Murder, Minors, Selective Serotonin Reuptake Inhibitors, and the Involuntary Intoxication Defense

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This article examines the clinical and legal aspects of the involuntary intoxication defense, primarily as it relates to violent acts perpetrated by minor and adult patients who have been prescribed selective serotonin reuptake inhibitors (SSRIs) and related psychoactive medications in a therapeutic context. The Model Penal Code recognizes the involuntary intoxication defense and its potential applicability to cases in which the defendant's criminal behavior is believed to be associated with prescription medication use. Two case reports of juvenile murderers who attributed their violent behavior to SSRI treatment are presented. Selected pertinent case law is reviewed. Currently there is a lack of convincing scientific evidence that clearly confirms or negates the postulated relationship between antidepressant agents and violent behavior. However, the use of the involuntary intoxication defense will likely continue to increase due to the growing number of novel psychotropic medications being developed and marketed along with advances in the scientific understanding of their actions and side effects.

This article examines the use of the involuntary intoxication defense for defendants who assert that adverse psychiatric effects from the therapeutic use of selective serotonin reuptake inhibitors (SSRIs) and related antidepressant compounds has led them to commit violent crimes. The clinical and legal aspects of this controversial topic will be addressed, including selected pertinent case law with an emphasis on its applicability to minors. Two case reports of juvenile murderers who attributed their violent behavior to SSRI treatment are included.

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Clinical Aspects

SSRIs are the most widely prescribed antidepressants worldwide, with fluoxetine at the forefront.[1] The neurotransmitter serotonin is believed to have a modulatory effect on aggression in both man and animals, perhaps through its effects on the central nervous system's behavioral inhibition system,[2] and serotonin

may be especially relevant to impulsive aggression.[3] It is postulated that pharmacologic agents which increase serotonergic function may be able to diminish aggression, although controlled clinical trials to prove that SSRIs and related serotonergic agents can decrease aggressive behavior in man are lacking.[4–7]

There are limited clinical studies and case reports to suggest that SSRIs can reduce aggression in various treatment populations including depressed outpatients,[8] patients with personality disorders and associated impulsive aggression,[9, 10] mentally retarded patients,[5] autistic patients,[11] and patients with Huntington's disease.[12]

However, not all studies have found SSRIs to have a positive effect on aggression in man. Troisi *et al.*[13] described an increase in aggressive behavior inpatients with mental retardation and epilepsy treated with fluoxetine. In a review of all deaths in Maryland over a four-year period, Frankenfield *et al.*[14] found that a significantly greater number of decedents who had been taking fluoxetine died from violent suicides than those who had been on tricyclics. Bost and Kemp[15] made a similar discovery in a study looking at fluoxetine-related deaths in Dallas County, Texas. In a postmarketing surveillance study examining adverse drug reactions, Fisher *et al.*[16] noted that 1.4 percent of fluoxetine-treated patients reported an increase in anger/aggression, a significantly higher percentage than among sertraline-treated patients. This finding raises the possibility that SSRIs may vary in their effects on the expression of aggression.

Other antisocial behaviors than interpersonal aggression have been related to SSRI use. Kleptomania was reportedly induced in three adults who were started on SSRIs for depression.[17] Their stealing behaviors began one to two months after initiation of either fluoxetine or fluvoxamine. Glancy[18] reported on two adult males who, after starting SSRI treatment for depression, engaged in diverse illegal behaviors including auto theft, robbery, shoplifting, and property offenses. These men, 29 and 32 years of age, respectively, had no history of previous arrests, impulsivity, or substance abuse. One of the men reported the onset of insistent, repetitive thoughts of purchasing a gun and committing robberies that resolved after SSRI discontinuation.

In children and adolescents, there is one study and several case reports in which SSRIs were found to incite or worsen aggressive behavior. Constantino *et al.*[19] reported a significant increase in verbal aggression, physical aggression toward objects, and aggression toward self in a sample of 19 adolescent inpatients being treated with fluoxetine, paroxetine, or sertraline. These researchers cautioned against the use of SSRIs strictly for the treatment of aggression in children and adolescents. They based this caveat, in part, on research involving developing rodents, which suggests that the long-term use of SSRIs can lead to a compensatory down-regulation of serotonin receptor production, thereby possibly leading to a greater likelihood of aggressive behaviors in the future.[19, 20]

There is a strong correlation between aggression and suicide,[3] and self-directed

aggression has also been associated with SSRI use. The most cited study is a case series of six patients by Teicher *et al.*[21] in which fluoxetine allegedly led to intense suicidal preoccupation. King *et al.*[22] described six children and adolescents who had *de novo* or intensified self-injurious ideation following treatment with fluoxetine for obsessive-compulsive disorder. Two of these youth had the onset of disturbing violent thoughts and behaviors toward others as well. A 12-year-old boy experienced a nightmare about killing his classmates; the dream continued to feel real even after he awoke. He also had several days of thoughts involving killing himself and the death of his parents. A 14-year-old girl not only developed intense suicidal ideation and behaviors after beginning fluoxetine, but also became violent toward hospital staff, injuring several of them. Tricyclic antidepressants also have been linked to the development of suicidality.[23]

Non-SSRI antidepressants with 5-HT uptake inhibiting properties have been implicated in the promotion of aggression as well. Twenty-five years ago, Capstick[24] wrote about the side effect of aggressive episodes inpatients taking clomipramine, a potent 5-HT reuptake inhibitor. He stated that the aggression appeared to be related to irritability, typically occurred several weeks into treatment, and may be more common in obsessional patients. More recently, Meyer *et al.*[25] suggested that clomipramine, when combined with alcohol, can result in the release of aggressive impulses in those with personality anomalies.

Alarcon *et al.*[26] described two cases of adolescents with obsessive-compulsive disorder who were treated with clomipramine and developed uncharacteristic symptoms of hostility, aggressiveness, rage, and paranoia. The 14-year-old boy reported the onset of "the desire to attack somebody," and the 11-year-old boy "punched a female classmate and then ran away from school." These aggressive symptoms began in both patients after approximately seven weeks of clomipramine therapy. Intense suicidal ideation also developed in one of these cases. Brasic *et al.*[27] reported on a series of five boys with autism and mental retardation; three of them developed extreme aggression and agitation when placed on higher doses of clomipramine. Aggression as a paradoxical response to traditional tricyclic antidepressants has also been described in adults and children.[28,29]

Case Reports

Case 1 AA, a 16-year-old boy, was charged with first degree murder and kidnapping. He was accused of beating to death an elderly woman. This daytime crime occurred in his neighborhood shortly after he left his home to calm down following an argument with his mother. The victim, a stranger to him, reportedly complained about the volume of his radio as she passed him on the street, and he attacked her in response. He had drunk several beers earlier this day. AA had been in five fights during his life, one resulting in an assault and battery charge. His only other arrest was for stealing beer from a store. He had never seriously injured anyone before murdering this woman.

Seven weeks before the crime, he had his first psychiatric hospitalization for depression, suicidal ideation, and violent threats toward his parents. His discharge diagnoses included major depressive episode, oppositional defiant disorder, attention deficit disorder, alcohol abuse, and a mathematics disorder. One week into his hospitalization, he was started on sertraline (50 mg daily). After being on sertraline for two weeks, he described the onset of sexual and aggressive fantasies and dreams primarily involving rape of teenage girls and the killing of male youths, using both his hands and weapons. He also complained of paranoia, feeling that eyes were staring at him, worsened depression, being in a "daze," decreased concentration, and insomnia. He killed the elderly victim six weeks after beginning sertraline.

AA had experienced several neuropathic incidents during his life. He was born prematurely at 8 months, delivered by cesarean section. As an infant, he suffered from perinatal anoxia and required 10 days of hospitalization for respiratory distress syndrome and jaundice. At the age of 18 months, he had a near-drowning episode and required cardiopulmonary resuscitation and hospitalization. In junior high school, he suffered from loss of consciousness and a concussion after being punched, after which incident he also complained of chronic tinnitus.

Case 2 BB, a 17-year-old boy, was convicted on charges of first degree murder, burglary, and sexual assault. He admitted to breaking into the apartment of a neighbor who was a young mother and a stranger to him. He held her at knife point and attempted to rape her but was unable to achieve an erection. He then killed her by stabbing her in the head and shooting her in the face with a handgun. He denied the use of alcohol or illicit drugs on the day of the crime. He had numerous previous criminal charges including burglaries, retail thefts, arson, and criminal mischief. However, he had never been violent toward other persons prior to his arrest for murder.

BB first saw a mental health professional one month before his arrest. During this initial court-ordered psychiatric consultation, he was placed on fluoxetine (20 mg daily) for depression. BB explained that he had felt emotionally dead inside for as long as he could remember up to this point and had always kept his emotions under tight control. After beginning fluoxetine, he experienced escalating feelings of anger and confusion and felt physically activated. After three weeks of antidepressant therapy, he developed "nonstop" thoughts of raping and killing his mother, with whom he reportedly had a good relationship. He felt as though he was no longer in control of his emotions. One week later, he "snapped" and fatally attacked his neighbor. He remembered feeling "wired and anxious" prior to the assault.

BB had also experienced neuropathic events during his life. He suffered head trauma at the age of three when he was caught under a merry-go-round; this resulted in extensive head bruising and a large laceration. During his childhood, he suffered from debilitating migraine headaches. At the age of 17, he struck his head during a motorcycle wreck, resulting in

unconsciousness for approximately five minutes.

Legal Aspects

The excuse of criminal action due to involuntary intoxication from prescription medication has evolved from cases dating back as early as 1915. In *Perkins v. United States*,[30] the defendant took an excessive dose of his prescription medication and killed a passenger on a steamship. The court stated that a person "is bound to take notice of the warning appearing on a prescription [but] . . . if the defendant had good reason to infer. . . that he would fall [asleep]. . . from a larger dose, then he would not be legally responsible for acts committed in a violent frenzy which he had no reason to anticipate."[30] The Model Penal Code recognizes that involuntary intoxication can result from prescribed medication: "Self-induced intoxication means intoxication caused by substances that the actor knowingly introduces into his body, the tendency of which to cause intoxication he knows or ought to know, unless he introduces them pursuant to medical advice or under such circumstances as would afford a defense to a charge of a crime."[31]

In such circumstances, legal responsibility is excused or mitigated, however, only if one of the statutory elements of the crime is "intent," because intent can be negated by involuntary intoxication. The defense of involuntary intoxication is used to demonstrate that the accused did not have the mental capacity to form the intent to commit a crime. Mental capacity is relevant because most actions, to be considered a crime, must involve a prohibited act and a mental element (intent), although there are a few crimes that are "strict liability" crimes and do not involve any intent. For example, in many jurisdictions, driving under the influence of alcohol or drugs is a strict liability crime.[32] However, in *City of Minneapolis v. Altimus*,[33] an accused could defend against a charge of driving under the influence where intoxication resulted from a prescribed drug and the defendant was not aware of the side effect of intoxication.

Crimes with an intent element are either general intent or specific intent. A general intent is simply the intent to do the prohibited act and may be inferred from the commission of the act itself. However, if the person committed the act under force or duress, then he or she did not have the intent necessary to be guilty of the crime. Other crimes require a specific intent on the part of the accused. Specific intent is the subjective desire to accomplish an act. This special mental element must be established by the State for an accused to be guilty of those crimes that require specific intent.[34] For example, first degree or premeditated murder is a specific intent crime. Involuntary intoxication is usually considered a complete defense to any crime requiring intent, although voluntary intoxication is only a defense to specific intent crimes, and some courts hold that it is not a defense at all.[35]

Each state adopts its own criminal code, and thus criminal defenses, including the defense of involuntary intoxication, will vary from state to state. In Colorado, involuntary intoxication cannot be

self-induced and occurs when the defendant ingests an intoxicating substance without knowing it or ingests a substance not known to be an intoxicant.[35] In Texas, intoxication is involuntary if the person who ingests the substance is unaware that it is an intoxicant, if the person is medically prescribed to take the substance, or if the person ingests the substance due to force or duress.[36] In Georgia, a person is not guilty of a crime when, at the time of the act constituting the crime, the person did not have sufficient mental capacity to distinguish between right and wrong because of involuntary intoxication. Furthermore, involuntary intoxication means intoxication caused by the consumption of a substance through excusable ignorance or the coercion, fraud, artifice, or contrivance of another person. Addiction resulting from reliance on a physician's prescription could constitute such excusable ignorance.[37]

A number of courts have equated the defense of involuntary intoxication to the defense of temporary insanity under the umbrella of the M'Naghten test.[38–40] The historic M'Naghten rule for insanity holds that a defendant is relieved of criminal responsibility if, at the time of the wrongful act, the defendant "was laboring under such a disease of the mind, as not to know the nature and quality of the act he was doing; or if he did know it, that he did not know what he was doing was wrong."[41]

Various courts have recognized that involuntary intoxication can occur as a result of the use of prescription medication. In *People v. Turner*,[35] the defendant was convicted of aggravated robbery. The conviction was reversed and remanded for a new trial primarily because the trial court refused to use the defendant's tendered jury instruction on involuntary intoxication. In this case, the defendant had taken approximately 25 bultalbital tablets (a barbiturate), five at a time, within the twenty-six hours prior to committing the offense. Butalbital had been prescribed for him to relieve migraine headaches. He stated that he thought the medicine would put him to sleep and testified that he had never been warned about the perils of an overdose. The court stated that the general rule is "where the intoxication is caused by an overdose of a [prescription] medicine. . . the resulting intoxication. . . has been considered voluntary or involuntary depending primarily upon whether the individual should have known that intoxication would ensue."[35]

In *People v. Caulley*,[42] a first degree murder conviction was reversed and remanded for a new trial. In that case, the defendant shot and killed his wife after ingesting three to five triazolam tablets a day for about a week prior to the shooting, although the prescribed dosage was one or two tablets a day. He was also being treated with amitriptyline and alprazolam. The court stated that the trial court should have instructed the jury in regard to involuntary intoxication if the jury found that the defendant did not know the side effects of triazolam.

Additionally, in *Brancaccio v. State*,[43] first degree murder and kidnapping convictions were reversed due to the failure of the trial court to instruct the jury as to an involuntary intoxication defense. Here, the defendant was taking the prescription

drug sertraline to treat his depression. The court found that infrequent side effects of this medication include aggressive reactions and hallucinations and that the defendant had experienced personality changes after taking sertraline. The court quoted Phillip E. Hassman in saying ". . . a patient is entitled to assume that an intoxicating dose would not be prescribed or administered by a physician; where intoxication results from medicine which has been prescribed (and taken as prescribed) or administered by a physician, such intoxication is generally considered involuntary."[44] It is not clear how this court would have ruled if the defendant had not taken the prescribed dose of the sertraline.

As outlined earlier, a defendant who voluntarily became intoxicated will still be liable for general intent crimes. In a trial, the judge should offer instructions to the jury on involuntary intoxication if the accused properly raises this affirmative defense. When a defendant takes prescribed medications, and as a result, alleges that he or she did not have the mental capacity to commit a crime, then the jury often must decide whether the accused knew that the drugs would cause intoxication. Generally, the fact that a drug requires a prescription will put the person on notice that an excessive dose could be dangerous.[30]

Recently, several actions against drug manufacturers and physicians have been allowed to go forward that allege that the use of fluoxetine or other psychotropic medications caused the patient to commit suicide or a crime. For example, in *Adams v. Rios*,[45] the family of a woman who shot and killed her ex-husband while taking triazolam filed suit against the prescribing doctors and hospital. The plaintiffs alleged that adverse side effects from the triazolam had caused her violent behavior. Summary judgment in favor of the defendants was reversed.

Furthermore, in *Forsyth v. Eli Lilly and Co.*,[46] Eli Lilly's motion to dismiss was denied and its motion for summary judgment was granted in part and denied in part. In this case, a patient murdered his wife and subsequently committed suicide after taking fluoxetine for a period of two weeks. The plaintiffs alleged that the patient committed these actions as a direct result of taking fluoxetine.

Discussion

This article has reviewed the involuntary intoxication defense as it relates to violent behavior and the therapeutic use of antidepressant medication, primarily the SSRIs, in minors and adults. Additionally, case law pertaining to other psychoactive medications has been briefly addressed. Currently, there is a lack of convincing scientific evidence that clearly confirms or negates the postulated relationship between antidepressant agents like the SSRIs and violent acts. Also contributing to this murkiness is the multifactorial nature of aggression.

Of note, neither of the two case reports in this article successfully raised the involuntary intoxication defense; one court would not allow it to be considered by the jury, and in the other case the defense counsel declined to pursue it, apparently from a lack of awareness of the clinicolegal issues.

Seven different types of aggression based on animal models have been described by Moyer,[47] which are theoretically applicable to man. "Irritable aggression" is the category that best describes uncharacteristic aggressive behavior in the patient with increased aggression from SSRI treatment, and it applies also to the case reports presented in this article. This type of aggression can be elicited by external stimuli (i.e., pharmacologic agents) or discomfort/pain, is more common in males, and typically has nonspecific targets of attack involving another organism or an inanimate object.[48]

Another category, "sex-related aggression," must also be considered in the two cases described in this article; both boys described the new onset of violent sexual fantasies preceding their crimes, and the victims were female strangers. SSRIs can have a marked impact on sexual functioning, and there is evidence that they have the capacity to alter the expression and intensity of the sexual drive. Carek[49] described the case of an adolescent male treated for depression and associated violent impulses who developed a "bothersome" sexual preoccupation on sertraline.

Thus, it is plausible but unproved that SSRIs may infrequently contribute to the occurrence of both irritable and sex-related aggression. Yet other risk factors in combination with SSRI treatment likely are needed to set the stage for the elicitation of an intensified and distorted aggressive drive that culminates in violence. For instance, it is well established that brain damage is a predisposing factor to violent behavior.[50] Perhaps neuropsychiatric vulnerabilities, subclinical brain injury, personality disturbance, psychiatric illness (i.e., depression, anxiety), obsessional violent thoughts, and preexisting antisocial tendencies must be present in certain combinations before murderous aggression will erupt in the susceptible patient taking an SSRI.

One can safely predict that the involuntary intoxication defense will be increasingly used in future legal cases involving patients taking SSRIs and related medications who have committed violent acts. Novel psychotropic medications are being introduced to the market at a growing rate, and more than 50 percent of approved drugs are found to have serious adverse effects not detected before approval.[51] Future research findings in tandem with evolving case law will help clarify when the involuntary intoxication defense can be most appropriately raised in the courtroom.

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