Preface

Despite its relevance to science as well as society, aggression remains an understudied topic in the basic neurosciences and in the psychopharmacological management and treatment of patients. The present volume is intended to appeal to both clinical practitioners and preclinical researchers who seek to enhance their understanding of basic molecular and cellular processes, neural circuitry, and behavioral mechanisms that are critical for the motivation and expression of aggressive behavior. The current contributions advance our insights into neurobiological mechanisms and begin to identify genes and gene networks which—in interaction with environmental triggers—render aggressive behavior more or less likely to occur. It is evident that the current research proceeds in a more rational, mechanistic way relative to its serendipitous beginnings. For example, long before the sites and mechanisms of action of lithium or benzodiazepines were understood, it was discovered that they calm agitated and aggressive individuals (Cade 1949; Randall et al. 1960).

From a psychiatric perspective, research on aggression has been impeded by inadequate recognition of these behavioral domains in consecutive versions of the Diagnostic and Statistical Manual, discouraging the development of compounds and interventions with specific anti-aggressive effects. One cardinal criterion for novel medications in this area should be their degree of specificity for reducing aggressive behavior relative to undesirable adverse effect profiles. Quantitative ethological methods enable the comparison of reducing aggressive acts with effects on other elements in the behavioral repertoire to learn about the behavioral specificity of novel compounds.

A fundamental challenge in aggression research is the distinction of the neurobiological mechanisms mediating escalated pathological aggressive behavior relative to those for species-typical patterns of behavior that are necessary for the survival of the organism (Miczek et al. 2013). In humans, of course, this distinction is further compounded by legal, ethical, and societal restriction on aggression no matter the biological concomitants. The neural circuits of different kinds of mammalian aggression have begun to be delineated by immunohistochemistry of immediate-early gene expression, intracranial microinjection, in vivo microdialysis,
optogenetics techniques in experimental animals, and high resolution functional imaging techniques. It is now feasible to conceptualize neurocircuits for different kinds of aggressive behavior to encompass nuclei in the mesencephalon projecting to hypothalamic, amygdaloid, septal, and hippocampal sub-nuclei, loops between striatum and thalamus with frontal and prefrontal structures and important feedback to limbic and mesencephalic nuclei (chapters by Kruk; Gobrogge; Bedrosian and Nelson; Barr and Driscoll; Takahashi and Miczek; Haller; Morrison and Melloni; de Almeida et al.). Identifying not only the neural structures and projections, but also the precise molecular processes within these critical cell groups that mediate escalated aggressive behavior remains an urgent task.

A most instructive example is our emerging understanding of the role of serotonin, the most intensively investigated neurotransmitter system that has been linked to aggression. It is evident that the classic serotonin deficiency hypothesis that associates defects in synthesis, release, receptor activation, or metabolism to a heightened propensity to engage in aggressive behavior has been replaced with a framework that incorporates a much more nuanced set of modulatory and regulatory mechanisms. The current contributions (Barr and Driscoll; Takahashi and Miczek; Morrison and Melloni; Bedrosian and Nelson; Gobrogge; Beck et al.; Buckholtz et al.) illustrate how serotonergic activity is modulated by a cascade of direct and indirect systems that range from nitric oxide synthase, neuropeptides and neurosteroids to excitatory and inhibitory amino acids and thereby reduce or intensify aggressive behavior.

We invite you to be inspired by the current contributions which we hope will renew interest in the neurobiology of aggressive behavior and reactivate this largely neglected area of research.

References


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