction between testosterone, serotonin, and aggressive behavior suggests that testosterone and serotonin interact to predict dominance behavior, but not necessarily aggressive behavior (Bernhardt, 1997). For example, one study that was discussed in this review (Bonson & Winter, 1992) used male rats to examine this interaction. They found that increased testosterone and decreased serotonin predicted an increase in dominance behavior during a competition task between two male rats. In this study, aggressive behavior occurred during the task, albeit infrequently (Bonson & Winter, 1992). Thus, Bonson and Winter's (1992) study suggests that a competition task between males elicits dominance behavior but not necessarily aggressive behavior. Similarly, Bernhardt's (1997) review concluded that increased testosterone and decreased serotonin predicts an increase in dominance behavior rather than aggressive behavior. The current study did not differentiate between aggressive behavior and dominance behavior because we employed a self-report measure (i.e., LHA AG) that assesses a broad range of aggressive behavior. Thus, it is plausible that the LHA AG subscale was unable to account for dominance behavior, which could explain the lack of support for a moderating effect of serotonin on the testosterone-aggression relationship. Future studies should employ a behavior-based measure that involves competition and/or status challenge (e.g., TAP; Taylor, 1967) when assessing aggression in attempt to further clarify the role of dominance behavior in the testosterone-aggression relation in men.

Bivariate analyses in Pharmacochallenge Sample revealed a positive correlation between cortisol response to paroxetine and LHA AG scores, suggesting that blunted cortisol response to paroxetine is positively associated with aggressive behavior. That is,

decreased serotonin activity is associated with aggressive behavior, which is consistent with expectations. Furthermore, cortisol response to paroxetine and baseline total testosterone levels, when entered simultaneously, each contributed significant unique variance to the prediction of life history of aggression. Furthermore, when cortisol response to paroxetine and baseline free and total testosterone levels were entered with the interaction terms (baseline free testosterone × cortisol response and baseline total testosterone × cortisol response), baseline total testosterone and cortisol response to paroxetine made significant unique contributions to predicting life history of aggression, whereas baseline free testosterone did not. First, increasing LHA AG scores predicted decreasing baseline total testosterone levels, suggesting that individuals who experience higher rates of other-directed aggressive behavior have decreased total testosterone levels. As discussed previously, this finding is inconsistent with previous studies and should be clarified in future research. It was suggested in the previous discussion that considering cultural and situational context in which past aggressive behaviors occurred is important when investigating the relation between testosterone and aggression. Second, decreasing (i.e., blunted) cortisol responses to paroxetine predicted increasing LHA AG scores. This finding indicates that individuals with compromised serotonin functioning (i.e., lower levels of 5-HT) experience higher rates of other-directed aggressive behavior, which is consistent with expectations. There is evidence that specific clinical populations, particularly personality-disordered individuals and aggressive individuals (Almeida, Lee, & Coccaro, 2010), possess abnormalities in the serotonergic system, which includes decreased 5-HT availability in the central nervous system (Almeida et al., 2010). This biological marker is believed to cause blunted cortisol responsivity to serotonergic

agents, such as SSRIs (e.g., paroxetine; Berman et al., 1997). Thus, it follows that aggressive individuals with decreased responsivity to serotonergic agents exhibit blunted cortisol responses to paroxetine.

Life History of Antisocial Behavior

The hypothesis that baseline free and total testosterone would be positively correlated with life history of antisocial behavior was not supported in either subsample. Contrastingly, LHA AB scores were negatively correlated with total testosterone in Pharmacochallenge Sample, but this relation was not found in the larger Baseline Sample, so this finding should be viewed cautiously. Furthermore, contrary to hypotheses, baseline total testosterone made a significant unique contribution to the prediction of antisocial behavior at both Step 1 and Step 2 of the regression analysis. Specifically, decreasing baseline total testosterone predicted increasing LHA AB scores, which was inconsistent with expectations. With regard to the literature, previous findings suggest that testosterone is positively associated with antisocial behavior, but the strength of this relation appears to vary depending on the social context in which antisocial behaviors occurred. For example, it has been found that challenges to social status (e.g., low socioeconomic status or competition with another male) strengthen the relation between testosterone and antisocial behavior in men (Dabbs & Morris, 1990). The current study did not employ a behavior-based task (e.g., competition task) and did not assess the nature of the social or situational context in which past antisocial behaviors occurred, only the frequency of these behaviors. Our findings are not in line with any previous studies, as no known studies have reported a negative correlation between testosterone

and antisocial behavior. Accordingly, this finding should be viewed cautiously given that total testosterone and LHA AB scores were not related in the larger Baseline Sample.

Contrary to hypotheses, serotonin activity did not moderate the relationship between baseline testosterone (free and total) and life history of antisocial behavior. Prior to the current study, no known study has examined the moderating effect of serotonin on the relation between testosterone and antisocial behavior; thus, this hypothesis was made on the basis that increased testosterone levels (van Honk & Schutter, 2007) and decreased serotonin levels (LeMarquand et al., 1997) have been implicated separately in the development of antisocial behavior. One explanation for these findings, taken together, may be that antisocial behavior, as one construct, is not associated with testosterone or serotonin. Instead, testosterone and serotonin may instead be directly associated with distinct specific components, or subtypes, of antisocial behavior. To demonstrate, Rowe et al.'s (2004) findings suggest that testosterone is positively related to socially dominant (e.g., violating social norms) and nonaggressive (e.g., manipulating or deceiving others, impulsivity, lack of remorse; American Psychiatric Association, 2000) antisocial behaviors, but not related to aggressive antisocial behaviors (e.g., frequent physical fighting; American Psychiatric Association, 2000). Thus, increased testosterone levels may contribute to the dominance- and/or nonaggressive-related components of antisocial behavior, but not contribute to other antisocial behavior components. Taken together, there is evidence for the existence of variables, which were not considered in the current study, that influence the relation between testosterone and antisocial behavior. By applying such a concept to serotonin, it can be suggested that, given that increased serotonin is associated with increased ability to inhibit impulsive behavior (Witte et al.,

2009), decreased serotonin activity may only be associated with the reckless, impulsive, and risk-taking component of antisocial behavior rather than antisocial behavior as one construct. Thus, given that the LHA AB subscale assesses a broad range of antisocial behavior, it is reasonable to suggest that this subscale may be unable to assess specific, narrow components of antisocial behavior (e.g., social dominance behavior) and their relation to testosterone and serotonin, which could account for the unexpected findings between these variables in the current investigation. Future studies examining biological variables as they relate to specific components or subtypes of antisocial behavior should consider moderators and assessment measure properties when examining the relations between testosterone, serotonin, and antisocial behavior. Furthermore, it would be especially beneficial to employ a multimeasure approach in the assessment of antisocial behavior, including a competition or status challenge task as well as self-report measures that assess the context in which these behaviors occurred.

Consistent with expectations, cortisol was negatively correlated with life history of antisocial behavior. This finding is in line with previous research which suggests that low levels of cortisol contribute to increased rates of antisocial behavior (Popma et al., 2006). A leading explanation for this relationship is that individuals with a high threshold for autonomic arousal are generally less reactive to stress, which causes decreased secretion of cortisol (given that cortisol is secreted during autonomic arousal; Popma et al., 2006). This low reactivity to stressful situations is believed to be a biological marker, particularly in men, for the development of antisocial behavior (Popma et al., 2006). A growing body of literature theorizes that subjective feelings of anxiety inhibit stimulus-seeking behavior (Raine, 2002). Thus, an individual who is relatively unreactive to

stressful situations likely fails to inhibit antisocial behavior. Accordingly, it is suggested that individuals with a high threshold for autonomic arousal are biologically predisposed to engage in stimulus-seeking behavior, such as theft or reckless driving, as these individuals are biologically disinhibited and must participate in relatively more stimulating experiences to achieve autonomic arousal (Raine, 2002). By contrast, individuals with a low threshold for autonomic arousal are more reactive to stressful situations and thus secrete more cortisol on average (Popma et al., 2006). Because of this lower threshold for arousal, these individuals experience stronger subjective feelings of anxiety in stressful situations, contributing to their ability to inhibit antisocial behavior (Popma et al., 2006).

Life History of Self-Aggression

Because testosterone has been implicated as a biological marker for aggressive behavior, it was hypothesized that baseline free and total testosterone would be positively related to life history of self-aggression given that the construct of self-aggression is subsumed under the construct of aggressive behavior. Furthermore, based on the available literature, it was hypothesized that cortisol would also be positively related to self-aggression. However, these hypotheses were not supported. Taken together, our findings suggest that testosterone and cortisol are unrelated to the processes underlying the manifestation of self-aggressive behavior in men. This result is inconsistent with a previous study which suggests that cortisol is positively related to self-injurious behavior (Mcardle, 2004). There is limited evidence to explain this inconsistency, as no other known studies, with exception to Mcardle (2004), have examined the relationship between cortisol and self-injurious behavior. Furthermore, despite the multitude of

research examining the relationship between testosterone and aggression in men, there are no known studies that have examined the role of testosterone in self-aggression specifically in men prior to the current investigation. Thus, the neurobiological processes involved in male self-injury remain poorly understood. However, given that the LHA SA subscale consists of only two items that are relatively broad and nonspecific (frequency of past self-aggressive behavior and suicide attempts), it is plausible that the LHA SA subscale is a less than adequate measure for assessing the underlying mechanisms of self-aggressive behavior. Furthermore, there is evidence that men generally have a low base-rate of endorsing the items on the LHA SA subscale (Coccaro et al., 1997). Exploratory analyses revealed that this was indeed the case for the current study, as nearly ninety-five percent (n = 93) of participants in Baseline Sample did not endorse either item on this subscale, resulting in a LHA SA score of zero for these participants (out of a possible score of 10). Approximately 3% (n = 3) of participants had an LHA SA score of 2, 1% (n = 1) of participants had an LHA SA score of 3, and 1% of participants had an LHA SA score of 4. It is therefore reasonable to suspect that the low base-rate of responding to the LHA SA items in the current investigation contributed to the finding that cortisol and testosterone were not related to self-aggression.

The hypothesis that serotonin activity would moderate the relation between testosterone (free and total) and life history of self-aggression was not supported. Because there are no known studies that have examined this relationship, the hypothesis that serotonin activity would moderate the relationship between testosterone and self-aggression was made on the limited basis that decreased serotonin is associated with increased self-injurious behavior (McCloskey et al., 2009b), and that increased

testosterone is positively associated with aggressive behavior (e.g., Berman et al., 1993). According to the results of this study, testosterone, serotonin activity, and cortisol, when considered individually or combined, are not part of the biological processes involved in self-aggressive behavior in men. It appears that a complex interaction of variables, which may be independent of these biological variables, predicts self-aggressive behavior in men. This interaction remains unspecified and should be a focus of future studies in an effort to better understand and predict, and therefore better treat, self-aggressive behavior in men. Furthermore, as mentioned previously, there were limitations regarding the use of the LHA SA subscale for this sample, which could account for the current study's lack of findings regarding the effects of testosterone, cortisol, and serotonin activity on self-aggression. It may be beneficial for future studies in this area to use a multimeasure approach in the assessment of self-aggression, which should include using both a self-report measure and a laboratory-controlled behavior-based measure (e.g., self-aggression paradigm; SAP; Berman & Walley, 2003) rather than using only a self-report measure in the assessment of self-aggressive behavior. It appears that this may be a more comprehensive approach to clarifying the underlying processes involved in male self-injurious behavior.

Life History of Aggressive, Antisocial, and Self-Aggressive Behavior

One purpose of the current study was to extend the previous literature regarding the relation between aggressive, self-aggressive, and antisocial behavior. Research suggests that these constructs are each related (Vermeiren et al., 2002). As discussed previously, one study found that exposure to violence is positively related to self-aggressive behavior and suicide risk in male and female adolescents, with aggressive

antisocial behavior predicting a positive relation between these variables in boys but not girls (Vermeiren et al., 2002). However, further evidence of the relation between these constructs is limited. The findings of the current study confirm previous findings which suggest that aggressive, self-aggressive, and antisocial behavior are related constructs. Consistent with the existing literature, our results show that aggressive, self-aggressive, and antisocial behavior are positively related to each other.

Free and Total Testosterone

A goal of the current study was to examine the differential value of using free and total testosterone when examining the role of testosterone in aggressive, self-aggressive, and antisocial behavior in men. According to the results of the current study, using total testosterone appears to be more valuable than using free testosterone when assessing male aggressive and antisocial behavior. Specifically, total testosterone contributed significantly more to the variance in the prediction of aggressive and antisocial behavior than free testosterone. Furthermore, despite not making a significant contribution to the prediction of self-aggressive behavior, total testosterone had a much lower *p* value than free testosterone in both Step 1 and Step 2 of the regression analysis. Taken together, the results of the current study suggest that total testosterone may be a more accurate representation of plasma testosterone levels when examining testosterone's role in aggressive, self-aggressive, and antisocial behavior.

Limitations of the Study and Suggestions for Further Research

There are limitations to consider when interpreting our results. Women were excluded from the sample pool because they were beyond the scope of the current investigation for two reasons: women have generally low levels of serum T and low life

history of aggression scores compared to men, and women represented a proportionally small number of participants across the two datasets. A further limitation was that the sample size of both Baseline Sample (N = 98) and Pharmacochallenge Sample (n = 34) was limited, reducing the power of the statistical analyses. Thus, it is possible that certain results were not obtained simply because of the limitations in sample size. Another limitation is the relative lack of ethnic diversity in both subsamples. Specifically, Baseline Sample and Pharmacochallenge Sample were 79.8% and 68.6% Caucasian, respectively. A similar limitation is the limited age range of participants, as most individuals were young adults (i.e., in the 20-29 range). The restricted age and relative lack of ethnic diversity of both samples certainly affect the generalizability of the results.

Upon examination of our results, it is clear that a multimeasure approach (i.e., using both self-report and behavior-based measures) is needed to better assess externalizing behavior in men. It appears that a competition and/or social-related status challenge task would be ideal in the assessment of aggressive and antisocial behavior. Furthermore, it seems that administering a self-report measure that inquires about the social, cultural, and situational context in which aggressive, self-aggressive, and antisocial behaviors occurred would be beneficial. Unfortunately, the broad-based LHA may have been unable to (a) clearly define the context in which past behaviors occurred, or (b) differentiate between specific components of aggressive, self-aggressive, and antisocial behavior. If self-report measures are used in future studies to assess externalizing behavior, it is important that these measures are designed to assess for the desired component of the behavior, as aggressive, self-aggressive, and antisocial behavior

capture a range of subtypes. Future studies should consider this suggestion when choosing which assessment measures to employ.

Conclusion

The main purpose of the current study was to extend the previous research by examining the effects of total and free testosterone on aggressive behavior (and related constructs), as well as the role of serotonin activity in the T-aggression relationship in men. As exploratory analyses, the effects of cortisol on aggression and related constructs were also examined. Our results suggest that cortisol is negatively related to antisocial behavior, which is consistent with previous research. Furthermore, the results showed that blunted cortisol response to paroxetine predicted higher rates of aggressive behavior, which is also consistent with previous research. However, other findings were not consistent with previous findings. Based on previous research, it can be concluded that testosterone may be more closely related to social dominance behavior rather than aggressive or antisocial behavior. Furthermore, it appears that social dominance behavior also influences the interaction between testosterone and serotonin on aggressive behavior. Social dominance behavior can certainly overlap with aggression and antisocial behavior (Bernhardt, 1997), but it appears that social dominance behavior is the primary behavior elicited in response to increased testosterone and decreased serotonin.

APPENDIX

LHA (COCCARO ET AL., 1997)

INSTRUCTIONS:

Conduct a "semi-structured" interview so that the following items may be rated. Please note that only reported actual behavior (e.g., verbal and/or physical) can be rated in the assessment of an item category. Aggressive thoughts, attitudes, and fantasies are not counted. It is important to rate any events that have occurred over the subject's lifetime (including years as a teenager and young adult).

0 = no events

1 = one event

2 = "a couple" or "a few" (i.e., 2-3 events)

3 = "several" or "some" (i.e., 4-9 events)

4 = "many" or "numerous" (i.e., 10+ events)

5 = "so many events that they can't be counted"

ITEM CATEGORIES:

A. Temper tantrums (i.e., behavioral manifestations in response to frustration; screaming, ranting and raving, throwing things, etc.).

   Since you were an adolescent, have you had times that you were so frustrated that you threw things, screamed, ranted and raved?

   Number of events from 13 yrs. to present:

B. Physical fighting (e.g., history of physical fights with other people whether or not the subject started the fight or not).

Since you were an adolescent, have you been involved in physical fights with other people, whether started by you or someone else?

Number of events from 13 yrs. to present:

C. Verbal fighting (e.g., history of verbal arguments in which an angry voice/profanity/insults/threats are used. Note: polite disagreements are not to be scored as positive).

Since you were an adolescent, have you had times that you were involved in verbal arguments in which an angry voice, profanity, or threats were used? Polite disagreements are not to be considered.

Number of events from 13 yrs. to present:

D. Specific assaults on other people (i.e., including children, whether during a physical fight or not, with the specific intent to hurt/harm someone).

Since you were an adolescent, have you ever assaulted another person (adult or child), whether during a physical fight or not, with the specific intent of hurting or harming them?

Number of events from 13 yrs. to present

E. Specific assaults on property or pets/animals (i.e., hitting, throwing, breaking objects, windows, dishes, etc. Note: intent should be to harm or intimidate others).

Since you were an adolescent, have you ever assaulted an animal, pet, or property, with the intent to harm or intimidate others, which involved hitting, throwing, breaking objects, etc.?

Number of events from 13 yrs. to present:

F. (1) Specific assaults on self (i.e., self-injurious, but not suicidal, in nature).

Since you were an adolescent, have you ever tried to hurt or harm yourself in any way, other than suicide attempts?

Number of events from 13 yrs. to present:

(2) Suicide attempts (i.e., method used, hospitalization, etc.)

Since you were an adolescent, have you ever attempted suicide? If so, what did you do? What happened? Did you receive any treatment, hospitalization, etc.?

Number of events from 13 yrs. to present:

G. School disciplinary problems (i.e., reprimand by school principal, suspension, expulsion).

Since you were an adolescent, have you ever had any school disciplinary problems, such as a reprimand from the principal, suspension, or expulsion?

Number of events from 13 yrs. to present:

H. Problems with supervisors at work (e.g., behavioral outbursts in response to authority reprimands, demotions, or terminations due to aggressive/impulsive behaviors).

Since you were an adolescent, have you ever had any problems with supervisors at work, such as behavioral outbursts in response to authority reprimands, demotions, or terminations due to aggressive or impulsive behaviors.

Number of events from 13 yrs. to present:

I. Antisocial behavior not involving the police (e.g., lying, stealing, prostitution, DUI, involvement in illegal operations, violations of the rights of others, trespassing, vandalism, robbery, etc.).

Since you were an adolescent, have you ever demonstrated any antisocial behavior not involving the police, such as lying, stealing, prostitution, DUI, involvement in illegal operations, violations of the rights of others, trespassing, vandalism, robbery, etc.? Have you ever done anything which could have involved trouble with the police but you were not caught?

Number of events from 13 yrs. to present:

J. Antisocial behavior involving the police (e.g., warnings, arrests, and/or convictions for misdemeanor or felony offenses).

Since you were an adolescent, have you ever demonstrated any antisocial behavior involving the police, such as warnings, arrests or convictions for misdemeanor or felony offenses?

Number of events from 13 yrs. to present:

Aggression Score (sum items A-E): _____

Self-Injury Score (sum items F1 and F2): _____

Antisocial Score (sum Items G-J): _____

TOTAL SCORE (sum of all items): _____

Categories:	A-E	Aggression
	F	Self-injury, Suicide
	G-J	Antisocial

REFERENCES

Almeida, M. Lee, R., & Coccaro, E. F. (2010). Cortisol responses to ipsapirone challenge correlate with aggression, while basal cortisol levels correlate with impulsivity, in personality disorder and healthy volunteer subjects. *Journal of Psychiatric Research, 44,* 874-880.

American Psychiatric Association (2000). *Diagnostic and statistical manual of mental disorders* (4th ed., text rev.). Washington, DC: Author.

Archer, J., Graham-Kevan, N., & Davies, M. (2005). Testosterone and aggression: A reanalysis of Book, Starzyk, and Quinsey's (2001) study. *Aggression and Violent Behavior, 10,* 241-261.

Brooks, J. H., & Reddon, J. R. (1996). Serum testosterone in violent and nonviolent young offenders. *Journal of Clinical Psychology, 52*, 475-483.

Berman, M., E., Gladue, B., & Taylor, S. (1993). The effects of hormones, Type A behavior pattern, and provocation on aggression in men. *Motivation and Emotion, 17*, 125-138.

Berman, M. E., Tracy, J. I., & Coccaro, E. F. (1997). The serotonin hypothesis of aggression revisited. *Clinical Psychology Review, 17*, 651-665.

Berman, M. E., McCloskey, M. S., Fanning, J. R., Schumaker, J. A., & Coccaro, E. F. (2009). Serotonin augmentation reduces response to attack in aggressive individuals. *Psychological Science, 20,* 714-720.

Berman, M. E., & Walley, J. C. (2003). Imitation of self-aggressive behavior: An experimental test of the contagion hypothesis. *Journal of Applied Social Psychology, 33*, 1036-1057.

Bernhardt, P. C. (1997). Influences of serotonin and testosterone in aggression and dominance: Convergence with social psychology. *Current Directions in Psychological Science, 6,* 44- 48.

Bonson, K. R., & Winter, J. C. (1992). Reversal of testosterone-induced dominance by the serotonergic agonist quipazine. *Pharmacology, Biochemistry and Behavior, 42,* 809-813.

Book, A. S., Starzyk, K. B., & Quinsey, V. L. (2001). The relationship between testosterone and aggression: A meta-analysis. *Aggression and Violent Behavior, 6,* 579-599.

Bornovalova, M. A., Tull, M. T., Gratz, K. L., Levy, R., & Lejuez, C. W. (2011). Extending models of deliberate self-harm and suicide attempts to substance users: Exploring the roles of childhood abuse, posttraumatic stress, and difficulties controlling impulsive behavior when distressed. *Psychological Trauma: Theory, Research, Practice, and Policy, 6,* 1-11.

Bradshaw, C. P., Rodgers, C. R. R., Ghandour, L. A., & Garbarino, J. (2009). Social–cognitive mediators of the association between community violence exposure and aggressive behavior. *School Psychology Quarterly, 24,* 199-210.

Coccaro, E. F., Beresford, B., Minar, P., Kaskow, J., & Gerocioti, T. (2007). CSF testosterone: Relationship to aggression, impulsivity, and venturesomeness in adult males with personality disorder. *Journal of Psychiatric Research, 41,* 488-492.

Coccaro, E. F., Berman, M. E., & Kavoussi, R. J. (1997). Assessment of life-history of aggression: Development and psychometric characteristics. *Psychiatry Research, 73*, 147-157.

Dabbs, J. M., & Morris, R. (1990). Testosterone, social class, and antisocial behavior in a sample of 4,462 men. *Psychological Science, 1*, 209-211.

Danel, T., Vantyghem, M. C., & Touitou, Y. (2006). Responses of the steroid circadian system to alcohol in humans: Importance of the time and duration of intake. *Chronobiology International, 23*, 1025-1034.

Farrell, S. F., & McGinnis, M. Y. (2003). Effects of pubertal anabolic-androgenic steroid (AAS) administration on reproductive and aggressive behaviors in male rats. *Behavioral Neuroscience, 117*, 904-911.

First, M. B., Gibbon, M., Spitzer, R. L., & Williams, J. B. W. (1998). Computer-assisted SCID – Clinical version (CAS-CV) [Computer software]. North Towanda, NY: Multi-Health Systems, American Psychiatric Association Press.

Gradinger, P., Strohmeier, D., & Spiel, C. (2009). Traditional bullying and cyberbulling: Identification of risk groups for adjustment problems. *Journal of Psychology, 217*, 205-213.

Haltigan, J. D., Roisman, G. I., Susman, E. J., Barnett-Walker, K., & Monahan, K. C. (2011). Elevated trajectories of externalizing problems are associated with lower awakening cortisol levels in midadolescence. *Developmental Psychology, 47*, 1-7.

Hanson, M. D., & Chen, E. (2010). Daily stress, cortisol, and sleep: The moderating role of childhood psychosocial environments. *Health Psychology, 29*, 394-402.

Higley, J. D., Mehlman, P. T., Poland, R. E., & Taub, D. M., (1996). CSF testosterone and 5-HIAA correlate with different types of aggressive behaviors. *Biological Psychiatry, 40,* 1067-1082.

Horwitz, S. H., Santiago, L., Pearson, J., & Larussa-Trott, M. (2009). Relational tools for working with mild-to-moderate couple violence: Patterns of unresolved conflict and pathways to resolution. *Professional Psychology: Research and Practice, 40,* 249-256.

Inoff-Germaine, G., Arnold, G. S., Nottelmann, E. D., Susman, E. J., Cutler, G. B., & Chrousos, G. P. (1988). Relations between hormone levels and observational measures of aggressive behavior of young adolescents in family interactions. *Developmental Psychology, 24,* 120-139.

Keleta, Y. B., Lumia, A. R., Anderson, G. M., & McGinnis, M. Y. (2007). Behavioral effects of pubertal anabolic androgenic steroid exposure in male rats with low serotonin. *Brain Research, 1132,* 129-138.

Kojima, H., Terao, T., Iwakawa, M., Soya, A., Inoue, N., Shiraishi, Y., . . . Nakamura, J. (2003). Paroxetine as a 5-HT neuroendocrine probe. *Psychopharmacology, 167,* 97-102.

Kuepper, Y., Alexander, N., Osinsky, R., Mueller, E., Schmitz, A., Netter, P., . . . Hennig, J. (2010). Aggression-interactions of serotonin and testosterone in healthy men and women. *Behavioural Brain Research, 206,* 93-100.

LeMarquand, D., Pihl, R. O., Young, S. N., Tremblay, R. E., Palmour, R. M., & Benkelfat, C. (1997). Tryptophan depletion and behavioral disinhibition in men at risk for alcoholism and antisocial behavior. In Raine, A., Breenan, P. A.,

Farrington, D. P., & Mednick, S. A. (Eds.), *Biosocial bases of violence* (pp. 337-339). New York, NY: Plenum Press.

Lumia, A. R., & McGinnis, M. Y. (2010). Impact of anabolic androgenic steroids on adolescent males. *Physiology & Behavior, 104*, 1-6.

McAndrew, F. T. (2009). The interacting role of testosterone and challenges to status in human male aggression. *Aggression and Violent Behavior, 14*, 330-335.

Mcardle, E. T. (2004). HPA-axis reactivity to interpersonal stress in young adults who self-injure. *Dissertation Abstracts International Section B: The Sciences and Engineering, 64*, 5226.

McCloskey**,** M. S., Berman, M. E., Echevarria, D. E., & Coccaro, E. F. (2009a). Effects of acute alcohol intoxication and paroxetine on aggression in men. *Alcohol: Clinical and Experimental Research, 33*, 1-10.

McCloskey, M. S., Ben-Zeev, D., Lee, R., Berman, M. E., & Coccaro, E. F. (2009b). Acute tryptophan depletion and self-injurious behavior in aggressive patients and healthy volunteers. *Psychopharmacology, 203*, 53-61.

Nazian, S. J. (1986). Concentrations of free testosterone, total testosterone, and androgen binding protein in the peripheral serum of male rats during sexual maturation. *Journal of Andrology, 7*, 49-54.

Popma, A., Jansen, L. M. C., Vermeiren, R., Steiner, H., Raine A., Van Goozen, S. H. M., . . . Doreleijers, T. A. H. (2006). Hypothalamus adrenal pituitary axis and autonomic activity during stress in delinquent male adolescents and controls. *Psychoneuroendocrinology, 31*, 948-957.

Popma, A., Vermeiren, R., Geluk, C. A. M. L., Rinne, T., van den Brink, W., Knol, D. L., . . . Doreleijers, T. A. H. (2007). Cortisol moderates the relationship between testosterone and aggression in delinquent male adolescents. *Biological Psychiatry, 61*, 405-411.

Poustka, L., Maras, A., Hohm, E., Fellinger, J., Holtmann M., Banaschewski, T., . . . Laucht, M.(2010). Negative association between plasma cortisol levels and aggression in a high-risk community sample of adolescents. *Journal of Neural Transmission, 117*, 621-627.

Raine, A. (2002). Annotation: The role of prefrontal deficits, low autonomic arousal and early health factors in the development of antisocial and aggressive behavior in children. *Journal of Child Psychology and Psychiatry, 43*, 417-434.

Rowe, R., Maughan, B., Worthman, C. M., Costello, E. J., & Angold, A. (2004). Testosterone, antisocial behavior, and social dominance in boys: Pubertal development and biosocial interaction. *Biological Psychiatry, 55*, 546-552.

Sato, S. M., Schulz, K. M., Sisk, C. L., & Wood, R., I. (2008). Adolescents and androgens, receptors and rewards. *Hormones and Behavior, 53*, 647-658.

Salas-Ramirez, K. Y., Montalto, P. R., & Sisk, C. L. (2008). Anabolic androgenic steroids differentially affect social behaviors in adolescent and adult male Syrian hamsters. *Hormones and Behavior, 53*, 378-385.

Salas-Ramirez, K. Y., Montalto, P. R., & Sisk, C. L. (2010). Anabolic steroids have long-lasting effects on male social behaviors. *Behavioural Brain Research, 208*, 328-335.

Schatzberg, A. F., & Nemeroff, C. B. (2001). *Essentials of clinical psychopharmacology*. Washington, DC: American Psychiatric Association.

Shoal, G. D., Giancola, P. R., & Kirillova, G. P. (2003). Salivary cortisol, personality, and aggressive behavior in adolescent boys: A 5-year longitudinal study. *Journal of the American Academy of Child & Adolescent Psychiatry, 42*, 1101-1107.

Siever, L. J. (2008). Neurobiology of aggression and violence. *American Journal of Psychiatry, 165*, 429-442.

Taylor, S. P. (1967). Aggressive behavior and physiological arousal as a function of provocation and the tendency to inhibit aggression. *Journal of Personality, 35*, 297-310.

van Honk, J., Schutter, D. J. L. G. (2007). Testosterone reduces conscious detection of signals serving social correction: Implications for antisocial behavior. *Psychological Science, 18*, 663-667.

Vermeiren, R., Ruchkin, V., Leckman, P. E., Deboutte, D., & Schwab-Stone, M. (2002). Exposure to violence and suicide risk in adolescents: A community study. *International Society for Research in Child and Adolescent Psychopathology, 30*, 529-537.

Wingfield, J. C. (1985). Short-term changes in plasma levels of hormones during establishment and defense of a breeding territory in male song sparrows, Melospiza melodia. *Hormones and Behavior, 19*, 174-187.

Witte, A. V., Floel, A., Stein, P., Savli, M., Mien, L. K., Wadsak, W., . . . Lanzenberger, R. (2009). Aggression is related to frontal serotonin-IA receptor distribution as revealed by PET in healthy subjects. *Human Brain Mapping, 30*, 2558-2570.

Yang, S. J., Shin, D. W., Noh, K. S., & Stein, M. A. (2007). Cortisol is inversely correlated with aggression for those boys with attention deficit hyperactivity disorder who retain their reactivity to stress. *Psychiatry Research, 153*, 55-60.

Yap, M., Mascord, D. J., Starmer, G. A., & Whitfield, J. B. (1993). Studies on the chronopharmacology of ethanol. *Alcohol and Alcoholism, 28*, 17-24.

Yi, Y. (1989). On the evaluation of main effects in multiplicative regression models. *Journal of the Market Research Society, 31*, 133-138.