Serotonin and Impulse Aggression: Not So Fast
Joel Wallman

The quest to root violent criminality in organic shortcomings has a long and, viewed with the wisdom of hindsight, sometimes silly history. Lombroso’s diagnostic taxonomy of criminal physical features, the phrenology of Gall, Kretschmer’s body typing and, more recently, the attempt to link the XYY or “supermale” genetic constitution to criminality are textbook cases of fruitless efforts to explain bad behavior as the outcome of bad biology.

Contemporary endeavors are, on the whole, far more sound in their scientific methods, if thus far not much more compelling. Studies linking persistent impulsive aggression to deficits or excesses of various juices of the brain (dopamine, GABA, MAOA), the nether regions (testosterone, estrogen), or parts in between (adrenal steroids) have yielded occasionally suggestive but generally equivocal findings. The same applies to research on areas of the brain, the most traveled in this search being the frontal and temporal lobes, amygdala, and hypothalamus.

One promising exception is the neurotransmitter serotonin. Dozens of studies have found that people with documented histories of impulsive violence have, on the average, a reduction in function of the serotonin system relative to people without such a profile. This has been found whether serotonin function is assessed by lumbar spinal tap of cerebrospinal fluid to determine the quantity of serotonin’s metabolic byproduct or by less direct measures, such as the magnitude of biochemical response to ingestion of a substance that increases serotonin production.

These and other methods are quite removed from direct assay of serotonin function in the brain, but the correlation between serotonin deficit and impulsive violence, both self- and other-directed, is a recurrent finding nonetheless. Moreover, studies in nonhuman animals in which serotonin levels were experimentally reduced through chemical intervention found an increase in aggressive behavior (compared to control animals subjected to identical delivery of an inert substance), suggesting that the correlation found in human research reflects a true causal relationship.

In the serotonin deficit, then, we seem to have a constitutional flaw underlying the syndrome of impulsive violent behavior. If serotonin abnormalities are truly linked in a specific way to aggression as opposed to behavior problems more generally, then we have a window into not just patologies of aggression but the normal neurobiology of aggression as well. This discovery also provides a basis for intelligent conjecture about the selective forces governing the evolution of both serotonin and aggression in animals in general, primates more specifically, and humans in particular.

Yet one needn’t be a student of neurotransmitters to wonder about the specificity of the connection between serotonin and aggression. A regular reader of New York Times articles on human behavior and health, for example, might well be troubled in attempting to collate the implicit claim that serotonin is the “aggression chemical” with reports that underactive serotonin circuits are also the cause of migraines (July 24, 1996, section C, p. 8), extreme shyness (May 18, 1999, section C, p. 1), obsessive-compulsive disorder (February 16, 1997, section 13CN, p. 3), anxiety and pessimism (November 29, 1996, section A, p. 1), and “restless leg” syndrome (night cramps) (April 10, 1996, section C, p. 10). A survey of popular books on the virtues of keeping one’s serotonin up will reveal that a deficit of this substance is responsible for craving and hence addiction to gambling, drugs, sex, and food (The Craving Brain, Ronald Ruden and Marcia Byalick); that, in addition to controlling emotion, serotonin is in charge of “intellect” (Naturally Slim & Powerful, Philip Lipetz and Jean Zevnik); and that serotonin is the culprit in insomnia (5-HTP: The Natural Way to Boost Serotonin and Overcome Depression, Obesity and Insomnia, Michael T. Murray). Combine this litany of affliction with the knowledge that tens of millions of people are being prescribed Prozac, a serotonin enhancer, on the apparently well-established medical belief that depression derives from—yes—a serotonin deficit, and, unless all of these reports and claims are dismissed as baseless, one is justified in concluding that a serotonin shortage manifests itself in a congeries of emotional and behavioral problems, including but by no means limited to aggression.

That conclusion is certainly consonant with the fact that serotonergic neurons, which reside in the brainstem, project their axons into many and functionally diverse regions of the brain, including the amygdala, hypothalamus, hippocampus, cerebellum, and temporal and prefrontal regions of the cerebral cortex. It would be surprising, given this wide ramification, if abnormalities of the serotonin system affected aggression in a specific way.

Just how sound are the numerous studies reporting a specific association between diminished serotonin function and violent behavior? A meta-analysis of this literature by Balaban and colleagues (1996) is illuminating. From 70 studies, Balaban chose 39 that provided sufficient information for an analysis employing the variables Balaban thought pertinent to answering the question. The subjects in these studies fall into three categories: violent psychiatric patients, nonviolent psychiatric or neurological patients, and normal, healthy control subjects. Not all studies employed all three groups, but a typical finding of those that did was reduced serotonin in the violent psychiatric group compared to both the nonviolent patients and normal controls, with no difference between the latter two, indicating that serotonin deficiency is associated specifically with violent psychiatric conditions rather than with serious psychiatric problems in general.

However, there are non-psychiatric sources of variability in serotonin level, and few of the serotonin studies take them into account (i.e., statistically control for them) in all subject categories used. In particular, serotonin (actually 5-HIAAA, its main break-down product) measured at the lumbar level through spinal tap is lower in males, goes up with age, and declines with stature. (Serotonin diffuses out of the brain into the cerebrospinal fluid. From there, most of it is transported to the bloodstream; the fraction making it...
Using those studies in the set of 39 that provided information on height, age, and sex of normal controls, Balaban computed the effects of those variables alone on serotonin level. These values were then used to adjust the measured serotonin levels in all studies for subject categories for which mean height and age and male-female ratio were published. Because the three subject categories happened to consistently differ in these traits, correcting for these non-psychiatric determinants of serotonin level yields results that are quite different from what is typically reported: violent psychiatric patients do indeed have somewhat lower levels than normal controls, but so do the non-violent psychiatric and neurological patients, and the psychiatric groups do not differ from each other. In short, people with a history of being in an institution or under psychiatric or neurological treatment have lower levels of serotonin than normal nonpatients.

In addition to the reasons adduced above for questioning the usefulness of low serotonin as a marker for impulsive aggression, there are reports in the scientific literature that, while far from refuting the claim that low serotonin increases impulsive aggression, contradict it and thus warrant weighing in the balance. These are not simply studies that fail to find a relationship between low serotonin and aggression—unless the relationship were extremely strong in a statistical sense, one would expect a certain number of studies to come up empty by chance even if the relationship were generally valid. One kind of contradictory finding is the observation in at least two studies that highly aggressive children evince not a reduction but an increase in serotonin function. (Castellanos et al. 1994; Halperin et al. 1994). And there is the much-cited discovery in a large Dutch family of an association between a genetic deficiency of the enzyme MAOA and impulsive violent behavior (Brunner et al. 1993). What has gone unremarked on in the discussion of this finding (which, predictably, was heralded in the non-technical media as the revelation of a "gene for aggression") is the problem it poses for the other major putative organic cause of abnormal aggression, serotonin. For MAOA is the enzyme that, among other functions, breaks down serotonin, which means that the affected men in this group would, arguably, have an excessively high level of serotonin. And, finally, the same primate experiments mentioned earlier, which showed that altering serotonin level affects behavior, also provide evidence that serotonin is equally a result of behavior. If the dominant male is removed from a group of vervet monkeys, an aggressive contest for dominance results. The male that ascends to top rank will experience an increase in serotonin level, and the exiled alpha male, if not returned to its group, will undergo a serotonin drop (McGuire and Troisi 1998). To the extent that it is legitimate to extrapolate to humans, this observation calls into question the assumption that serotonin abnormality precedes the behavioral problems with which it has been linked.

The correct inference from all of the foregoing is not that anyone low on the serotonin scale should be a dangerous, depressed, and overweight compulsive gambler, torn between shyness and nymphomania, who would be kept awake at night by their headaches and restless legs even if they didn't suffer from insomnia. It is rather that serotonin is not a very discriminating marker for violence and that the neuropsychological and neurochemical characteristics that accompany low serotonin—whether as causes, consequences, or both—are not limited to brain regions that govern aggression.

But what if there were no ambiguity about the serotonin-aggression relationship? If it were clearly established that underactive serotonin circuits increased the risk for serious aggressive behavior, and only that risk, what insight would be gained into human violence? Would it help us understand the shocking increase in youth homicide in the United States beginning in the middle 1980s or the decrease of recent years? Would it clarify why the rate of violent crime has declined in New York, Los Angeles, and Tampa but increased in New Orleans and Richmond, why Nevada's murder rate is 10 times higher than South Dakota's, or why the U.S. rate is 15 times higher than Britain's?

The explanation of these facts will come not from research in neurobiology but from understanding economic forces, variation in cultural mores regarding the acceptability of violence, diversity in the kinds and efficacy of means of informal and formal social control, and availability of firearms. A reasonable response to this assertion would be to suggest that individual differences in serotonin could explain why this person rather than the next succumbs to the distinctive mix of violence-promoting influences impinging on a given neighborhood, ethnic group, class, or nation. I am rather pessimistic about the potential of this approach, however. But that may just be the serotonin talking.

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References


