Are Persecutory Delusions Amenable to Treatment?

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An understudied but overrepresented disorder among mentally ill offenders is delusional disorder, particularly of the persecutory subtype. There is a common assumption that pure persecutory delusions are hopelessly resistant to treatment,[1] including medications. Several current popular and otherwise comprehensive textbooks on the treatment of mental disorders neglect the treatment of delusional disorders altogether.[2] Moreover, empirical research supporting efficacy and effectiveness in the treatment of such delusions is scant and little known. There have been no controlled studies of specific agents in the treatment of delusional disorders.[1] Treatment efforts are typically confounded by the individual's psychotic denial of illness and resistance to accepting pharmacotherapy. Deluded individuals, who keep their distortions to themselves until arrested for an act resulting from such delusions, reject psychotropic medications because of persistent distrust and even delusional incorporation of those who treat them.

From correspondence with colleagues in forensic inpatient settings, an impression emerges that two standards of care are provided, depending on whether the model in effect is treatment driven or rights driven.

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Not only is the availability of pharmacotherapy for the unwilling patient determined by the weight given treatment needs in civil mental health law, but there is great jurisdictional variation concerning the treatment of forensic patients. In some states, for example, psychiatrists must follow the civil mental health code when seeking court-enforced medication for an incompetent defendant. In other states, the state's interest in restoration of competency is given more weight, and criteria are not so stringent. Even within a state, one court may insist on hearings for treating incompetent defendants with medication, whereas others do not. If the standard of care is treatment driven, medication is more likely to be prescribed. With medication, even if delusions remain indelible, the affective intensity and drive to action are disengaged from them. This substantial, though incomplete, improvement can then allow the patient to be transferred to a less restrictive setting and eventually even to be discharged to outpatient care. On the contrary, with a strongly rights-driven model, the patient is less likely to receive refused medications. The patient with a primary delusional disorder and no other significant disturbance in mood or thought can seem quite normal during the medication hearing, thwarting the psychiatrist's efforts to persuade the judge of the reasonableness of psychotropic medication. Without empirical evidence to support treatment and a robust consensus within the field, the psychiatrist hesitates to recommend treatment for an unaccepting patient whose manner and speech suggest litigiousness[3] and undue anticipation of side effects.

Without medicine, the patient, already committed based on a violent, delusion-driven act, remains deluded and dangerous, and commitments are peri-

odically renewed. This outcome presumes that the patient's autonomy is enhanced by respecting the patient's right to decide and to avoid potential medication side effects. But, if medication would have made a difference, autonomy that comes from logical, realistic, self-serving thinking may have been seriously restricted.

The problem in pursuing this inquiry into effective treatment for pure persecutory delusions is the dearth of relevant empirical data. Pharmaceutical companies have supported a substantial volume of high-quality research to test the efficacy of antipsychotic drugs in the treatment of schizophrenia and antidepressants in the treatment of depressive disorders, but have eschewed research on patients with pure persecutory delusions. Overly suspicious, querulous, contentious, and unwilling but otherwise intelligent individuals are not attractive research subjects. Also, from the perspective of the pharmaceutical industry, developmental research on uncommon psychiatric disorders is not nearly as revenue generating as research designed to develop a better chemical for a far more common disorder.

Nonetheless, there are sound reasons for applying drug trial research to patients with pure persecutory delusions. The lengthy confinements of such patients, reminiscent of custodial care before the advent of modern psychopharmacotherapy, are expensive. If specific drugs are shown to be effective in ameliorating pure persecutory delusions and their resultant untoward behaviors, it may help explain the neurotransmitter involvement of efficacious medications for other disorders with prominent delusions.

We begin inquiry into this problem by first defining the phenomenon of pure persecutory delusions. We then review studies on the course of delusional disorders and summarize studies that pertain to the effectiveness of psychotropic drugs in the treatment of delusional disorders. Finally, in summarizing and reconciling these findings, we discuss implications for the clinician concerned with the treatment and care of offenders with delusional disorder, paranoid type.

The Concept: Pure Persecutory Delusions

Perhaps the greatest frustration for anyone who attempts to review the research literature on this phenomenon is the lack of a consistently applied diagnosis.[4] Studies of paranoid disorders commonly include, for example, subjects with schizophrenia who have paranoid delusions as well as other serious symptoms. Thus, the psychopathologies represented in these studies are too heterogeneous for meaningful comparisons or meta-analysis. Thus, we begin with an attempt to define this phenomenon and to limit our focus accordingly.

For purposes of this inquiry, we focus on those disorders referred to as delusional disorders in DSM III,[5] DSM III-R,[6] DSM-IV,[7] and DSM-IV-TR,[8] as well as those in International Classification of Diseases (ICD)-10.[9] Even with the help of multiple editions involving two diagnostic systems, not many studies limit the focus to pure delusional disorders, let alone pure persecutory delusions. Other syndromes not recognized as mental disorders in standard diagnostic nomenclature (e.g., the misidentification syndrome[10]) are not included in our review of delusional disorders. All criteria are not listed herein—only the essential, inclusion criterion and some comments about other criteria that could affect treatment prognosis. The essential criterion for delusional disorders in DSM IV-TR,[8] similar to that in earlier editions, beginning with DSM III, is presence of "[n]on-bizarre delusions (i.e. involving situations that occur in real life, such as being followed, poisoned, infected, loved at a distance, or deceived by spouse or lover, or having a disease) of at least one month's duration."[8] Types of delusional disorders, with nearly self-explanatory names, are erotomanic, grandiose, jealous, persecutory, somatic, mixed, and unspecified.

Some of the very criteria used to define the disorder could be expected to diminish the likelihood of effective treatment. For example, the minimum of one month's duration increases interrater reliability and reduces confusion with other disorders, but is likely to reduce the probability of effective treatment. Expressed in other words, if treatment with medication is begun early, before the delusion has had time to petrify, chances for a favorable response may be improved. Criterion B[8] requires exclusion of schizophrenia, for which antipsychotic medications have been shown to be effective, although variably, in bringing psychotic symptoms, including persecutory delusions, under control. Similarly, disturbed mood lasting longer than the "delusional periods" must be excluded, and mood disorders, too, have effective pharmacotherapeutic interventions. Also included in this discourse are articles dealing with pure delusional disorder and the treatment of pure persecutory

delusions, even without reference to the inclusion and exclusion criteria of specific diagnostic manuals.

Kennedy *et al.*[11] studied a series of 15 patients, all with the diagnosis of a paranoid delusional disorder and all hospitalized after a violent event. Fear and anger were prominent in all cases and occurred together in most. The affective states were pervasive and typically were found many months before the violent offense. The affective states were so pervasive as to be associated in three cases with violent behavior against victims who were not incorporated into the delusions.

One of the hallmarks of delusions has been the total conviction the patient attributes to his belief. Frosch[12] described this as the "fixity" of the delusions. He reports that this fixity delusion derives from multiple sources—one being the kernel of truth that is typically associated with a pure delusion. "In other words, the sense of conviction of the reality of a delusion may be related not only to the historical truth of the content of the delusion, but to the regressive reappearance of a whole series of associated psychic phenomena coeval with past experiences" (Ref. 12, p 146). Fixity may also be related to the defensive and protective functions of the delusion—a denial of one reality replaced by a subjective one. The patient's "psychic survival" seems to depend on adherence to this fixed false belief. From a psychodynamic perspective, any faltering could lead to dissolution and disintegration of the self.

Neurologic conditions associated with delusions may provide clues regarding the pathophysiology of pure delusions. "The neurological conditions most commonly associated with delusions are conditions that affect the limbic system and the basal ganglia" (Ref. 13, p 513). The mesolimbic area has been described as the brain region responsible for both hallucinations and delusions.[14] The multiple causation of delusions suggests the possibility that multiple brain areas are involved and may help to explain the delusions' relative resistance to treatment.

Besides a seat for delusions, the limbic system is one area where violent and aggressive behaviors originate. Aggression found in delusional individuals may be triggered or exacerbated by symptoms other than the delusion itself. Marino *et al.*[15] reported that among patients with delusional disorder, 50.7 percent had a mood disturbance. Thirty-five percent had a recurrent form and in 42 percent of these, the onset preceded the delusion disorder by a considerable time interval. Their results did not suggest that delusional disorder was a form of mood disturbance, but rather that the mood disorder represented a possible co-diagnosis with delusional disorder.

Preliminary Pharmacotherapeutic Considerations

Before focusing on the course of pure persecutory delusions and their response to pharmacotherapy, some preliminary comments about pharmacotherapy for paranoid delusions in general and potential accompanying affective states are relevant.

The significant role of affective symptoms in delusions provides the psychiatrist with more options. The newest antipsychotic drugs, the atypical antipsychotics (AAs), affect many more neurochemicals than the typical antipsychotics (TAs), which primarily result in D-2 receptor blockade. Recent studies report that AAs appear to reduce hostility and aggression in psychotic patients.[16–20] There are enough data to show mood improvement with olanzapine and risperidone in patients who have schizophrenia and the depressed and manic phases of bipolar disorder.[14] A recent study showed the superiority of olanzapine in the treatment of acute mania.[21] Future studies should reveal similar results with quetiapine and ziprasidone. The chemical formula of ziprasidone is consistent with antidepressant and anxiolytic agents.[14] The AAs should be more favorable than the TAs in the treatment of delusional disorders, because of their demonstrated efficacy in thought disorders and presumed modulating effects on associated symptoms of mood and anxiety.

AAs have a favorable side-effect profile compared with TAs. The AAs exhibit reduced extrapyramidal symptoms (EPS), and some show little or no elevation in prolactin levels (e.g., olanzapine, clozapine). These benefits would be especially attractive for treating the paranoid patient because "paranoid patients are usually very sensitive to all side effects of drugs" (Ref. 22, p 93).

Some clinicians recommend treating the delusional disordered patient with mood stabilizers if antipsychotic drugs fail.[13] The psychiatrist should also consider augmentation with mood stabilizers if AAs are not sufficient.

Phillips and McElroy[23] recently reported favorable results with fluvoxamine in treating delusional patients who also had body dysmorphic disorders (BDDs). Results of this open-label study involving

30 subjects suggest that both BDD and attendant delusions may respond to selective serotonin reuptake inhibitors (SSRIs). Thus, antipsychotics, mood stabilizers, and antidepressants may each have a role in future algorithms for the treatment of delusions in general or pure persecutory delusions in particular. New pharmacotherapeutic approaches may improve the paranoid patient's condition to a level at which the patient can begin to benefit from psychotherapy.

Course and Outcome of Delusional Disorders

A prospective, follow-up study of delusional disorders by Opjordsmoen[24] in Norway, indicates that patients with delusional disorders have outcomes comparable to those in patients with schizophrenia and schizophreniform disorders and less favorable outcomes than in patients with affective disorders. After a mean of 10 and 30 years, the study followed-up 91 patients with diagnosed schizophrenia, 47 with schizophreniform disorder, 35 with schizoaffective disorder, 54 with major affective disorder, 18 with other mostly organic disorders, and 53 with paranoid disorders. Those patients whose delusions appeared to have been reactive to a precipitating factor showed a favorable prognosis. Approximately one fifth of the delusional patients eventually showed deterioration into a schizophrenic condition. Another subgroup manifested a more chronic, persistent course. Unfortunately, for purposes of the present inquiry, treatments were not described. However, the observation that it was difficult to keep patients with paranoid disorder in treatment may provide a clue as to why treatment was sometimes less than satisfactory in these patients.

Retterstøl[25] conducted a similar follow-up study using DSM III diagnostic categories. Although patients with paranoid and schizophrenic disorders showed a worse outcome than those with affective and schizoaffective disorders, approximately one of three patients with Kraepelin's paranoia showed no psychotic symptoms when seen at follow-up. Retterstøl concludes, ". . . paranoia is not always chronic, and . . . the well-used maxim 'once paranoia—always paranoia' is not true" (Ref. 25, p 283). Unfortunately, information on the type of treatment provided was too scant to allow any impressions about which treatments or medications were most effective.

Opjordsmoen[26] reported a study of 72 patients during their first hospital admissions who were reevaluated after a mean of 10 years—42 of them after 27 years. A significant predictor of outcome was duration of symptoms before hospitalization. Those who had been delusional for more than six months showed a decidedly worse course, and those who had been symptomatic for more than two years, worse yet. Again, treatments were not described, and there is therefore no way of ascertaining what might have improved the course. These findings at least raise the possibility, however, that the longer a delusional disorder goes untreated, the more resistant it becomes to treatment. Conversely, those with paranoid delusional disorders may be more amenable to medication if treated early in the course of the illness.

From a sample of 239 patients with a diagnosed paranoid state and hospitalized at the Phipps Clinic (The Johns Hopkins University Hospital, Baltimore, MD) between 1913 and 1940, Stephen *et al.*[27] studied 60 patients who retrospectively met the DSM IV criteria for delusional disorder. All the patients had follow-up for more than five years and had no prior hospitalizations. The delusions were subtyped as 73 percent persecutory, 18 percent jealous, 3 percent grandiose, 3 percent somatic, and 2 percent erotomanic. On follow-up, 52 percent were rated as unimproved and 27 percent as recovered.

The outcome of this study, conducted before the introduction of drug treatments, was contrasted with that of patients discharged from Phipps Clinic between 1949 and 1959, when antipsychotic drugs were beginning to be used. During this later period, only 26 percent were rated as unimproved compared with 52 percent in the years before drug treatments were available. The rates of complete recovery remained the same (27% versus 22%) during both these periods. Although the recovery rates were the same, the higher percentage of patients from the drug-treatment era showed that partial response may have been due to a softening of delusions as a result of pharmacotherapy.

Studies of the Effectiveness of Pharmacotherapy for Delusional Disorders

In a double-blind study,[28] seven patients with delusional disorder (DSM III-R) treated with pimozide (median dose, 4.57 ± 1.9 mg) for six weeks, showed no favorable responses on the Brief Psychiatric Rat-

ing Scale (BPRS) scores, global assessment of functioning (GAF), or in the severity or fixity of delusions. One of the limitations of this study is the short treatment duration of six weeks, which may not have been long enough for the desired changes to occur. Also the median dose of pimozide used in this study was lower than the *PDR*-recommended[29] dose of 10 mg or of 0.2 mg/kg of body weight. It is noteworthy that delusions of all seven patients had persecutory themes, and the duration of illness was 6 to12 years. This raises the question of whether the long duration of illness before treatment could have contributed to the treatment failures in this study.

Munro,[30] in contrast, states that treatment of "monodelusional disorders" (i.e., DSM III-R paranoid (delusional) disorder) can be "strikingly successful."[30] Several case reports indicate that pimozide may be effective in the treatment of delusional disorders.[31] This diphenylbutylpiperidine antipsychotic has been used in the treatment of Tourette's syndrome, acute agitated psychosis, schizophrenic symptoms, and monosymptomatic delusional conditions. Conditions corresponding to specific types of delusional disorder include erotomania,[32] pathologic jealousy,[33] hypochondriadic psychosis,[33] delusional parasitosis,[34] delusional pseudocyesis,[35] delusional infestation,[35] and delusional dysmorphosis.[36]

In a 1995 literature review of 1,000 articles on paranoid delusional disorder, Munro and Mok[37] concluded that 80.8 percent of patients made a full or partial recovery, adding that this compares favorably with the treatments of other psychiatric disorders. However, among the numerous references, only a few clearly concerned treatment of the delusional disorder about which we are most interested: the persecutory type. Without the benefit of controlled studies, the question arises whether, even with such case reports, the persecutory type of delusional disorder would show the same positive response as these other types.

Regarding the persecutory type in particular, Ungvari and Hollokoi[38] reported the successful treatment with pimozide of an 85-year-old man. The delusional thinking of this patient subsided as did his talk about litigation. Antidepressants have also been used with favorable outcome.[1] Trazodone was used successfully when antipsychotic drugs had no effect on a patient's persecutory delusions and associated symptoms of anxiety.[39]

Discussion

Relatively little has been written about the treatability, or lack thereof, of the persecutory type of delusional disorders. Yet individuals with such disorders are not uncommon in forensic patients and should compel our studied attention because of the considerable clinical, legal, and ethical challenges they present. Of special concern is the presumed immutable nature of their delusions, often thought to be unresponsive to medication. Without effective treatment, extended civil or criminal commitments harken back to the preantipsychotic era of custodial confinement with little hope for improvement. The lack of empirical studies on treatment of this disorder is a serious deficiency at a time when greater emphasis is placed on evidence-based medicine in clinical work and on evidentiary standards in courtroom testimony.

However, what little exists in the way of studies yields results that are not entirely hopeless. Although the prognosis is not as favorable as that of affective disorders, it may not be much worse than that for other major psychiatric disorders. Other types of delusional disorders have shown response to antipsychotic medication, and at least a few case reports indicate a favorable result for pharmacotherapy of the persecutory subtype in particular.

For the willing and cooperative patient, combined psychotherapy, designed to minimize distrust, and pharmacotherapy may offer the best hope for symptom amelioration and optimal level of functioning. The choice of antipsychotic drug, always offered with full informed consent, must be based on the patient's individual presentation, what little exists in the way of supportive literature, individualized risk-benefit analysis, and careful monitoring for the desired response. An antipsychotic medicine may reduce the intensity and continued expansion of the delusional system. A mood-altering or impulse-controlling medicine may reduce the drive to act on the basis of a delusion. An important point should not be understressed: Even without eradication of a delusion, control over the drive to act on the delusion may make the difference between treatment in the community and long-term hospital care. Thus, even this modest change in the patient's mental condition can constitute a substantial improvement in level of functioning and autonomy.

The real challenge occurs when the patient with pure persecutory delusions refuses recommended pharmacotherapy and presents an ongoing threat to others if not confined. Allowing time for a relatively trustful therapeutic relationship to develop may result in the patient's eventual ability to appreciate the logic of a pharmacotherapeutic trial. But temporizing too long may also allow the delusions to become more firmly implanted and resistant to change. Moreover, extended hospitalization without medication may allow time for the patient to incorporate staff into the persecutory delusional system and to become more distrustful of and uncooperative with staff members, thereby further frustrating efforts at successful treatment.

If medication is offered to a voluntary patient, it should be considered for the unwilling patient. In either case, this presumes the medication has a therapeutic rationale, it has been used successfully by others, the results of successful use have been published, and a risk-benefit analysis favors treatment. If the administration of medication cannot yet be based on rigorous research, neither can it be based only on guesswork. The treatment, even if empirical, can be clinically appropriate and offer reasonable hope for improvement.

The second phase of analysis is both philosophical and legal. Even if the medication is clinically appropriate, should it be forced on an unwilling patient? A patient's-rights perspective is that involuntarily administered mind-altering medication is more intrusive and, therefore, more restrictive than extended involuntary hospitalization. The patient's rights ought to prevail, especially when mild side effects of the medication are probable. Serious side effects, although improbable, are known risks, and the favorable effect on symptoms and dysfunction elude quantitative prediction. The likelihood of extended hospitalization without medication can be included in this equation, but, without a present emergency, the patient should decide, having been apprised of the consequences of opting for or against pharmacotherapy.

Although more apt to be categorized as a best-interest approach, an alternative view is arguably just as considerate of a patient's rights. Pharmacotherapy not only enhances the possibility of symptom improvement, restores the level of functioning, and perhaps prevents further expansion and crystallization of the delusional system, it also offers the possibility of reducing the drive behind the delusions, permitting hospital discharge with follow-up in the community. Rather than mind restricting, the medication is mind liberating. It brings the possibility of a less tortured existence and improved functioning, and it can serve as the key to real, physical liberty. Brief decisional encroachment thereby results in substantial physical liberty and unfettered mental, functional, and decisional autonomy in the long run.

Whether the clinician errs in the direction of encroachment on the treatment decision, to enhance other freedoms, or in the direction of respecting the patient's right to decide, even in the face of likely extended hospitalization without improvement, raises the question of the patient's capacity to make treatment decisions. From a legal standpoint, if the patient is unable to make a rational decision regarding medical treatment, the appropriate court can find the patient to be incompetent and appoint a guardian to make treatment decisions on the patient's behalf. The practicality of this approach depends, of course, on the laws pertaining to competency in the given jurisdiction, as well as the infrastructure for providing guardians and supporting their effective functioning as guardians. Typically, competency-guardianship hearings are reserved for discussion of medical issues and not psychotropic medicine *per se*, because enforced psychotropic medication is covered in mental health law. However, the mental health law is not always completely clear and helpful when applied to patients with pure delusional disorders, who can present a danger to others when living freely in the community, but not necessarily while in the closely supervised and structured setting of a hospital. If the law for court-enforced medication requires that the patient pose an ongoing danger to others, unanswered in the hospitalized patient is whether the danger would be present were it not for the physical control of the patient's current hospitalization.

The mental health law concerning court-enforced medication may include a criterion that because of mental illness the patient is unable to make a rational treatment decision in his or her best interest. The patient with pure persecutory delusions often has enough awareness of reality and expectations from others to provide rational objections to taking medication. At the same time, the patient can harbor delusional beliefs that are the true reasons for the patient's refusal of medications, yet the patient

knows enough not to reveal the delusions during the court hearing or when evaluated for a second opinion.

Having determined that the proposed medication is clinically appropriate, that the patient's liberty and autonomy interests would be best served by pharmacotherapy, and that the patient lacks the capacity to make a rational treatment decision, the clinician then applies such findings to the legal criteria that apply to court-enforced medication. In court, the clinician cannot testify based on empirical research alone that the medicine will, more likely than not, be efficacious. The clinician can say, however, that medication appears to have been used effectively in similar cases and therefore offers improved probability of symptom improvement and eventual ability to function in the community. In clinical practice, the clinician is doing what is reasonably thought to be best for the patient; in the courtroom, the clinician is honest and objective, neither over- nor understating the case.

If nothing else, it is hoped that this analysis underscores the critical importance of quality research into efficacious psychotropic agents and reasonable algorithms for the treatment of pure persecutory delusions. Once the hoped for pharmacotherapeutic approaches are developed and validated, patients afflicted with this disorder will presumably join patients with other disorders who have benefited immeasurably from the gratifying results of productive psychopharmacologic research over the past half century.

Conclusions

The treatment of pure persecutory delusions, not an uncommon challenge in forensic inpatient settings, is fraught with both therapeutic and legal barriers. It is commonly assumed that the disorder is hopelessly immutable and particularly resistant to pharmacotherapeutic interventions. Literature review, however, suggests that the prognosis is not invariably so grim and provides evidence, although meager or tangential, that medication has been helpful in specific cases. A reasoned approach, taking into account available literature, is recommended when the clinician must decide whether court-ordered medication is appropriate for the noncompliant patient with pure persecutory delusions. This commentary cries out for further research on the treatment of delusional disorder, persecutory type, and particularly on pharmacotherapeutic approaches that, even if unable to erase the delusion, can at least reduce their intensity, drive to action, and resultant disturbing behaviors.

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