Abstract

The author distinguishes between the putative neuroleptic-induced disorders of tardive dysmentia and supersensitivity psychosis. The distinction is made with regard to clinical features, response to pharmacological intervention, and proposed etiologies. It is suggested that tardive dysmentia is due not to dopaminergic supersensitivity but to some other neurotoxic phenomenon associated with the use of neuroleptic drugs. The possibility that cholinergic mechanisms are involved in the tardive dysmentia syndrome is examined. Finally, the potential for such drug-induced disorders to confuse diagnosis is highlighted.

The article by Wilson, Garbutt et al. (1983) proposing the concept of tardive dysmentia and Garbutt's (1984) subsequent response to Mukherjee's (1984) criticism suggests yet another neuroleptic-induced iatrogenic syndrome. Wilson et al. (1983) attribute the clinical findings of tardive dysmentia to the development of dopaminergic (DA) supersensitivity analogous to tardive dyskinesia's putative etiology (Tarsy and Baldessarini 1974). Their hypothesis therefore is similar to the one proposed by Chouinard and his associates (Chouinard and Jones 1978, 1980; Chouinard et al. 1978) and others (Ungerstedt and Ljungberg 1977; McCarthy 1978; Davis and Rosenberg 1979; Forrest and Fahn 1979). Yet, clinically, the syndrome of tardive dysmentia described is different from that of neuroleptic-induced supersensitivity psychosis. According to Wilson, Garbutt et al. (1983), tardive dysmentia is characterized by loud speech, unstable mood, excessive approach to the examiner, excessive words, and euphoria. Neuroleptic-induced supersensitivity psychosis, in contrast, is manifested as the positive symptoms of schizophrenia, i.e., delusions and hallucinations. Although some overlap might be expected between these two syndromes in their clinical presentation, Wilson et al. (1983) state clearly that patients with tardive dysmentia did not seem more psychotic in the sense of showing greater delusional ideation, hallucinations, or formal thought disorder. How therefore does one integrate these two putative syndromes related to DA supersensitivity?

The proposal of neuroleptic-induced supersensitivity psychosis was based on the theory that DA supersensitivity developed in response to neuroleptic exposure in mesolimbic or mesocortical DA tracts. Based on this hypothesis, the syndrome was explained as being analogous to the clinical characteristics of a DA supersensitivity disorder; i.e., the patients would manifest an appearance of psychotic symptoms closely contingent upon neuroleptic dose decrease or discontinuation due to uncovering of DA supersensitivity by removal of DA receptor blockade. Psychotic symptoms would respond rapidly to a reinstitution of neuroleptic medication due to masking of the DA supersensitivity by reinstitution of DA receptor blockade. Psychotic symptoms would appear in the aforementioned manner only after substantial exposure to neuroleptic treatment, thus allowing for DA supersensitivity to develop. Tolerance to the antipsychotic affect of the drug would appear due to a reininstitution of neuroleptic medication due to masking of the DA supersensitivity by reinstitution of DA receptor blockade. Psychotic symptoms would appear in the aforementioned manner only after substantial exposure to neuroleptic treatment, thus allowing for DA supersensitivity to develop.
disorders were presumably due to the same drug-induced phenomenon. In fact, with further study, such a correlation has not been found (Chouinard and Jones 1982). Also, certain features of the two disorders are different, including the tendency for supersensitivity psychosis to be more easily reversible (Chouinard and Steinberg 1984). A number of possible explanations for these findings can be offered. One explanation would be that the two syndromes are not due to the same pathophysiological mechanism. Thus, tardive dyskinesia, although suggested to be a dopaminergic supersensitivity phenomenon, may in fact be caused by a different neurotoxic mechanism. This may be especially true for irreversible forms of tardive dyskinesia. The same neurotoxic mechanism may, in turn, be that which leads to the correlation of tardive dyskinesia found by Wilson et al. (1983) with the syndrome of tardive dysmentia.

Tardive dysmentia would not be due to DA supersensitivity and would be different from neuroleptic-induced supersensitivity psychosis, both in terms of its clinical presentation and its response to pharmacological intervention.

A key point to make with regard to the work of Wilson et al. (1983) is that no attempt within the study was made to examine the possibility that this syndrome is a DA supersensitivity syndrome that follows some of the patterns we have proposed for the supersensitivity psychosis syndrome. Indeed, no attempt was made to assess other potential etiologies for the syndrome. The authors simply found a correlation between tardive dysmentia and tardive dyskinesia. As Mukherjee (1984) has suggested, many possible explanations can be given for this correlation. On the other hand, the two syndromes may be due to similar pathophysiological mechanisms related to neuroleptic exposure. It would therefore be interesting to use pharmacological probes in an attempt to delineate that common mechanism without accepting it simply as DA supersensitivity. Given the chronic exposure to neuroleptics that constitutes the history of the patient population studied by Wilson et al. (1983) where an average of 17 years of drug treatment was present, most of these patients have undoubtedly been treated extensively with low potency neuroleptics. As a result, the effects of such neuroleptics would not be confined to dopamine receptor blockade, in that action of low potency neuroleptics occurs at multiple receptor sites. Although Mukherjee (1984) has pointed out that the syndrome does not completely resemble dementia as suggested by the title of Wilson, Garbutt et al.'s article, a demented syndrome putatively caused by drug exposure might be more likely related to changes in cholinergic activity caused by neuroleptics and antiparkinsonian medication than to dopaminergic supersensitivity. Also, the euphoric aspect of the tardive dysmentia syndrome could explain the abuse potential for antiparkinsonian drugs taken chronically, if cholinergic mechanisms are indeed a key element in the syndrome's etiology. It would therefore be interesting to assess changes in the tardive dysmentia syndrome that might occur in response to drugs affecting cholinergic activity.

Finally, Wilson et al. (1983) suggest that the tardive dysmentia syndrome may result in a rediagnosis of some schizophrenic patients as manic-depressive patients, given that some of the symptoms resemble those of mania. If one considers supersensitivity psychosis, a contrasting hypothesis can be entertained. Manic-depressive patients exposed to neuroleptics for control of mania may potentially develop neuroleptic-induced supersensitivity psychosis which, if not recognized, could lead to neuroleptic dependency and positive symptoms of schizophrenia. Such patients could ultimately be cast into the diagnostic entity of schizoaffective disorder or schizophrenia. The point to be made, of course, is that illnesses as severe as manic-depressive psychosis and schizophrenia, which require treatment with highly toxic medications such as neuroleptics, can best be understood and studied before drug treatment and the effects of institutionalization have taken their toll.

References


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Commentary

Introducing their concept of tardive dysmentia, Wilson et al. (1983) postulated a neurotoxic effect of neuroleptic medication as a possible etiological factor. Noting an association between dysmentia and dyskinesia ratings, they further speculated that the pathophysiological changes responsible for the proposed behavioral syndrome were similar to those leading to tardive dyskinesia (TD), viz. dopaminergic (DA) supersensitivity, and referred to tardive dysmentia as a "behavioral equivalent of tardive dyskinesia."

Jones (*Schizophrenia Bulletin, this issue*) has highlighted the differences between an earlier proposed concept of DA supersensitivity psychosis (Chouinard and Jones 1978) and tardive dysmentia. He argues convincingly against viewing DA supersensitivity as a pathophysiological basis for tardive dysmentia and proposes an as yet unidentified neurotoxic phenomenon as a probable basis for this proposed disorder. Like Wilson et al. (1983), Jones appears to favor tardive dysmentia being a neuroleptic-induced disorder and introduces the perspective of cholinergic system dysfunction.

While these speculations are interesting, the validity of the tardive dysmentia concept remains to be unequivocally established and the choice of the term "dysmentia" has already been questioned (Mukherjee 1984).

We have just concluded a preliminary exploratory study of this proposed syndrome in a group of 60 chronic psychiatric inpatients. Tardive dysmentia assessments were made using the scale described in Wilson et al. (1983) by a psychiatrist blind to the proposed concept. The tardive dysmentia scale, as proposed, showed modest internal consistency (coefficient alpha = .66). Principal components factor analysis yielded two factors with Eigenvalues greater than one. Factor 1 had high loadings on loud speech, excess words, and approach to the examiner. Factor 2