

Legal Fallacies of Antipsychotic Drugs

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Advances in the biological sciences have dramatically improved the understanding of schizophrenia and related psychotic illnesses. One of the most compelling findings is the substantial degree to which cognition is impaired in these illnesses and the remedial effects that antipsychotic drugs have in treating these cognitive impairments. Despite these promising discoveries, legal cases and scholarship remain replete with pejorative associations with antipsychotic drug action. References to antipsychotic medications as mind-altering drugs and their effects as “synthetic sanity” misconstrue the beneficial effects these medicines have on cognition. We review the prevailing legal attitude of antipsychotic medications and contrast these views with prevailing scientific knowledge. We conclude that legal opinion is misinformed about the effects of antipsychotic medications on cognition.

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One of the persisting quagmires in modern psychiatry and law has been the disparity between current scientific knowledge regarding mental illnesses and legal scholarship, court decisions, and public policy regarding these illnesses. Within the past two decades in particular, the surge of scientific information regarding the pathogenesis of schizophrenia and related illnesses—aided by multiple neuroimaging techniques¹; genetic studies^{2,3}; and neurodevelopmental,⁴ amino-acid, and oxidative-stress models⁵ of psychiatric illness—has greatly expanded the knowledge base and confidence within psychiatry as to the nature of these illnesses.⁶ Among the most prominent of these advances has been an appreciation of the importance of negative symptoms,^{7,8} impaired cognition,^{9–11} and the therapeutic qualities of antipsychotic medications beyond treating the overt, positive symptoms of psychosis.^{12,13}

These developments build on the growing understanding that untreated psychosis engenders extensive detrimental consequences related to progno-

sis,^{14,15} while consistent treatment with antipsychotic medications is associated with improved long-term outcomes.^{16–18} Consequences of treatment nonadherence include a fourfold increase in the risk of suicide,¹⁹ a near fourfold increase in relapse,²⁰ and an increased risk of violent behavior.²⁰ In addition, nonadherence is associated with increased rates of hospitalization, use of emergency psychiatric services, arrests, violence, victimizations, poorer mental functioning, poorer life satisfaction, greater substance use, and more alcohol-related problems.^{21,22} The rate of treatment nonadherence among patients with psychotic disorders varies widely, but a recent meta-analysis places the rate at about one-quarter of all patients.²³

Schizophrenia is unquestionably a disease of the brain. A plethora of neuropathological studies have demonstrated that it is associated with substantial anatomical and functional abnormalities in the brain.^{24–28} These include volumetric loss of gray matter in the frontal lobes,^{29,30} enlarged lateral ventricles,^{31,32} and atrophic temporal and prefrontal lobes.³³ While the absence of gliosis in these illnesses places them outside the domain of traditional neurodegenerative disorders, evidence of neuronal atrophy and apoptosis,^{34,35} decreased neuropil,³⁶ abnormal neuronal density,^{37,38} and progressive structural brain changes^{39,40} suggests a progressive neurodevelopmental disorder with plausible atypical neurodegenerative aspects.^{39,41}

Despite these compelling findings, the law remains replete with negative associations between

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psychotic illnesses and effective treatments, especially antipsychotic medications. The case of *Sell v. United States*⁴² neglected any meaningful discussion regarding the propensity of antipsychotic medications to improve cognitive abilities in persons with schizophrenia and related psychotic disorders and the detriment that patients incur when allowed to forgo proper psychiatric treatment. The *Sell* decision continues an enduring skepticism by the courts and legal scholars toward psychiatric treatment, which is evident by its continued reference to antipsychotic medications as “mind-altering drugs”⁴³ that produce “synthetic sanity,”⁴⁴ denoting a misconstrued appreciation for the pathogenesis of psychotic illnesses, the meaning of recovery from a biomedical perspective, and the benefits of pharmacological agents used in the treatment of psychoses.

In this review, the legal approach toward antipsychotic medications will be explored by focusing on case law and legal scholarship surrounding involuntary administration of antipsychotic medications to incompetent defendants, prison inmates, and civilly committed patients. Current scientific understanding regarding psychotic illnesses, particularly cognition, and the capacity of antipsychotic medications to improve cognitive abilities will be examined. Furthermore, the hazards of untreated psychosis will be discussed, particularly in light of the emerging neuropsychiatric literature on the phenomenon of duration of untreated psychosis (DUP) and neurotoxicity through glutamate dysregulation in psychotic illnesses. Finally, a call for a more informed public policy and legal perspective on severe mental illnesses will be discussed, focusing on diminishing the continued stigma associated with these illnesses that current legal authority, represented by cases such as *Sell*, inadvertently perpetuate by their continued depreciatory position toward effective treatments.

Seminal Legal Cases

Competency to Stand Trial

A fundamental concept of American criminal law is that defendants cannot be tried for any crime unless they have a factual and rational understanding of the charges against them, a rudimentary knowledge of the criminal proceedings, and the ability to assist their attorneys in their defense. Known as competence to stand trial, this doctrine evolved from 17th-century English jurisprudence and has been firmly

incorporated into American criminal law as a constitutional right. As such, it is unsurprising that competency evaluations remain one of the most common areas of forensic psychiatry practice.⁴⁵ Its cornerstone in both forensic practice and criminal law reflects the strong penchant in American jurisprudence toward individual culpability and moral blameworthiness.⁴⁶

Criminal defendants can be found incompetent to stand trial for a variety of reasons, including stable characteristics such as low intelligence levels. However, most competency deficits result from severe mental disorders, usually psychotic illnesses, that are fluid in nature and amenable to treatment.⁴⁷ The long-recognized principal method for treating psychotic illnesses is pharmacotherapy with antipsychotic medications.^{48,49} Unfortunately, as many clinicians, researchers, and family members of those afflicted with these devastating illnesses have known for decades, psychosis frequently entails a loss of insight and deluded thinking that leaves the afflicted person unable to understand the benefits of treatment.⁵⁰ Although antipsychotic medications are effective in restoring rationality in persons with psychosis, denial of illness and paranoia often necessitate involuntary treatment. Such treatment, unsurprisingly, is often necessary for competency restoration, and pharmacotherapy is the chief method of restoration.⁵¹

Perhaps the quintessential case that provides insight into the court's concerns regarding involuntary administration of antipsychotic medications for restoration of competency is *Riggins v. Nevada*, decided in 1992.⁵² Riggins was convicted of murder and sentenced to death. Upon appeal, he claimed that the denial of his motion during trial to suspend administration of thioridazine infringed on his constitutional right to privacy and presentation of his presumably psychotic demeanor during his insanity defense. Justice O'Connor, writing for the majority, held that the forcible administration of antipsychotic medication violated Riggins' Sixth and Fourteenth Amendment rights. The Court held that testimony by defense experts regarding the alleged disabling effects of thioridazine on Riggins' ability to interact with counsel, produce testimony, or comprehend the trial proceedings was pervasive and that Riggins should have enjoyed the right to forgo treatment, allowing the jurors “to assess Riggins' demeanor fairly” (Ref. 52, pp 137–8). The strong presumption

that antipsychotic medications interfere with the defendants' ability to communicate with their attorneys and present their "true" demeanor is a theme passionately endorsed by many legal scholars.⁵³⁻⁵⁵

Eleven years later, in *Singleton v. Norris*,⁴⁴ the Eighth Circuit considered whether a death row inmate could be restored to competency involuntarily after adjudication, to face the death sentence. A sharply divided court held that such practice was constitutionally permissible. Judge Heaney, writing for the dissent in a revealing opinion regarding the legal perception of antipsychotic medications, called Singleton's restored competency "artificial" and that "drug-induced sanity is not the same as true sanity." The dissent also cited as authoritative several legal scholars who claimed that "despite their beneficial effects, antipsychotic drugs merely *mask* the debilitating symptoms of major mental disorders" and provide only "synthetic sanity" (Ref. 44, p 1034; emphasis added).

Again in 2003, the courts ruled on involuntary administration of antipsychotic medications and competency in the decisive case, mentioned earlier, of *Sell v. United States*.⁴² In *Sell*, the United States Supreme Court considerably limited the practice of involuntary restoration by citing its concerns that antipsychotic medications can infringe on a defendant's constitutional rights under the Sixth and Fourteenth Amendments. Justice Breyer, writing for the majority and citing the American Psychological Association's *amicus curie* brief claiming that psychosis can resolve without pharmacologic interventions, held that the sedation accompanying administration of antipsychotic medications can "interfere" with defendants' communication with their attorneys, prevent them from "rapidly reacting" to trial developments, and diminish the expression of emotions (Ref. 42, pp 185-6). Consequently, the Court held, involuntary administration of antipsychotic medications for purposes of restoration may only occur in limited circumstances. The requirements being that: (1) the administration of psychotropics must be for an important governmental interest; (2) they must directly further that interest; (3) it must be "substantially likely" that administration of psychotropics will restore competency; (4) the psychotropics must be "unlikely" to interfere with the ability of a defendant to communicate with his/her attorney; (5) less intrusive measures are unlikely to restore compe-

tency; and (6) the medication must be medically appropriate.

Prison Inmates With Psychotic Disorders

In 1990, the United States Supreme Court held in *Washington v. Harper*,⁴³ that inmates with severe mental illnesses, who are deemed to be dangerous to themselves or others, can be forcibly medicated without the need for a full judicial hearing. The inmate, Walter Harper, was convicted of robbery and incarcerated in state prison from 1976 to 1980, housed mainly in the prison's mental health unit. He was subsequently released on parole on the condition that he receive mental health treatment in the community. After assaulting two nurses, Harper's parole was revoked, and he was returned to prison, where he initially voluntarily received antipsychotic medications, but later refused treatment. The state, relying on the Supreme Court's prior holding in *Vitek v. Jones*,⁵⁶ held an administrative hearing, finding Harper in need of treatment and ordered that he be involuntarily medicated. Harper filed a civil suit, alleging that the state's practice violated his federal constitutional rights of due process, equal protection, and free speech.

Justice Stevens, writing the dissenting opinion, held that the administration of antipsychotic drugs was akin to electroconvulsive therapy or psychosurgery and unfortunately introduced into the Court's lexicon the term "mind-altering drugs" as synonymous with antipsychotic medications (Ref. 43, pp 240-1). In citing the Supreme Court of Massachusetts case *In re Guardianship of Roe*,⁵⁷ Justice Stevens noted as pervasive that court's conclusion that antipsychotic drugs have a "well-established likelihood of severe and irreversible adverse effects" (Ref. 43, p 241; internal quotations omitted). Justice Stevens further held that:

The State might seek to compel Harper to submit to a *mind-altering drug* treatment program as punishment for the crime he committed in 1976, as a "cure" for his mental illness, or as a mechanism to maintain order in the prison. The Court [majority opinion] today recognizes Harper's liberty interest only as against the first justification [Ref. 43, p 241; emphasis added].

Cases of Treatment Over Objection

Similar to cases of competency to stand trial and penological interest, involuntary administration of antipsychotic medications have been addressed by the courts in a variety of other contexts, most prominently in cases of civil treatment over objection. The

courts have acknowledged in these circumstances as well the compelling state interests of involuntary pharmacotherapy and the individual liberty interests of the afflicted patient. Analogous to the court's perception of antipsychotic drugs in competency cases and prison inmate cases, however, cases of civil treatment over objection provide further illumination as to the mindset of the judiciary and legal community that these treatments invariably exert harmful effects on cognition, and hence, infringe on constitutional rights.

The decisive case of *Riese v. Mary's Hosp. & Med. Ctr.*,⁵⁸ is emblematic of most cases of civil treatment over objection. Ms. Riese had a history of chronic schizophrenia since her early 20s, but was successfully treated with thioridazine, allowing her to avoid hospitalization for over 10 years. After she began to have bladder problems, her doctors switched her to molindone, which was ineffective. In 1985, Ms. Riese was voluntarily admitted for exacerbation of her psychotic symptoms and was eventually treated again with thioridazine. After Ms. Riese became agitated and refused further medication, she was converted to involuntary status, given intramuscular injections, and required further hospitalization for her active psychotic symptoms. Ms. Riese sued, contending that California law provided her with a right to refuse antipsychotic medication on the grounds of privacy and free speech.

Justice Kline, writing for the majority, held that absent a judicial determination of incompetency, informed consent was required before treatment with antipsychotic medications was permissible. Citing that these medications were “by intention mind altering” and “possess a remarkable potential for undermining individual will and self-direction” and may result in “sudden death” (Ref. 58, p 203), the court held that psychiatric hospitalization for psychosis alone did not presume incompetency, and thus, the hospital had violated Ms. Riese's constitutional rights. In a footnote, the court also held that:

The cited cases protect against intrusions into the mind by means of lie detector tests or therapists' disclosures. While the present case does not involve such forced revelations of the content of the mind, the changing of thoughts contested here is *no less intrusive* [Ref. 58, p 208, fn 11; internal citations omitted, emphasis added].

The court also found New York's similar determination persuasive. Referencing to the watershed case, *Rivers v. Katz*,⁵⁹ that mental illness “often strikes only

limited areas of functioning, leaving other areas unimpaired” (Ref. 58, p 210; citing Ref. 59, p 342), the court showed a deep misunderstanding of the pervasiveness of psychotic symptoms and impaired judgment that often accompany acute exacerbations of psychosis.

The safeguarding of individual liberties is an important function of the courts. Indeed, antipsychotic medications are associated with numerous side effects, including tardive dyskinesia, neuroleptic malignant syndrome, dyslipidemia, and metabolic syndrome.^{60,61} Tolerability is a major factor in patient dissatisfaction with these agents,⁶² and the global blockade of dopamine inherent in these drugs reduces hedonic pleasure and motivation.^{63,64} Indeed, there is much room for improvement in the pharmacological armamentarium of treatments for psychotic illnesses. But the implication that such medicines are mind controlling and have the propensity to sabotage intentionality of free thinking shows a fundamental misunderstanding of the effects that these life-saving medications have in millions of people. More crucially, the notion that antipsychotic drugs impair cognition in persons with psychosis is in direct opposition to the wealth of scientific studies that have demonstrated just the opposite—that these medicines improve cognition.

Neurocognition in Schizophrenia

Perhaps the greatest scientific achievement in the realm of schizophrenia and related illnesses within the past 15 years has been the appreciation and intensive study of comorbid cognitive impairments that usually accompany these chronic illnesses. Conclusive evidence has demonstrated that the severity of cognitive deficits is strongly linked with long-term prognosis and overall functioning.⁶⁵ Consequently, vigorous research has focused on identifying aspects of these impairments and exploring effective treatments.⁶⁶ A variety of impairments have been identified, with the most salient aspects being visual processing, sustained attention, memory, executive functioning, and general intelligence.

Visual Processing

One of the first cognitive deficits to be identified in schizophrenia was the inability of those afflicted to discriminate between multiple visual cues.⁶⁷ Visual processing is a cognitive process that allows interpretation of a vast array of visual stimuli. This vital cog-

nitive ability was first observed by the 17th century philosopher Sir William Hamilton. Recent research has shown that persons with schizophrenia have particular deficits with backward masking, which prevents them from interpreting the first stimulus (icon) in a series of visual cues (mask).⁶⁸

Although the exact mechanism behind impairment of backward masking remains unknown, it is believed to involve a disruption of the magnocellular and parvocellular pathways that leads to either disruption of the icon or overemphasis of the mask.⁶⁹ The importance of visual processing deficits in schizophrenia is that they impair a person's ability to scan the environment quickly, create an internal representation of the environment, and extract relevant information. Thus, inherent in this deficit is the difficulty in making transitory perceptual judgments when presented with multiple visual cues in the environment.

Sustained Attention

Attention is an invaluable process of cognitive functioning. In schizophrenia, impaired attention has been observed for many decades by researchers and has been a focal point of many neuropsychological studies.⁶⁹ From a neurocognitive perspective, attention contains several subcomponents, many of which are impaired in schizophrenia.⁷⁰ Sustained attention is a process that allows a person to identify and select a target (signal) among extraneous targets (noise). When the task is completed over time, this facet of attention is referred to as vigilance.

While vigilance decrement (i.e., the loss of vigilance during execution of a task) does not appear severely impaired in schizophrenia,⁷¹ deficits in vigilance levels (i.e., the overall vigilance given to the task at hand), latent inhibition, and selective attention are prevalent.⁷² Selective attention is the ability to pay attention to one source of sensory input while disregarding others. Latent inhibition is the ability to adapt to changing rules that give emphasis to a stimulus. In schizophrenia, deficits in selective attention and latent inhibition have been well documented.⁷³

Both impairments have obvious relevance to persons with schizophrenia involved in legal proceedings, since attention can be defined as a cognitive process necessary for complex situations that require a person to discriminate among multiple sensory inputs. As discussed in *Sell*, the ability of defendants to "rapidly react" to changing situations (Ref. 42, pp

185–6) in the courtroom necessarily implies intact attention on the part of the defendant, and thus, its impairment is significant for mentally ill defendants.

Memory

Impairment in the ability to learn and recall information from past events is a hallmark feature of schizophrenia.^{74,75} While an exhaustive review of the memory deficits involved in schizophrenia is beyond the scope of this article, the putative impairments observed generally include deficits in explicit and working memory. Explicit memory includes tasks that rely on conscious recollection of specific, previous events that can be articulated. Numerous studies have shown that persons with schizophrenia have impairments in domains of explicit memory, including verbal recall^{76,77} and, to a lesser extent, recognition memory.⁷⁸

In addition, working memory deficits have been observed in medicated and medication-naïve persons with schizophrenia.⁷⁹ Working memory is the process of actively holding information in consciousness and manipulating it in service of guiding behavior. Working memory deficits usually persist throughout the course of schizophrenia⁸⁰; however, findings in several studies suggest that some atypical antipsychotic medications may be associated with improvement in working memory.^{81–83}

The importance of memory cannot be overstated. Memory is believed to be crucial in learning⁸⁴ and its value in everyday functioning is intuitive. The ability to form new memories and recall past events is strongly related to a person's overall ability to form a coherent, functional understanding of the environment. Memory impairment has also been associated with those at high risk of psychotic illnesses.⁸⁵ In addition, results of several studies suggest that schizophrenia is associated with other impairments of memory, including semantic⁸⁶ and visual memory,⁸⁷ as well as prominent encoding deficits⁸⁸ that further disrupt the capacity of persons with schizophrenia to adduce logically the stimuli in their environment.

Executive Functioning

Executive functioning is a fundamental attribute of higher cognitive functioning in primates.⁸⁹ This concept refers to a host of neurocognitive activities that are involved in planning, problem solving, and alternating between tasks. It appears to be more disturbed than other neurocognitive deficits in schizo-

phrenia and most likely involves decreased activity in the prefrontal cortex.⁹⁰ Executive functioning may be related to working memory,⁹¹ and the failure of additional studies to find an association between these two aspects of cognition probably is representative of the heterogeneity of schizophrenia.

Impairment in executive functioning has been associated with negative symptoms, including avolition and alogia,⁹² and may be associated with poor insight,⁹³ occupational competence,⁹⁴ and independent living,⁹⁵ although methodical problems limit these last two findings.⁶⁹ Surely, impairments in executive functioning have direct relevance to persons with mental illness who are involved in legal proceedings. The ability to assist counsel competently, weigh the risks and benefits of plea-bargaining conditions, and appreciate the potential long-term repercussions of court orders necessarily involves abilities related to planning and abstract thinking.

General Intelligence

Schizophrenia is associated with low intelligence quotients (IQ), even when family and environmental factors are controlled for,⁹⁶ and low IQ appears during childhood before the development of symptoms of schizophrenia.⁹⁷ Whether intelligence in schizophrenia is a mediating factor that is independent of the illness or a marker of the genetic predisposition remains unclear, yet poor performance on neuropsychological measures of intellectual abilities appears independent of general intelligence.⁹⁸ Nonetheless, there is evidence of an association between low intelligence and risk of schizophrenia.⁹⁹ Low intelligence and schizophrenia are associated with earlier onset of illness and worse prognosis.^{100,101} The prevalence of low intelligence in schizophrenia is estimated at about 18 percent.¹⁰²

Duration of Untreated Psychosis and Neurotoxicity

The idea that active psychosis is fundamentally related to a neurotoxic process dates back to the early days of psychiatry. Emil Kraepelin is well-known for conceptualizing psychosis as an illness of invariable deterioration, presumably resulting from neuronal death.¹⁰³ The neurodevelopmental hypothesis, however, has been the dominant paradigm for the past several decades. It posits that schizophrenia is borne through early developmental insults that manifest in later life as the disease.¹⁰⁴ Recent discoveries have

challenged this theory and suggest that psychotic illnesses such as schizophrenia involve progressive changes in brain structure and function that signal an atypical neurodegenerative process.

Role of Glutamate

Glutamate is an excitatory amino acid implicated in the pathology of psychotic illnesses. Its role has been discerned from animal models of exposure to phencyclidine (PCP) and involves activity of *N*-methyl-D-aspartate (NMDA) receptors.¹⁰⁵ NMDA receptors play a crucial role in memory, learning, synaptic development and neuroplasticity, sensory information, and coordinated movements.¹⁰⁶ It is theorized that glutamatergic dysregulation occurs via secondary pathways, in which inhibition of NMDA receptors leads to disinhibition of cortical excitatory cholinergic neurons by way of decreased stimulation of inhibitory γ -aminobutyric acid (GABA) neurons, which leads to autoexcitotoxicity of glutamate.¹⁰⁷ Within this context, glutamate neurotoxicity leads to dopamine hyperactivity, which produces pathogenic destruction of neuronal function.

While histopathological studies have consistently failed to demonstrate large-scale neuronal loss in schizophrenia similar to that in other neurodegenerative disorders,¹⁰⁸ some have postulated that the reduced cancer rates in people with schizophrenia¹⁰⁹ are related to the accelerated apoptosis observed through abnormal expression of cortical Bcl-2 proteins in both treated and drug-naïve patients with schizophrenia.^{110,111} Significant neuronal reductions have been noted in the thalamus, nucleus accumbens,^{112,113} and GABAergic interneurons in layers II, III, V, and VI of the anterior cingulate of postmortem brains,¹¹⁴ and neuronal atrophy appears likely in schizophrenia.¹¹⁵ Agents that indirectly enhance NMDA receptor function via the glycine modulatory site have shown promise in treating negative symptoms and the impaired cognition observed in schizophrenia.^{116,117} These findings suggest some neurodegenerative process occurs in schizophrenia.

Duration of Untreated Psychosis

Within the past two decades, increased attention has been given to the duration of untreated psychosis (DUP) and its association with treatment response and functional outcome. Studies have examined the onset and duration of symptoms until the point of first treatment. Notably, this period appears quite

long^{118,119} and has spurred intense interest in early detection and treatment programs.¹²⁰ Although it remains unsettled whether DUP is pathogenic or is simply a marker of more malignant forms of psychosis,¹¹⁹ when viewed within the emerging theory of glutamate dysregulation and possible toxicity of untreated psychosis to the brain, DUP represents a possible reemergence of the neurodegenerative theory of schizophrenia^{39,121,122}—although some disagree with this assessment in favor of a disconnectivity hypothesis.¹²³ Nonetheless, a recent meta-analysis confirmed that DUP is associated with a host of negative outcomes,¹⁴ while another recent study demonstrated long-term DUP associations with poorer global functioning and increased positive symptoms.¹²⁴

Duration of untreated psychosis has been associated with a lack of acute treatment response,^{125,126} poor premorbid functioning,^{127,128} increased positive^{129,130} and negative symptoms,^{129,131} poorer outcome,¹³² and increased cognitive deficits.^{133,134} Others have found no relationship between DUP and some of these variables.^{135,136} Nonetheless, there is a growing consensus that DUP is an important prognostic factor in psychotic illnesses. Whether the deficits associated with DUP can be fully restored with proper treatment remains unknown; however, the long-term course and prognosis for those with long DUP appears poor.¹³⁷

Improvement of Cognition by Antipsychotic Medications

An abundance of studies have clearly demonstrated that consistent treatment with antipsychotic medications improves cognition in patients with schizophrenia and related psychotic disorders. However, the notion of psychotropic drugs as mind-altering by legal scholars and the courts is in no way a reference to their beneficial effects. They are viewed as “chemical straightjackets” impinging on free thought and the exercise of individual judgment.¹³⁸ The expansion of privacy rights rooted in the fundamental autonomy recognized by the courts since the 1960s is the touchstone of the right to refuse unwanted medical treatments.¹³⁹ Yet, it is well recognized that significant governmental interests, including personal safety, competence to stand trial, and the established right of the state to care for incompetent citizens under its *parens patriae* powers can override these rights.¹⁴⁰

Nonetheless, as demonstrated in this article, the courts are wary of involuntary treatment with anti-

psychotic agents because of the erroneous belief that these medications exert some form of mind control or altered state of consciousness. On the contrary, antipsychotic medications have the propensity to improve cognition in many areas directly relevant to competence, whether it is competence to stand trial or competence to make informed decisions regarding medical treatment. Indeed, antipsychotic medications restore cognitive capacities that are often severely impaired by psychosis—a disease of the brain.

Older Agents

For many years, it was presumed that the older, first-generation antipsychotic drugs had no effect or even a deleterious effect on cognition. Recent studies have disproven this conclusion. Many of the early studies examining these agents had methodological problems ranging from being underpowered to administration of excessively high dosages of the drugs.^{141,142} Indeed, the permissive use of haloperidol as a comparator agent, with its high extrapyramidal side effects was a primary reason for the use of perphenazine in the recent NIH Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE).¹⁴³

Studies have shown that first-generation antipsychotic medications are associated with improvement across a wide-range of cognitive domains, including executive functioning, sustained attention, memory, language function, time perception, and ocular motor function.¹⁴² Low-dose haloperidol has shown a more rapid onset and equal overall efficacy of cognitive improvement than the newer agent, risperidone, across measures of executive functioning, memory, sustained attention, and visual processing.¹⁴⁴ These results remain consistent, even accounting for concomitant use of anticholinergic medications.

Newer Agents

The 1990s saw a rapid transition of treatments for psychotic disorders, most notably the wide-spread use of newer, second-generation antipsychotic drugs. While older agents exerted their effects primarily on the D₂ receptor, newer agents exponentially expanded the number and type of receptors engaged in treatment. A wealth of data has been generated examining the effects of these second-generation drugs and their effects on cognition. The abundance of data strongly suggests that second-generation antipsychotic medications significantly improve a host of cognitive functions. These improvements include

performance on measures of verbal fluency,^{145–148} executive functioning,^{145,149,150} vigilance,^{148,151,152} sustained attention,^{145,153,154} memory,^{83,155,156} and numerous other cognitive processes.^{157–159} Moreover, the effects are sustained over time and are independent of positive symptom severity. Investigational drugs that directly target NMDA are in development¹⁶⁰ with the NMDA receptor coagonists glycine, D-serine, and D-cycloserine already showing promise for adjunctive remediation of the cognitive deficits seen in schizophrenia.^{116,161} In addition, reversible inhibitors of the enzyme acetyl cholinesterase have also been shown to improve these cognitive deficits.^{12,106,162}

Antipsychotic Medications and Persons Involved in Legal Proceedings

As demonstrated, patients with schizophrenia and related psychotic illnesses often have substantial deficits in a host of cognitive abilities. Antipsychotic medications, both typical and atypical, improve cognitive functioning in these patients. Cognitive abilities such as executive functioning, memory, and attention are surely important for any person involved in legal proceedings in which important issues including liberty interests are at stake. While antipsychotic medications are associated with several negative side effects, including many serious and debilitating diseases, forgoing treatment is associated with numerous negative outcomes, including severe impairments in cognition.

In referring to antipsychotic medications as “mind altering” or their effects as “synthetic sanity,” the legal community misconstrues their cognitive restorative properties in favor of a view akin to psychedelic drugs of abuse. Antipsychotic drugs do not override personal choice or intentionality or “control” the persons who receive them. On the contrary, abundant evidence suggests otherwise. That is, antipsychotic drugs improve cognitive capacities that are vitally important to persons involved in legal proceedings who have psychotic disorders. Consequently, in any legal system that values competent defendants who can appreciate the legal proceedings against them and assist in their defense, antipsychotic medications should be embraced for those defendants afflicted with severe mental illnesses.

Conclusions

Antipsychotic medications are not mind-altering drugs as construed by legal scholars and the courts. Rather, they are beneficial treatments that uncontroversially improve cognition among patients with psychotic disorders, including schizophrenia. Whether the task involves making competent and informed treatment decisions, assisting defense counsel during trial, or enduring the hardships of prolonged incarceration, these medicines enhance a person’s ability to make rational decisions. There is evidence that antipsychotic medications may prevent further clinical deterioration due to potentially permanent oxidative-stress processes occurring in the brains of those affected with psychotic disorders.^{163,164} The time is ripe and the evidence overwhelming that the deprecatory attitudes toward these life-saving medicines are unwarranted and contradictory to the aims of beneficence, autonomy, dignity, and justice that medical ethics and the law passionately seek. The onus is on the courts to make informed decisions regarding such important matters as civil commitment and competency and this necessarily entails an accurate and current understanding of questions brought before them. In terms of antipsychotic drugs, the first step is the declaration that antipsychotic medications are “mind-saving drugs.”

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