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Aggressive behavior: A comprehensive review of its neurochemical mechanisms and management

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ABSTRACT

Aggression is a deliberate series of actions that lead to harm, injury, or destruction of another organism, and is the most common factor promoting violent crimes. Beyond being the immediate cause of physical injury, aggressive behavior also produces profound long term emotional disabilities in its victims. When outburst of aggression is comorbid with DSM-IV-defined neuropsychiatric disorders, the offenders are usually given psychiatric care; however, when they appear normal or healthy, their most likely fate is punishment by the law. This punitive approach often increases aggression, thereby promoting the propensity for violent crimes. Antipsychotics are the drugs commonly used for treatment of aggression and violent outbursts. However, the uses of these drugs have serious side effects of catalepsy or impairment of sensorimotor performance. They also affect the defense or flight capabilities of organisms, which further limit their usefulness in aggression. Thus, there is a critical need to search for agents that can selectively reduce aggression without affecting other behaviors or causing any serious unwanted side effects. This review focuses on the types, neurochemical bases, and animal models of aggression, with a comprehensive appraisal of the pharmacological approach to the treatment of the disorder.

Contents

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1. Introduction

Aggression is a deliberate series of actions that lead to harm, injury, or destruction of another organism and is the most common factor promoting violent crimes. Beyond being the immediate cause of physical injury, aggressive behavior also produces profound long term emotional disabilities in its victims (Weinshenker & Siegel, 2002). When outburst of aggression is comorbid with DSM-IV-defined neuropsychiatric disorders, the offenders are usually given psychiatric care, but when they appear normal or healthy, their most likely fate is punishment by law (Weinshenker & Siegel, 2002). However, this punitive approach often increases aggression, thereby promoting the propensity for violent crimes.

Although aggression is detrimental to the society, it also serves as a useful defensive purpose for obtaining the desired goal of self-preservation in life threatening events (Moffitt et al., 2008; Moyer, 1968; Siegel & Victoroff, 2009). Mental illness, prolonged stress, poverty, and drug abuse are common factors that contribute to the higher rate of violence or aggressive outbursts (Gowin, Swann, Moeller, & Lane, 2010; Moffitt et al., 2008; Moss, Yao, & Panzak, 1990; Siegel & Victoroff, 2009; Weinshenker & Siegel, 2002). In vulnerable individuals, stress in particular, can lead to a subtype of depression characterized by anger, anxiety, and aggression (Barnett, Fagan, & Booker, 1991; Weinshenker & Siegel, 2002). Stress might be a strong factor that can precipitate aggression and predicts the severity of developing violence behavior (Barnett et al., 1991).

The major limitation in the study of aggression is the lack of suitable animal models with predictive validity of human aggression that can provide insight into the neural mechanisms underlying the disorder, as well as new targets of therapeutic intervention (Blanchard & Blanchard, 2003; Gowin et al., 2010; Moffitt et al., 2008; Miczek, Fish, De Bold, & De Almeida, 2002; Miczek, Weerts, Haney, & Tidey, 1994). The use of antipsychotics in the treatment of aggression is limited by serious adverse effects, which necessitate the search for agents that can selectively reduce aggression without affecting other behaviors or causing any serious unwanted side effects. Current research is now focused on the development of serenics (compounds with selective anti-aggressive activity) that stimulate specific subsets of 5-HT receptors that are critically involved in the initiation and execution of aggressive acts (Miczek et al., 2002; Moffitt et al., 2008). However, the complex neural mechanisms and lack of a unified classification scheme for the categorization of human aggression has contributed greatly to the slow pace in the development of specific anti-aggressive agents (Weinshenker & Siegel, 2002). The aim of this review is to discuss the types, neurochemical bases, and animal models of aggression, with an appraisal of the pharmacological approach to the treatment of the disorder.

2. Types of aggression

The lack of a unified classification scheme for the categorization of human aggression has contributed greatly to the slow pace in the development of new medicines with specific anti-aggressive properties (Weinshenker & Siegel, 2002). Various types of aggression have been described in literature based on the factors that trigger it. Moyer (1968) classified aggression into the seven different categories: (1) Fear induced-aggression: This occurs when the animal is placed in a position where escape is denied and turns, instead, to attack a second animal perceived as a threat. (2) Maternal-induced aggression: This is a form of an attack that occurs when an animal is placed close to its young ones and a second animal approaches. (3) Intermale-induced aggression: An attack occurring by a male toward another male, but not a female, in its immediate environment. (4) Irritable aggression: An attack occurring in response to a threat, intimidation, or to an environmental condition which is irritating. (5) Sex-related aggression: In humans, sexual arousal is frequently associated with increased levels of hostility or hostile fantasies. In animals, components of aggressive behavior are sometimes associated with sexual acts. The aggressive and sexual aspects appear as components of the same behavioral act, thus, creating difficulties in classifying these behaviors. (6) Territorial aggression: An attack occurring when an intruder enters into an area that an animal has determined for itself to be its own domain. This is commonly known as a resident–intruder model. Most often, tests involving the resident–intruder model utilize animals of the same species although a resident animal might also attack an intruder of a different species (Malone et al., 1998; Weinshenker & Siegel, 2002). (7) Predatory aggression: Specifically triggered by the presence of a prey within the visual field of the predator; this response can be elicited in experimental conditions by stimulating the lateral hypothalamus of the cat (Siegel, Roeling, Gregg, & Kruk, 1999). The response is characterized by stalking of an anesthetized rat, which is followed by a bite to the back of its neck, which continues until stimulation is terminated (Siegel et al., 1999). It is evident that all these forms of aggression are meant for the dual purposes of survival and reproduction whether for obtaining food, access to a mate or protection. However, the central question that may be asked is whether these aggressive behaviors are related by a common neural mechanism or to different mechanisms underlying them.

2.1. Bimodal classification of aggression

A number of investigators have attempted to classify aggressive behavior in animals or humans into affective defense and predatory attack (Weinshenker & Siegel, 2002). Affective defense is an aggressive response based on the presence of fear and/or threat, which may be real or perceived. Predatory attack has been understudied relative to affective defense, and consists of a purposeful and goal-directed attack with the absence of sympathetic arousal (Weinshenker & Siegel, 2002). Thus, the seven types of aggression belong to one of two categories, predatory attack or affective defense behavior (Eichelman, 1985; Malone et al., 1998). All categories of aggression that include fear-induced, maternal, intermale, sex-related, irritable, and territorial appear to have a similar common feature, namely an aggressive response based on the presence of elements of fear and/or threat that may be real or perceived. Thus, these categories of aggression may be classified as affective defense (Weinshenker & Siegel, 2002). The motivation frequently triggering aggressive responses may be pain, a threat of another organism of the same or different species, and territory perceived by the animal in question as its own (Malone et al., 1998). Moyer showed the unique characteristics associated with affective defense, which are submission and appeasement, together with their associated postural positions. Moreover, these forms of behavior have been clearly described in different species, including mice, rats, cats, dogs, and primates. Moyer argues that submission reflects an aggression-inhibiting mechanism that has survival value by signaling to the dominant animal that the fight is over (Weinshenker & Siegel, 2002). In addition, the posture adopted by the defeated animal makes it difficult for the dominant animal to continue its aggressive acts. The