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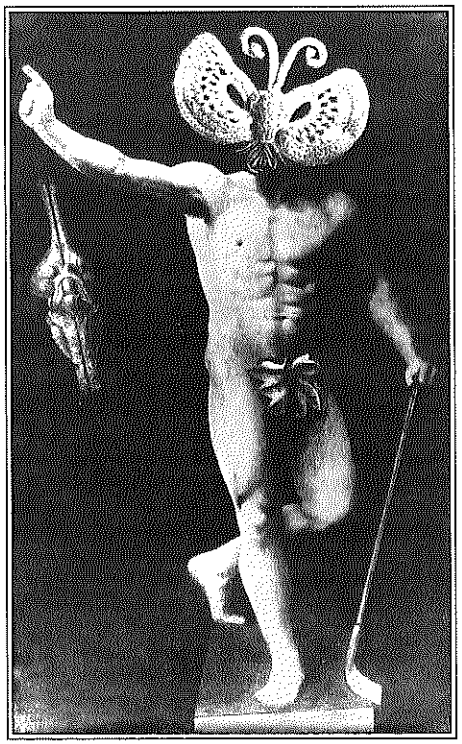
The Trouble with Testosterone

WILL BOYS JUST BE BOYS?



Max Ernst, Health Through Sports, *c. 1920;*
The Menil Collection, Houston

Face it, we all do it. We all believe in certain stereotypes about certain minorities. The stereotypes are typically pejorative and usually false. But every now and then, they are true. I write apologetically as a member of a minority about which the stereotypes are indeed true. I am male. We males account for less than 50 percent of the population, yet we generate an incredibly disproportionate percentage of the violence. Whether it is something as primal as having an ax fight in an Amazonian clearing or as detached as using computer-guided aircraft to strafe a village, something as condemned as assaulting a cripple or as glorified as killing someone wearing the wrong uniform, if it is violent, males excel at it.

Why should that be? We all think we know the answer. A dozen millennia ago or so, an adventurous soul managed to lop off a surly bull's testicles and thus invented behavioral endocrinology. It is unclear from the historical records whether this individual received either a grant or tenure as a result of this experiment, but it certainly generated an influential finding—something or other comes out of the testes that helps to make males such aggressive pains in the ass.

That something or other is testosterone.* The hormone

*Testosterone is one of a family of related hormones, collectively known as "androgens" or "anabolic steroids." They all are secreted from the testes

binds to specialized receptors in muscles and causes those cells to enlarge. It binds to similar receptors in laryngeal cells and gives rise to operatic basses. It causes other secondary sexual characteristics, makes for relatively unhealthy blood vessels, alters biochemical events in the liver too dizzying to even contemplate, has a profound impact, no doubt, on the workings of cells in big toes. And it seeps into the brain, where it binds to those same "androgen" receptors and influences behavior in a way highly relevant to understanding aggression.

What evidence links testosterone with aggression? Some pretty obvious stuff. Males tend to have higher testosterone levels in their circulation than do females (one wild exception to that will be discussed later) and to be more aggressive. Times of life when males are swimming in testosterone (for example, after reaching puberty) correspond to when aggression peaks. Among numerous species, testes are mothballed most of the year, kicking into action and pouring out testosterone only during a very circumscribed mating season—precisely the time when male-male aggression soars.

Impressive, but these are only correlative data, testosterone repeatedly being on the scene with no alibi when some aggression has occurred. The proof comes with the knife, the performance of what is euphemistically known as a "subtraction" experiment. Remove the source of testosterone in species after species and levels of aggression typically plummet. Reinstate normal testosterone levels afterward with injections of synthetic testosterone, and aggression returns.

To an endocrinologist, the subtraction and replacement

or are the result of a modification of testosterone, they all have a similar chemical structure, and they all do roughly similar things. Nonetheless, androgen mavens spend entire careers studying the important differences in the actions of different androgens. I am going to throw that subtlety to the wind and, for the sake of simplification that will horrify many, will refer throughout to all of these related hormones as "testosterone."

paradigm represents pretty damning proof: this hormone is involved. "Normal testosterone levels appear to be a prerequisite for normative levels of aggressive behavior" is the sort of catchy, hummable phrase that the textbooks would use. That probably explains why you shouldn't mess with a bull moose during rutting season. But that's not why a lot of people want to understand this sliver of science. Does the action of this hormone tell us anything about *individual* differences in levels of aggression, anything about why some males, some human males, are exceptionally violent? Among an array of males—human or otherwise—are the highest testosterone levels found in the most aggressive individuals?

Generate some extreme differences and that is precisely what you see. Castrate some of the well-paid study subjects, inject others with enough testosterone to quadruple the normal human levels, and the high-testosterone males are overwhelmingly likely to be the more aggressive ones. However, that doesn't tell us much about the real world. Now do something more subtle by studying the normative variability in testosterone—in other words, don't manipulate anything, just see what everyone's natural levels are like—and high levels of testosterone and high levels of aggression still tend to go together. This would seem to seal the case—interindividual differences in levels of aggression among normal individuals are probably driven by differences in levels of testosterone. But this turns out to be wrong.

Okay, suppose you note a correlation between levels of aggression and levels of testosterone among these normal males. This could be because *(a)* testosterone elevates aggression; *(b)* aggression elevates testosterone secretion; *(c)* neither causes the other. There's a huge bias to assume option *a,* while *b* is the answer. Study after study has shown that when you examine testosterone levels when males are first placed together in the social group, testosterone levels predict noth-

ing about who is going to be aggressive. The subsequent behavioral differences drive the hormonal changes, rather than the other way around.

Because of a strong bias among certain scientists, it has taken forever to convince them of this point. Behavioral endocrinologists study what behavior and hormones have to do with each other. How do you study behavior? You get yourself a notebook and a stopwatch and a pair of binoculars. How do you measure the hormones? You need a gazillion-dollar machine, you muck around with radiation and chemicals, wear a lab coat, maybe even goggles—the whole nine yards. Which toys would you rather get for Christmas? Which facet of science are you going to believe in more? Because the endocrine aspects of the business are more high-tech, more reductive, there is the bias to think that it is somehow more scientific, more powerful. This is a classic case of what is often called physics envy, the disease among scientists where the behavioral biologists fear their discipline lacks the rigor of physiology, the physiologists wish for the techniques of the biochemists, the biochemists covet the clarity of the answers revealed by the molecular biologists, all the way down until you get to the physicists, who confer only with God.* Hormones seem to many to be more real, more substantive, than the ephemera of behavior, so when a correlation occurs, it

*An example of physics envy in action. Recently, a zoologist friend had obtained blood samples from the carnivores that he studies and wanted some hormones in the sample assays in my lab. Although inexperienced with the technique, he offered to help in any way possible. I felt hesitant asking him to do anything tedious but, so long as he had offered, tentatively said, "Well, if you don't mind some unspeakable drudgery, you could number about a thousand assay vials." And this scientist, whose superb work has graced the most prestigious science journals in the world, cheerfully answered, "That's okay, how often do I get to do *real* science, working with test tubes?"

must be because hormones regulate behavior, not the other way around.

As I said, it takes a lot of work to cure people of that physics envy, and to see that interindividual differences in testosterone levels don't predict subsequent differences in aggressive behavior among individuals. Similarly, fluctuations in testosterone levels within one individual over time do not predict subsequent changes in the levels of aggression in that one individual—get a hiccup in testosterone secretion one afternoon and that's not when the guy goes postal.

Look at our confusing state: normal levels of testosterone are a prerequisite for normal levels of aggression, yet changing the amount of testosterone in someone's bloodstream within the normal range doesn't alter his subsequent levels of aggressive behavior. This is where, like clockwork, the students suddenly start coming to office hours in a panic, asking whether they missed something in their lecture notes.

Yes, it's going to be on the final, and it's one of the more subtle points in endocrinology—what is referred to as a hormone having a "permissive effect." Remove someone's testes and, as noted, the frequency of aggressive behavior is likely to plummet. Reinstate precastration levels of testosterone by injecting that hormone, and precastration levels of aggression typically return. Fair enough. Now this time, castrate an individual and restore testosterone levels to only 20 percent of normal and . . . amazingly, normal precastration levels of aggression come back. Castrate and now generate twice the testosterone levels from before castration—and the same level of aggressive behavior returns. You need some testosterone around for normal aggressive behavior—zero levels after castration, and down it usually goes; quadruple it (the sort of range generated in weight lifters abusing anabolic steroids), and aggression typically increases. But anywhere from roughly 20 percent of normal to twice normal and it's all the

same; the brain can't distinguish among this wide range of basically normal values.

We seem to have figured out a couple of things by now. First, knowing the differences in the levels of testosterone in the circulation of a bunch of males will not help you much in figuring out who is going to be aggressive. Second, the subtraction and reinstatement data seem to indicate that, nevertheless, in a broad sort of way, testosterone causes aggressive behavior. But that turns out not to be true either, and the implications of this are lost on most people the first thirty times you tell them about it. Which is why you'd better tell them about it thirty-one times, because it is the most important point of this piece.

Round up some male monkeys. Put them in a group together, and give them plenty of time to sort out where they stand with each other—affiliative friendships, grudges and dislikes. Give them enough time to form a dominance hierarchy, a linear ranking system of numbers 1 through 5. This is the hierarchical sort of system where number 3, for example, can pass his day throwing around his weight with numbers 4 and 5, ripping off their monkey chow, forcing them to relinquish the best spots to sit in, but, at the same time, remembering to deal with numbers 1 and 2 with shit-eating obsequiousness.

Hierarchy in place, it's time to do your experiment. Take that third-ranking monkey and give him some testosterone. None of this within-the-normal-range stuff. Inject a ton of it into him, way higher than what you normally see in a rhesus monkey; give him enough testosterone to grow antlers and a beard on every neuron in his brain. And, no surprise, when you then check the behavioral data, it turns out that he will probably be participating in more aggressive interactions than before.

So even though small fluctuations in the levels of the hormone don't seem to matter much, testosterone still causes

aggression. But that would be wrong. Check out number 3 more closely. Is he now raining aggressive terror on any and all in the group, frothing in an androgenic glaze of indiscriminate violence? Not at all. He's still judiciously kowtowing to numbers 1 and 2, but has simply become a total bastard to numbers 4 and 5. This is critical: testosterone isn't *causing* aggression, it's *exaggerating* the aggression that's already there.

Another example just to show we're serious. There's a part of your brain that probably has lots to do with aggression, a region called the amygdala.* Sitting right near it is the Grand Central Station of emotion-related activity in your brain, the hypothalamus. The amygdala communicates with the hypothalamus by way of a cable of neuronal connections called the stria terminalis. No more jargon, I promise. The amygdala has its influence on aggression via that pathway, with bursts of electrical excitation called action potentials that ripple down the stria terminalis, putting the hypothalamus in a pissy mood.

Once again, do your hormonal intervention; flood the area with testosterone. You can do that by injecting the hormone into the bloodstream, where it eventually makes its way to this part of the brain. Or you can be elegant and surgically microinject the stuff directly into this brain region. Six of one, half a dozen of the other. The key thing is what doesn't happen next. Does testosterone now cause there to be action potentials surging down the stria terminalis? Does it turn on that pathway? Not at all. If and only if the amygdala is *already* sending an aggression-provoking volley of action potentials down the stria terminalis, testosterone increases the rate of such action potentials by shortening the resting time between

*And no one has shown that differences in the size or shape of the amygdala, or differences in the numbers of neurons in it, can begin to predict differences in normal levels of aggression. Same punch line as with testosterone.

them. It's not turning on the pathway, it's increasing the volume of signaling if it is already turned on. It's not causing aggression, it's exaggerating the preexisting pattern of it, exaggerating the response to environmental triggers of aggression.

This transcends issues of testosterone and aggression. In every generation, it is the duty of behavioral biologists to try to teach this critical point, one that seems a maddening cliché once you get it. You take that hoary old dichotomy between nature and nurture, between biological influences and environmental influences, between intrinsic factors and extrinsic ones, and, the vast majority of the time, regardless of which behavior you are thinking about and what underlying biology you are studying, the dichotomy is a sham. No biology. No environment. Just the interaction between the two.

Do you want to know how important environment and experience are in understanding testosterone and aggression? Look back at how the effects of castration were discussed earlier. There were statements like "Remove the source of testosterone in species after species and levels of aggression typically plummet." Not "Remove the source . . . and aggression always goes to zero." On the average it declines, but rarely to zero, and not at all in some individuals. And the more social experience an individual had being aggressive prior to castration, the more likely that behavior persists sans *cojones*. Social conditioning can more than make up for the hormone.

Another example, one from one of the stranger corners of the animal kingdom: If you want your assumptions about the nature of boy beasts and girl beasts challenged, check out the spotted hyena. These animals are fast becoming the darlings of endocrinologists, sociobiologists, gynecologists, and tabloid writers. Why? Because they have a wild sex-reversal system—females are more muscular and more aggressive than males and are socially dominant over them, rare traits in

the mammalian world. And get this: females secrete more of certain testosterone-related hormones than the males do, producing the muscles, the aggression (and, as a reason for much of the gawking interest in these animals, wildly masculinized private parts that make it supremely difficult to tell the sex of a hyena). So this appears to be a strong vote for the causative powers of high androgen levels in aggression and social dominance. But that's not the whole answer. High up in the hills above the University of California at Berkeley is the world's largest colony of spotted hyenas, massive bone-crunching beasts who fight with each other for the chance to have their ears scratched by Laurence Frank, the zoologist who brought them over as infants from Kenya. Various scientists are studying their sex-reversal system. The female hyenas are bigger and more muscular than the males and have the same weirdo genitals and elevated androgen levels that their female cousins do back in the savannah. Everything is in place except . . . the social system is completely different from that in the wild. Despite being stoked on androgens, there is a very significant delay in the time it takes for the females to begin socially dominating the males—they're growing up without the established social system to learn from.

When people first grasp the extent to which biology has something to do with behavior, even subtle, complex, human behavior, there is often an initial evangelical enthusiasm of the convert, a massive placing of faith in the biological components of the story. And this enthusiasm is typically of a fairly reductive type—because of physics envy, because reductionism is so impressive, because it would be so nice if there were a single gene or hormone or neurotransmitter or part of the brain that was *it,* the cause, the explanation of everything. And the trouble with testosterone is that people tend to think this way in an arena that really matters.

This is no mere academic concern. We are a fine species

with some potential. Yet we are racked by sickening amounts of violence. Unless we are hermits, we feel the threat of it, often as a daily shadow. And regardless of where we hide, should our leaders push the button, we will all be lost in a final global violence. But as we try to understand and wrestle with this feature of our sociality, it is critical to remember the limits of the biology. Testosterone is never going to tell us much about the suburban teenager who, in his after-school chess club, has developed a particularly aggressive style with his bishops. And it certainly isn't going to tell us much about the teenager in some inner-city hellhole who has taken to mugging people. "Testosterone equals aggression" is inadequate for those who would offer a simple solution to the violent male—just decrease levels of those pesky steroids. And "testosterone equals aggression" is certainly inadequate for those who would offer a simple excuse: Boys will be boys and certain things in nature are inevitable. Violence is more complex than a single hormone. This is endocrinology for the bleeding heart liberal—our behavioral biology is usually meaningless outside the context of the social factors and environment in which it occurs.

FURTHER READING

For a good general review of the subject, see E. Monaghan and S. Glickman, "Hormones and Aggressive Behavior," in J. Becker, M. Breedlove, and D. Crews, eds., *Behavioral Endocrinology* (Cambridge, Mass.: MIT Press, 1992), 261. This also has an overview of the hyena social system, as Glickman heads the study of the Berkeley hyenas. For technical papers on the acquisition of the female dominance in hyenas, see S. Jenks, M. Weldele, L. Frank, and S. Glickman, "Acquisition of Matrilineal Rank in Captive Spotted Hyenas: Emergence of a Natural Social System in Peer-Reared Animals and Their Offspring," *Animal Behavior* 50 (1995): 893; and L. Frank, S. Glickman, and C. Zabel, "Ontogeny of Female Dominance in the Spotted Hyaena: Perspectives from Nature and Captivity," in P. Jewell and G. Maloiy, eds., "The Biology of Large African Mammals in Their Environment," *Symposium of the Zoological Society of London* 61 (1989): 127.

I have emphasized that while testosterone levels in the normal range do not have much to do with aggression, a massive elevation of exposure, as would be seen in anabolic steroid abusers, does usually increase aggression. For a recent study in which even elevating into that range (approximately five times normal level) still had no effect on mood or behavior, see S. Bhasin, T. Storer, N. Berman, and colleagues, "The Effects of Supraphysiologic Doses of Testosterone on Muscle Size and Strength in Normal Men," *New England Journal of Medicine* 335 (1996): 1.

The study showing that raising testosterone levels in the middle-ranking monkey exaggerates preexisting patterns of aggression can be found in A. Dixson and J. Herbert, "Testosterone, Aggressive Behavior and Dominance Rank in Captive Adult Male Talapoin Monkeys *(Miopithecus talapoin)*," *Physiology and Behavior* 18 (1977): 539. For the demonstration that testosterone shortens the resting period between action potentials in neurons, see K. Kendrick and R. Drewett, "Testosterone Reduces Refractory Period of Stria Terminalis Neurons in the Rat Brain," *Science* 204 (1979): 877.