

## Introduction

# The Phenomenology and Treatment of Aggression Across Psychiatric Illnesses

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Aggression is a dimensional symptom that often brings individuals to psychiatric treatment and can make them difficult to manage, particularly in institutional settings such as nursing homes. On one end, the dimension of aggression encompasses increased activity and agitation and on the other, violent criminal behavior. Symptoms of aggression occur in a wide variety of psychiatric disorders, but currently no pharmacologic agent is approved specifically for the treatment of aggression. This Supplement is derived from a closed symposium at which a group of investigators discussed the development of pharmacologic protocols aimed at studying the treatment of aggressive behavior in a wide variety of psychiatric disorders.

Elizabeth B. Weller, M.D., and colleagues described the phenomenology, etiology, assessment, and pharmacologic treatment of aggression in children with attention-deficit/hyperactivity disorder (ADHD), conduct disorder, and pervasive developmental disorders. Although numerous pharmacologic agents have been tried in this population, most of the literature involves uncontrolled studies with small samples of patients.

Intermittent explosive disorder is characterized by the DSM-IV as discrete episodes of failure to resist aggressive impulses that result in serious assaultive acts or destruction of property. Susan L. McElroy, M.D., who studied the phenomenology, comorbidity, and treatment response of 27 subjects who met DSM-IV criteria for intermittent explosive disorder, suggested that explosive episodes in these patients, which often respond to mood-stabilizing drugs, may be linked to bipolar disorder.

Agitation, defined as motor restlessness such as fidgeting and pacing associated with inner tension, is a common and often troublesome symptom in major depression, according to Alan F. Schatzberg, M.D., and Charles DeBattista, M.D., D.M.H., who are currently in the midst of a controlled double-blind trial of divalproex versus placebo augmentation in patients who have agitated major depression and are being treated with selective serotonin reuptake inhibitors (SSRIs) or other antidepressants.

Approximately 30% to 40% of depressed patients experience anger attacks, sudden intense spells of uncharacteristic anger inappropriate to the situation at hand. Maurizio Fava, M.D., and Jerrold F. Rosenbaum, M.D., described the Anger Attacks Questionnaire, which was designed to identify the presence of such attacks, and noted that the attacks have disappeared in a majority of patients treated with the antidepressants—fluoxetine, sertraline, or imipramine.

While bipolar disorder is generally viewed as a disturbance of mood, prominent aspects of behavior that occur during depressive and manic states of bipolar disorder, including aggression, are not specific to mood syndromes and occur across many psychiatric states. Alan C. Swann, M.D., noted that severe hyperarousal beyond that usually associated with the

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classic manic or depressive episodes of bipolar disorder could result in a variety of behavioral or symptomatic disturbances, including aggression. Successful management of aggression in manic patients, he added, requires an integrated environmental and pharmacologic treatment that provides an externally coherent environment and internal resolution of the hyperarousal state.

Although not included in the DSM-IV criteria for posttraumatic stress disorder, anger and aggression are acknowledged features of this illness, reported Rachel Yehuda, Ph.D., who also stated that pharmacologic treatment generally benefits some, but not all, symptoms of posttraumatic stress disorder and that mood stabilization is generally the primary goal of treatment. Dr. Yehuda suggested a role for anticonvulsants in the treatment of the impaired impulse control and violent outbursts that often accompany posttraumatic stress disorder.

Eric Hollander, M.D., reported that anger and aggression are characteristics linking the ends of the spectrum of compulsive and impulsive disorders: obsessive-compulsive disorder (OCD) and borderline personality disorder. Serotonin dysfunction has also long been associated with both OCD and impulsive aggressive behavior, the latter of which is often found in borderline personality disorder. Mood stabilizers, including lithium, carbamazepine, and divalproex, have been found useful for aggression in small samples of patients with borderline personality disorder, but additional controlled trials with larger samples are needed.

Elderly patients with dementia are often placed in long-term care facilities because of agitated and aggressive behavior. Murray A. Raskind, M.D., suggested that aggression in this population is best understood as a product of the interaction of neurobiological, cognitive, and environmental factors. Treatment strategies should focus on improvement of cognition, control of the patient's environment, and mediation of neurobiological disruption. A number of agents have been tried, but controlled studies of drugs that appear promising such as anticonvulsants and SSRIs are lacking.

Primate models of aggressive behavior, described by Ned H. Kalin, M.D., are providing insights into the biological mechanisms that underlie such behavior. Defensive aggression in rhesus monkeys is related to extreme asymmetric right frontal activity in the brain and to high plasma cortisol concentrations. Offensive or impulsive aggression is associated with low serotonergic activity in the central nervous system and high levels of CSF free testosterone. Both forms of aggression in rhesus monkeys appear to be mediated by environmental factors, particularly disruptions to the mother-infant relationship.

Since aggressive behavior occurs in so many psychiatric disorders, it is important to identify the neuroanatomical circuitry implicated in aggression, said K. Ranga Krishnan, M.B., Ch.B. Most imaging studies in psychiatry currently focus on the cortex, but many behaviors associated with emotions are driven primarily at the subcortical level. Studies of patients with brain lesions provide evidence that frontal lobe impairment may be related to aggression. Investigation of the case report literature may help demonstrate the relationships of the location of lesions to specific behaviors. As understanding of the neuroanatomical circuitry of aggression grows, the ability to successfully treat aggressive symptoms should also increase.

Investigating aggression as a dimensional syndrome or construct that occurs in the context of many DSM psychiatric diagnoses could include neuroimaging, genetic, and pharmacologic studies. Protocols are needed for controlled, head-to-head comparisons of specific agents that target aggressive symptoms in a variety of psychiatric disorders.