

# Commentary

## Testosterone and Aggression: More Than Just Biology?

Emil F. Coccaro

Carré *et al.* (1) have carried out a careful and thoughtful study in an area of human aggression that has long held the public in its thrall.

If you were a *Jeopardy!* contestant and the answer was: “Something we all have that makes us aggressive,” you would say, “Testosterone!” and you would win. Yes, but this would not be entirely true. It might be true if you were talking about lower-order mammals, but not necessarily humans. You might counter that we all know about “roid rage.” Yes, but this requires supraphysiological doses of testosterone (T)-like agents for more than a single dose. In addition, it has been clear for years that the relationship between aggression and baseline levels of T is, even if statistically significant, rather small in magnitude.

My research group looked at basal levels of cerebrospinal fluid T in a mixed group of personality-disordered individuals several years back and noted no relationship with aggression or impulsivity but a positive relationship with “venturesomeness” on the Eysenck Personality Questionnaire (2). This construct is a part of the larger construct of “sensation seeking” and represents “thoughtful” as opposed to “impulsive” sensation seeking. The critical difference between the two is that when venturesome people climb a mountain, they make certain they are prepared to engage in this potentially dangerous activity; they do not simply go off “half-cocked” and climb without making all the proper preparations. While not exactly the same as dominance, people high in venturesomeness likely share similar characteristics, such as assertiveness and self-assuredness.

The Carré *et al.* study goes much further than previous studies in that it performs a T challenge in a large group of healthy subjects and employs a laboratory assessment of aggressive responding rather than assessing aggression simply as a personality trait. Carré *et al.* also prospectively assess the relationship of dominance and self-control to the behavioral response to a single dose of T.

The results are exciting because they make clear the complex nature of the T/aggression relationship. T does not simply increase aggressive behavior in everyone but does so according to specific behavioral parameters. That is, acute T increases aggressive responding only in those high on dominance and/or low on self-control. This provides additional evidence of the importance of trait behavioral/personality dimensions to the effect of biologically active compounds. Aspects of personality are no longer a curiosity or a nuisance in research but instead are critical to our understanding of human behavior.

Also noteworthy is the corroborating data regarding the underlying mechanisms of this finding—specifically the role of

social cognition at the neurocircuitry level. That is, previous data indicated that exogenous T increases amygdala reactivity (3), reduced orbitofrontal activity (4), and reduced amygdala and orbitofrontal connectivity (5) in response to angry faces—which is what is observed in those with recurrent, problematic, impulsive aggressive behavior and intermittent explosive disorder (6,7). All of which make a compelling, and rich, story for our understanding of how T exerts its effect on brain and behavior.

Next time you appear on *Jeopardy!* and you are given the answer posed above, say, “Possibly testosterone...but it depends on the nature of your personality.” You might not win the round, but you would be correct.

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### Article Information

From the Department of Psychiatry and Behavioral Neuroscience, Biological Sciences Division, University of Chicago, Chicago, Illinois.

Address correspondence to Emil F. Coccaro, M.D., The University of Chicago, Psychiatry and Behavioral Neuroscience, Biological Sciences Division, 5841 South Maryland Avenue, MC 3077, Chicago, IL 60637; E-mail: ecoccaro@bsd.uchicago.edu.

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### References

1. Carré JM, Geniole SN, Ortiz TL, Bird BM, Videto A, Bonin PL (2017): Exogenous testosterone rapidly increases aggressive behavior in dominant and impulsive men. *Biol Psychiatry* 82:249–256.
2. Coccaro EF, Beresford B, Minar P, Kaskow J, Geraciotti T (2007): CSF testosterone: Relationship to aggression, impulsivity, and venturesomeness in adult males with personality disorder. *J Psychiatr Res* 41: 488–492.
3. Hermans EJ, Ramsey NF, van Honk J (2008): Exogenous testosterone enhances responsiveness to social threat in the neural circuitry of social aggression in humans. *Biol Psychiatry* 63:263–270.
4. Mehta PH, Beer J (2010): Neural mechanisms of the testosterone-aggression relation: The role of orbitofrontal cortex. *J Cogn Neurosci* 22:2357–2368.
5. van Wingen G, Mattern C, Verkes RJ, Buitelaar J, Fernández G (2010): Testosterone reduces amygdala-orbitofrontal cortex coupling. *Psychoneuroendocrinology* 35:105–113.
6. Coccaro EF, McCloskey MS, Fitzgerald DA, Phan KL (2007): Amygdala and orbitofrontal reactivity to social threat in individuals with impulsive aggression. *Biol Psychiatry* 62:168–178.
7. McCloskey MS, Phan KL, Angstadt M, Fettich KC, Keedy S, Coccaro EF (2016): Amygdala hyperactivation to angry faces in intermittent explosive disorder. *J Psychiatr Res* 79:34–41.

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