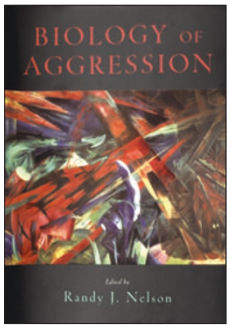
The many roots of aggression



Biology of Aggression

Edited by Randy J Nelson

Oxford University Press, 2005
528 pp, hardcover, $85.00
ISBN 0195168763

Reviewed by Jordan Grafman, Maren Strenziok & Frank Krueger

Aggression is critical to survival, but so is learning when to suppress aggressive impulses. Is it appropriate to head-butt someone who insults your sister during a world championship soccer game when a penalty could cost your team the trophy? Words may provoke, but context matters. Over normal development, impulsive aggressive tendencies diminish, reason rules, and strict social rules about aggression become a guidepost for navigating through adolescence and adulthood.

As the title suggests, *Biology of Aggression* is heavily weighted toward understanding the role of biology in aggressive behavior. This timely volume covers genetics, neurotransmitters, hormones, development, pharmacology and psychophysiology. Almost all the chapters are up to date, point out weaknesses in previous investigations and suggest future directions—a real help to the novice in this area. Of course, one principal reason that neuroscientists study aggression is to learn how to modulate it in humans and perhaps how to cope with it in other species. This book provides a good yardstick to measure where we stand in attaining those goals, while making clear that we are not yet able to predict with any useful degree of precision who will be aggressive and when they will be aggressive.

In humans, aggression comes in many forms: verbal, physical, sexual; with or without a weapon; impulsive or premeditated. As noted in the book, a major problem is the absence of a widely acceptable definition for aggression across different species and adequately validated scales for kind and severity of aggressive acts. Despite these inherent limitations, the book articulates some clear findings on the relationships of brain structure, chemistry, physiology and aggression.

Inappropriate aggression is generally associated with impaired executive cognitive processes, typically the abilities to resist impulses, to modulate behavior and to understand the consequences of one's behavior. These cognitive processes depend on the prefrontal cortex, which is impaired in many aggressive individuals. Neuropsychological tests show impaired executive function in adolescent and adult offenders. Structural magnetic resonance imaging and functional positron emission tomography imaging show that the aggressive population has high incidence of reduced prefrontal volume and metabolism. Similarly, aggressive individuals show high rates of neurological abnormality, with abnormally elevated rates of so-called frontal release signs. The theory that impairment in prefrontal cortical function occurs in and probably in part causes certain forms of aggressive behavior is further supported by clinical studies of brain-damaged subjects. For example, Vietnam veterans with prefrontal ventromedial brain injuries demonstrate more aggression after than before their injury. However, not all individuals with acquired prefrontal ventromedial lesions become aggressive.

Before recognizing the role of prefrontal cortex, researchers attributed aggression to the amygdala and other structures of the limbic system. The 'cold-hearted' manner of some of the most violent killers suggested possible abnormalities in how emotions are registered. This hypothesis has been borne out in part, as the book reports. Chronically aggressive individuals, both adult and adolescent, show reduced emotional reactivity, including diminished autonomic responses, as measured by skin conductance, heart rate changes and contraction of the facial muscles that cause one to wince when viewing an unpleasant scene. The most violent offenders—murderers—do not harbor the same implicit distaste for aggression that normal controls do.

This book clearly argues that pathological aggression is not a unitary construct but instead posits that there are different forms of aggression depending on factors ranging from genetic abnormalities, including polymorphism-biased susceptibility, to variation in levels of neurotransmitters, particularly serotonin. Abnormally low serotonin is found in the cerebrospinal fluid of violent offenders and in the brainstems of aggressive mice, and serotonin agonists decrease aggressive behavior in several animal species. In humans, selective serotonin reuptake inhibitors and antipsychotic agents may reduce aggression in some individuals. Aggression also depends on environmental context (such as scarcity of resources), social necessity (for status or to defend territory) and gender. Not surprisingly, males tend to be more physically aggressive than females.

The etiology of neurobiological impairments in the aggressive population requires further study. The book discusses a number of proposed causative factors, including genetics, prior head injuries and physical insults, and substance abuse. These factors certainly can contribute to impairment, but they are not present in all aggressive subjects, and not all individuals with head injuries become violent.

Studying the key variables identified in this book may help reduce aggression and recidivism in the adolescent and adult violent population, as well as persistent bullying at school. The most common treatment for aggressive individuals, incarceration, typically does not reduce aggression, as evidenced by the high rates of repeat offenses following release.

Biology of Aggression has some weaknesses, including redundancies of definition and description across chapters, an occasional chapter that seems out of place (for example, on submission) and perhaps a few chapters that are missing (one on the environmental causes of aggression would have been welcome), but all in all this book is the best of the recent group on this topic. ■

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Corrigendum: Selective inhibition of 2-AG hydrolysis enhances endocannabinoid signaling in hippocampus

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Nature Neuroscience **8**, 1139–1141 (2005); **Published online 7 August 2005**

Our paper identified 6-methyl-2-*p*-tolylaminobenzo[*d*]oxazin-4-one (URB754; Specs) as a monoacylglycerol lipase (MGL) inhibitor that enhances hippocampal depolarization-induced suppression of inhibition (DSI). However, in subsequent tests of non-commercial URB754, we failed to replicate these results, suggesting that a bioactive impurity was present in the commercial material. We have identified this impurity as bis(methylthio)mercurane (**Supplementary Results** online). Because this compound interacts with multiple targets, we tested another MGL inhibitor, methylarachidonylfluorophosphonate (MAFP), which prolonged DSI (**Fig. 1**), confirming that monoacylglycerol lipase contributes to the termination of DSI, as others have reported[1]. Another generation of endocannabinoid metabolism inhibitors is needed to test this hypothesis further.

Note: Supplementary information is available on the Nature Neuroscience website.

1. Szabo B *et al. J. Physiol. (Lond.)* **577**, 263–280 (2006).

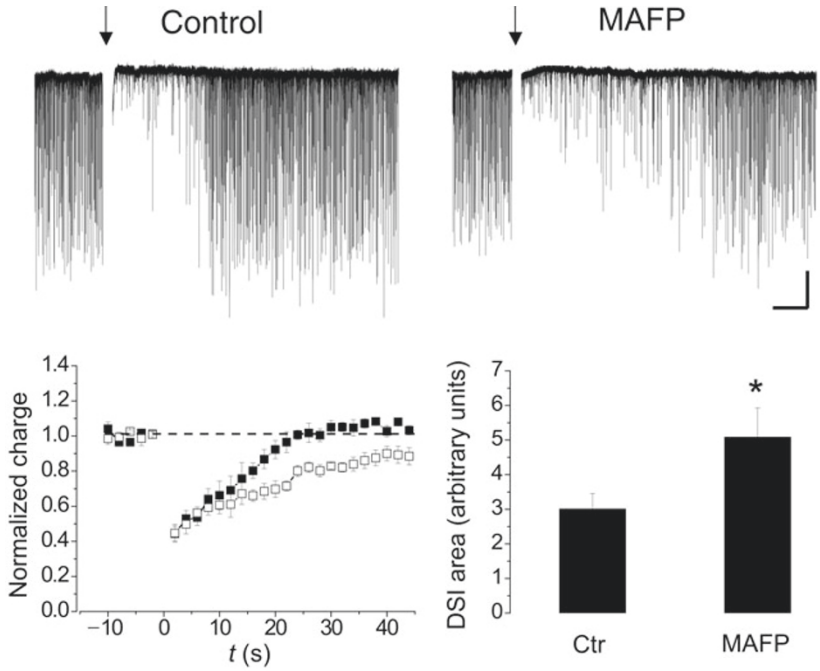

Figure 1 Effects of MAFP on DSI in hippocampal CA1 pyramidal cells. Top, traces from a representative experiment showing the effects of vehicle (ethanol, 0.00003%) or MAFP (Tocris, 45 nM) on the transient reduction of spontaneous inhibitory postsynaptic potentials (IPSCs) elicited by a depolarizing stimulus (arrow). Scale bars, 100 pA, 5 s. Bottom left, averaged time-course of DSI after administration of vehicle (solid squares) or MAFP (open squares). Bottom right, DSI area in the first 30 s after stimulus application was significantly larger in MAFP-treated than in control slices.

Erratum: Reduced sodium current in GABAergic interneurons in a mouse model of severe myoclonic epilepsy in infancy

Frank H Yu, Massimo Mantegazza, Ruth E Westenbroek, Carol A Robbins, Franck Kalume, Kimberly A Burton, William J Spain, G Stanley McKnight, Todd Scheuer & William A Catterall

Nature Neuroscience **9**, 1142–1149 (2006); **published online 20 August; corrected after print 13 December 2006**

In the version of this article initially published, the acceptance date was incorrect. The paper was accepted on 2 August 2006. This error has been corrected in the PDF versions of the article.

Erratum: The many roots of aggression

Jordan Grafman, Maren Strezniak & Frank Krueger

Nature Neuroscience **9**, 1347 (2006); **published online 26 October 2006; corrected after print 21 November 2006**

In the version of this article initially published, the second author's name was spelled incorrectly. The correct name should be Maren Strenziok. The error has been corrected in the HTML and PDF versions of the article.