EDITORIAL

IS SCHIZOPHRENIA MORE THAN ONE DISEASE ?

Recent evidence suggests that although the reliability of diagnosis, and particularly of the elicitation of symptoms, can be substantially improved, prediction of outcome remains highly uncertain unless the established progression of the disease be taken into account. An illness or group of illnesses described as schizophrenic can be reliably identified, but on the one hand, their demarcation from the affective disorders, and on the other, their subdivision, on grounds other than observed course into illnesses of good and poor prognosis remain unsolved problems.

Kendell, Brockington and Leff (1978) have compared the validity of six operational definitions of schizophrenia namely :

1. Langfeld's criteria for distinguishing true schizophrenia from schizophreniform psychosis (1960).
2. The presence of one or more of Schneider's symptoms of the first rank (1959).
3. The New Haven criteria (Astrachan **et al.**, 1972).
4. The "flexible criteria" derived empirically from data from the International Pilot Study of Schizophrenia (Carpenter **et al.**, 1975).
5. The Research Diagnostic Criteria of Spitzer **et al.**, (1975).
6. A diagnosis derived from P.S.E. ratings by the Catego program using the Catego class S+ to represent schizophrenia (Wing **et al.**, 1974).

The authors assessed the definitions' respective abilities to predict incomplete recovery from the index episode, persistent symptoms and poor social outcome. They found that all six definitions were more successful at predicting a poor symptomatic than a poor social outcome. Three sets of criteria (Langfeld's, 1960; Carpenter "flexible" 1973; and Spitzer Research Diagnostic Criteria, 1975) consistently predicted poor

outcome better than the presence of Schneider's first rank symptoms (1959) or the New Haven criteria (Astrachan **et al.,** 1972).

The belief that the primary disturbance in schizophrenia is chemical has long been plausible, that it is a disturbance of neurohumoral function is supported by observations that schizophrenic symptoms can be exacerbated in a patient and provoked in non-psychotic individuals by drugs that act on specific transmitters.

Craw (1980) summarized the Neurohumoral hypothesis of schizophrenia as follows :

1. Serotonin deficiency (Gaddum, 1954; Wooley and Shaw, 1954). The argument that LSD psychosis resembles schizophrenia and that LSD blocks serotonin receptors. Against this that PM studies showed that serotonin turnover was not decreased and serotonin receptors remained unchanged.

2. Dopamine neurone overactivity (Randrup and Munkvad, 1965). Evidence for this hypothesis is : a) Amphetamine psychosis resembles acute paranoid schizophrenia. b) Amphetamines increase dopamine release. c) Antipsychotic drugs block dopamine receptors. Against this theory, the fact that in PM studies dopamine turnover is not increased.

3. Dopamine receptor supersensitivity (Bowers, 1974). The argument with this hypothesis is as the above theory and PM studies showed evidence of increase of dopamine receptors.

4. Noradrenaline neurone degeneration (Stein and Wise, 1971). The argument here is that reward processes are mediated by central noradrenergic systems and anhedonia is a core feature of chronic schizophrenia. PM studies showed evidence against this hypothesis, that dopamine B-hydroxylase is not reduced.

5. Mono-amine oxidase deficiency (Murphy and Wyatt, 1972). It

was observed that platelet MAO activity is reduced in some schizophrenic patients, but PM studies showed no reduction in MAO activity.

At present, therefore the only change found consistently in the PM studies of the schizophrenic brains is an increase in the numbers of dopamine receptors.

If specific neurohumoral systems are disturbed in schizophrenia, we expect some subtle changes in pituitary hormone secretions. There is good evidence that the tuberoinfundibular dopamine system inhibits prolactin release. If dopamine release was increased in schizophrenia it might be predicted that prolactin secretion would be unusually low. A significant positive relationship between increase prolactin secretion and antipsychotic potency has been demonstrated (Langer **et al.,** 1977).

It was shown by some investigators that some schizophrenics present with pneumo-encephalography ventricular enlargement (Story 1966, Young and Crampton 1974). In the first computerized tomography (Johnstone **et al.,** 1978) increased ventricular size was correlated with negative symptoms and evidence of intellectual impairment.

Two syndromes in schizophrenia :

It seems probable from above data of neurohumoral changes on one hand and the pathological changes in the brain on the other hand, that we have two types of schizophrenia as described by Crow (1980).

	Type I	**Type II**
Known as :	Acute schizophrenia.	Chronic schizophrenia.
Symptoms :	Hallucinations, delusions, thought disorder. (Positive symptoms)	Affective flattening, poverty of speech, loss of drive. (Negative symptoms)
Response to Neuroleptics:	Good.	Poor.
Outcome :	Reversible.	? Irreversible.
Intellectual impairment :	Absent.	Sometimes present.
Pathological process :	Increased dopamine receptors.	Cell loss and structural changes in the brain.

Crow (1980) discussed the possibility of these two syndromes. It seems that two syndromes can be distinguished in those currently as schizophrenic and that each may be associated with a specific pathological process. The first (the type I syndrome, equivalent to "acute schizophrenia", and characterized by the positive symptoms — delusions, hallucinations, and thought disorder) is in some way associated with a change in dopaminergic transmission; the second process (the type II syndrome, equivalent to the "defect state," and characterized by the negative symptoms — affective flattening and poverty of speech) is unrelated to dopaminergic transmission but may be associated with intellectual impairment and, perhaps, structural changes in the brain. Type I symptoms are reversible ; type II symptoms, which are more difficult to define, may indicate a component of irreversibility. The former predict a potential response to neuroleptics; the latter are more closely associated with a poor long-term outcome. Episodes of type I symptoms may be followed by development of the type II syndrome, and both may be present together. Type II symptoms, however, define a group of illnesses of graver prognosis. They occasionally occur in the absence of the type I syndrome (for example, in "simple" schizophrenia), but because these symptoms are not well defined the diagnosis in these cases is difficult to establish.

This hypothesis of two diseases should not add to the nosological difficulties of schizophrenia but should stimulate us for further thoughts regarding the aetiology, management and prognosis of this illness.

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