

Alcohol, Serotonin, and Aggression

ROBERT O. PIHL, PH.D., AND JORDAN B. PETERSON, PH.D.

Deficiencies in the brain chemical serotonin are associated with increased tendency to violence and victimization. Alcohol consumption interacts with serotonin levels to increase the likelihood of aggression.

The role of brain chemistry in regulating behavior is difficult to determine, especially in behavior as complex as aggression.

Bushman and Cooper (1990) define aggression as "behaviour directed towards the goal of injuring another living being, who is motivated to avoid such treatment" (p. 341).

Aggression itself is not a mental disorder. A tendency to display aggressive behavior is considered an aspect of personality, rewarded under certain circumstances, punished under others. Thus, it is not aggression itself, but the inappropriate display of aggression, that society defines as abnormal. The set of all acts defined as aggressive is therefore heterogeneous in the extreme.

Despite the difficulties involved, research has shed light on some chemical processes by which the brain regulates aggression. The brain chemical serotonin is one chemical that may play a key role in promoting aggressive behavior. Alcohol is known to facilitate aggression in persons with defects in serotonin-related processes. This article will explore the interactions between alcohol, serotonin, and aggression.

SEROTONIN

Serotonin is a neurotransmitter, a chemical by which nerve cells communicate with one another. The communicating ends of adjacent nerve cells are separated by a microscopic gap called a synapse. To

communicate, a nerve cell releases neurotransmitter molecules into the synapse. The neurotransmitter molecules cross the synapse and become bound to protein molecules (receptors) embedded in the surface of the other nerve cell. There are several types of receptor, each of which binds a specific type of neurotransmitter. The binding of a neurotransmitter to the appropriate receptor sets off a chain of events within the receiving nerve cell. The ultimate effect of this process may be to stimulate or inhibit a particular type of brain activity.

Serotonin helps regulate many chemical processes in the brain, and it also helps regulate such functions as bodily rhythms, food and water intake, sexual behavior, and response to pain. Various mental disturbances, including depression, alcoholism,¹ obsessive-compulsive disorder, eating disorders, and sleep disorders, appear to be associated with reduced brain serotonin concentrations (Whitaker-Azmitia and Peroutka 1990).

The activity of serotonin is itself regulated by mechanisms that prevent excessive accumulation of serotonin in the synapse. One such mechanism is the reuptake of serotonin by the nerve cell that released it. Another mechanism is the

¹Throughout this article, we use the terms "alcohol abuse," "heavy drinking," "alcoholism," and "alcohol dependence." There is overlap among these terms in the alcoholism literature; therefore, our wording at any given point must rely on the terms used by the authors in each report cited.

action of enzymes that convert serotonin into inactive metabolites, or breakdown products (Cooper et al. 1982).

SEROTONIN AND AGGRESSION

Animal Studies

Various studies have compared serotonin function among members of animal species that display different levels of aggression when provoked. Brain serotonin concentration, difficult to assess directly, may be estimated by measuring the concentration of the serotonin metabolite 5-hydroxyindoleacetic acid (5-HIAA) in cerebrospinal fluid (CSF). In one study, the CSF of aggressive rhesus monkeys was found to contain reduced levels of 5-HIAA in comparison with the CSF of matched nonaggressive control animals (Higley et al. 1992). Conversely, animals selected for domesticity (reduced aggression), such as tame silver foxes and laboratory rats, appear to have higher levels of brain serotonin function compared with their wild, more aggressive counterparts (Popova et al. 1991).

Various laboratory chemicals can transiently modify serotonin function, producing alterations in serotonin synthesis, storage, release, or reuptake. For example, parachlorophenylalanine (pCPA), which inhibits serotonin synthesis, heightens irritability and various kinds of aggressive behavior among rats, mice, and vervet monkeys (see Chamberlain et al. 1987 for a brief review). This chemically induced increased aggression can be eliminated by the drug fluoxetine, an inhibitor of serotonin reuptake, which counters the effects of pCPA by increasing the concentration of serotonin in the synapse. The increased aggression can also be eliminated by 5-hydroxytryptophan, an amino acid from which the brain manufactures serotonin.

Serotonin function can be more permanently altered. For example, surgical, electrical, or chemically induced damage to key serotonin-producing structures of

ROBERT O. PIHL, PH.D., is a professor in the Department of Psychology and the Department of Psychiatry, McGill University, Montreal, Quebec, Canada.

JORDAN B. PETERSON, PH.D., is an assistant professor in the Department of Psychology, Harvard University, Cambridge, Massachusetts.

the brain profoundly decreases serotonin activity. Such damage produces aggressive behavior among members of various species and can be at least partly reversed by procedures that facilitate serotonin production or function (see Chamberlain et al. 1987).

Brain serotonin levels can also be manipulated dietetically. The amino acid L-tryptophan is the dietary factor from which brain cells synthesize 5-hydroxytryptophan and, subsequently, serotonin. Tryptophan-free diets, which decrease brain serotonin activity (Biggio et al. 1974), heighten aggression among rats, mice, and monkeys (see Chamberlain et al. 1987). Figure 1 schematically illustrates behavioral differences among vervet monkeys fed diets supplemented with, balanced in, or depleted of tryptophan. Tryptophan depletion increased aggression among males, particularly during social interactions (such as competition during feeding) that tend to elicit aggression.

Human Studies

Reduced brain serotonin function is associated with heightened vulnerability to depression, increased risk of violent suicide, propensity to exhibit aggressive or impulsive behavior, and susceptibility to alcohol abuse both among persons with psychiatric disorders and among the general public. All of these manifestations appear causally linked; the presence of one appears to substantially heighten risk for any or all of the others (see Virkkunen and Linnoila 1993).

A variation of the dietary tryptophan-depletion procedure has been designed for application to humans. During this procedure, human volunteers ingest an amino acid beverage devoid of L-tryptophan. Ingestion of this biologically unbalanced mixture hampers the utilization of tryptophan already present in the body, thereby interfering with ongoing serotonin synthesis. After 5 or 6 hours, brain serotonin concentrations are reduced, alterations in food selection occur (Young et al. 1988), and mood disturbances appear in both recovering depressives (Delgado et al. 1990) and in normal subjects (Young et al. 1985). One study demonstrated increased aggression following ingestion of such a tryptophan-depleted beverage (Pihl et al. unpublished data). Tryptophan supplementation, by contrast, appears to reduce aggressive displays among very aggressive psychiatric patients (Morand et al. 1983; Volavka et al. 1990).

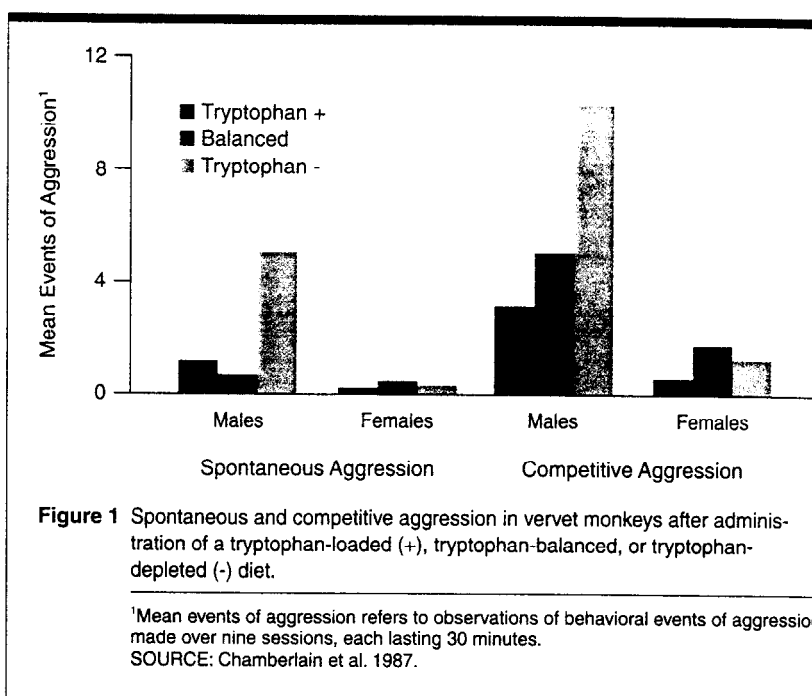


Figure 1 Spontaneous and competitive aggression in vervet monkeys after administration of a tryptophan-loaded (+), tryptophan-balanced, or tryptophan-depleted (-) diet.

¹Mean events of aggression refers to observations of behavioral events of aggression made over nine sessions, each lasting 30 minutes.
SOURCE: Chamberlain et al. 1987.

Suicide frequently occurs in association with depression and may result from a mixture of depression and aggression, both of which are associated with reduced serotonin activity. Five out of seven studies reviewed by Mann and colleagues (1990) reported decreased 5-HIAA levels in the brainstems of suicide victims. Many studies have also found a relationship between low serotonin activity (assessed by cerebrospinal 5-HIAA levels) and the level of violence in suicide attempts (reviewed in Mann et al. 1990).

Nerve cells often respond to depletion of a neurotransmitter by increasing the number or sensitivity of the receptors that bind that neurotransmitter. This process, known as upregulation, serves to damp excessive fluctuations in a neurotransmitter's activity. Three out of four relevant studies reported increased numbers of a serotonin-specific receptor in the brains of suicide victims. An additional report described upregulation of this receptor in the brains of deceased depressed patients who died of causes other than suicide. These studies of receptor upregulation, together with the results of the 5-HIAA studies described above, confirm the association of low serotonin activity with depression and suicide (reviewed in Mann et al. 1990).

Reduced levels of cerebrospinal 5-HIAA are also found in other types of aggressive or impulsive populations: children who display severe cruelty to

animals or who are otherwise aggressive (see Kruesi et al. 1990); persons with extensive histories of aggressive behavior; men with poor impulse control; persons who repeatedly commit violent crimes; and impulsive, alcohol-abusing persons with a family history of male alcoholism (see Virkkunen and Linnoila 1993 for a review).

ALCOHOL AND AGGRESSION

After mood disorder, alcoholism is the most prevalent risk factor among persons who commit suicide (Roy and Linnoila 1990), and a high proportion of suicide victims were drinking heavily prior to time of death (Murdoch et al. 1990). A high proportion of perpetrators and victims of violent crime, perhaps the majority, have also been found to be intoxicated (according to various measurements) at the time of the crime (Murdoch et al. 1990). A high proportion of antisocial people² are alcoholic, and childhood conduct disorder³ may be the most reliable predictor of adult alcoholism (Pihl and Peterson 1992).

²A mental disorder characterized by a pattern of irresponsible and antisocial behavior since the age of 15

³A disturbance of conduct in people under 18, characterized by antisocial, often violent, behavior; often precursor to antisocial personality disorder.

SEROTONIN AND ALCOHOL

Brain serotonin activity may play a role in governing alcohol intake and in partly determining predisposition to alcohol abuse and dependence.

Animal Studies

Drugs designed to reduce serotonin activity have produced mixed effects on voluntary alcohol ingestion in rats. The serotonin-synthesis inhibitor pCPA most frequently (and paradoxically) *decreases* alcohol consumption. On the other hand, a nerve poison that decreases serotonin activity increases alcohol consumption in rats, at least under certain circumstances. Drugs designed to increase serotonin activity reduce voluntary alcohol consumption in rats. Serotonin, tryptophan, or 5-hydroxytryptophan reduce alcohol consumption, as do various serotonin reuptake inhibitors (reviewed in LeMarquand et al. in press).

Scientists have bred strains of rats that drink alcohol solutions in preference to water. The Preferring (P) and High Alcohol Drinking (HAD) strains were found to have reduced serotonin activity compared with their Nonpreferring (NP) or Low Alcohol Drinking (LAD) counterparts (LeMarquand et al. in press). Drugs that increase serotonin activity often reduce alcohol consumption in the P and HAD strains. However, the ALKO strain of alcohol-preferring rats appears to have higher levels of serotonin activity than do non-alcohol-preferring rats (McBride et al. 1989); this issue is still unresolved.

Short-term alcohol administration produces complex and contradictory effects on serotonin function among various animal species (reviewed in LeMarquand et al. in press). By contrast, chronic alcohol administration increases serotonin concentration in CSF and facilitates serotonin activity. Cessation of chronic consumption tends to decrease serotonin concentration concurrently with the appearance of alcohol withdrawal symptoms.⁴ Serotonin levels then gradually return to normal, providing abstinence is maintained (reviewed in LeMarquand et al. in press). The serotonin decrease associated with withdrawal may play a role in

initiating or maintaining the craving for alcohol that occurs during that period.

Human Studies

Studies of the effects of acute alcohol administration on serotonin activity in healthy, non-alcohol-abusing, nonalcoholic volunteers have produced results too contradictory to summarize here (LeMarquand et al. in press). However, studies assessing the effects of serotonin reuptake inhibitors have consistently demonstrated reduced alcohol intake among various groups of males: male social drinkers, mildly alcohol-dependent males, and alcohol-dependent males. These results buttress similar evidence derived from the animal studies described above.

Studies assessing indicators of serotonin function among alcoholic subjects have yielded interesting results. Alcoholics have reduced serotonin function as assessed by reduced levels of CSF 5-HIAA (Banki 1981) and by other measurements, particularly during withdrawal (Buydens-Branchey et al. 1989). A substantial body of evidence suggests that reduced serotonin function by itself is not necessarily a risk factor for alcoholism. Rather, serotonin deficiencies are associated with alcoholic predisposition among people characterized by depression, poor impulse control, abnormal glucose metabolism, heightened self- and other-directed aggression, abnormalities in daily bodily rhythms, and early onset of problematic alcohol use (reviewed by Virkkunen and Linnoila 1993). Such people may damage their already fragile serotonin system by abusing alcohol; this may increase serotonin activity in the short term but lower it in the long term, as described previously.

SEROTONIN, ALCOHOL, AND AGGRESSION

Serotonin

Serotonin governs brain activity in several ways that appear to affect the expression of aggression (Spont 1992). For example, the neurotransmitter dopamine appears to facilitate psychomotor activity⁵ motivated by reward and punishment.⁶ Serotonin appears to act as a brake on this

facilitation. Thus, serotonin depletion may increase the likelihood of physical activity aimed at acquiring a reward or deterring a punishment (Spont 1992).

Serotonin also modifies the response to threat. Threat is the learned association between punishment and the behavior that elicits punishment. When serotonin function is normal, anxiety, the emotional response to threat, inhibits socially inappropriate behavior such as aggression. When serotonin is depleted, anxiety loses its inhibitory effect while retaining its emotional intensity (Spont 1992). Thus, a person with low serotonin levels might display aggressive behavior despite intense anxiety induced by the threat of punishment.

In general, a person depleted of serotonin is more likely to appear depressed and aggressive, more driven by appetites (more motivated by food, water, sex, and drugs of abuse), and more impulsive (less able to control behavior in the face of threat). Such a person will find it difficult to stop engaging in a behavior once started, unless an alternative source of reward is present. He or she may be more likely to begin consuming alcohol and less likely to stop drinking as long as alcohol is present.

Alcohol

Although brain serotonin function may increase temporarily under the influence of alcohol, serotonin levels may subsequently drop below baseline levels (Virkkunen in press). This rebound effect may stimulate aggression among susceptible people exposed to rewarding or punishing stimuli, through mechanisms discussed above. Alcohol may also facilitate aggression through direct effects on other neurotransmitter systems, as discussed below.

Gamma-aminobutyric acid (GABA) is the main inhibitory neurotransmitter in the brain. The binding of certain drugs to the GABA receptor results in sedation and diminished anxiety. These drugs include alcohol, barbiturates, and tranquilizers such as Valium. Alcohol reduces the protective control of anxiety, so alcohol-intoxicated people may be more likely to engage in aggressive behavior (Pihl et al. in press).

Alcohol stimulates psychomotor activity, probably by increasing dopamine activity. Sensitivity to these psychomotor effects may be population specific. For example, young men with an extensive

⁵Muscular activity associated with mental processes.

⁶In this context, a reward is something that satisfies a need, and punishment is a painful physical or psychological stimulus.

⁴Alcohol withdrawal symptoms appear following prolonged heavy alcohol ingestion. These symptoms include tremors; anxiety; mood and sleep disturbances; and, in severe cases, convulsions.

family history of alcoholism are particularly susceptible to an alcohol-induced increase in heart rate, a phenomenon linked to dopamine activity (Pihl and Peterson 1992). Increased dopamine activity stimulates aggression. Increased serotonin activity suppresses dopamine-induced aggression, whereas decreased serotonin activity increases such aggression (reviewed above).

Consideration of alcohol's properties helps clarify the nature of the potential serotonin-aggression relationship. The serotonin-depleted person drinks, presumably thereby experiencing transient improvements in serotonin activity, followed by depletion of brain serotonin. Such a person's dopamine-driven psychomotor systems, accelerated by alcohol, might be more responsive to stimuli that elicit aggression.

Subsequent depletion of serotonin could hamper regulation of this alcohol-induced aggressive reaction. Anxiety levels, their role in behavioral control already compromised as a consequence of diminished serotonin activity, could be further reduced by alcohol's action at the GABA receptor. Ripe for impulsive manifestations of aggression, the serotonin-depleted drinker might be more likely to get into (temporarily rewarding) trouble.

CONCLUSION

Decreased brain serotonin activity appears to stimulate aggression. Specifically, persons with reduced serotonin activity may be more likely to use aggression to attain rewards or deter punishment, and they may be less sensitive to social control of such behavior. Social control in this context includes internalized social control, manifested, for example, as anxiety.

Impaired behavioral control induced by decreased brain serotonin levels may affect a person's response to alcohol. Decreased serotonin may lead to an inability to terminate drinking once started. The addition of alcohol to existing low serotonin levels profoundly affects the manifestation of aggression. Alcohol transiently enhances serotonin function, perhaps thereby initially moderating violent tendencies. However, serotonin activity may subsequently decrease below baseline levels. This decrease leads to increased impulsivity and reduced threat-induced control of behavior. Furthermore, alcohol can increase the capacity for

aggression by reducing anxiety and by enhancing motivated psychomotor activity. The combination of impulsivity with alcohol-induced fearlessness and hyperactivity appears prone to produce aggressive acts or to culminate in victimization. ■

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