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Correspondence

POSITIVE AND NEGATIVE SCHIZOPHRENIC SYMPTOMS AND THE ROLE OF DOPAMINE

DEAR SIR,

We somewhat hesitantly enter the discussion regarding the nature of the schizophrenias. The relationship between the acute syndromes with 'positive symptoms' and the chronic 'defect' states is an old subject of debate. Recently the alleged occurrence of a high incidence of neurological abnormalities in the defect states, together with a relative failure to respond to neuroleptic therapy and a high hereditary predisposition, led Kety to suggest that two distinct disease entities were likely to be involved in the acute syndromes and defect states rather than different stages or outcome of a single condition. Dr Tim Crow added observations on ventricular size and cognitive functioning to the list of differences and coined the terms Type 1 and Type 2 to label the two conditions.

In the discussion papers (*Journal*, October, 1980, **137**, 379–86), two hypotheses were presented by Dr Tim Crow and Dr Angus McKay relating the pathophysiology of the syndromes to changes in dopaminergic systems. McKay regards the defect state and positive symptoms as both explicable in terms of changes in dopaminergic activity, whilst Crow regards the syndromes as "independent dimensions reflecting different underlying pathological processes". Both seem to regard the pathological basis of the defect state as irreversible, representing widespread but subtle brain damage.

Much of the evidence cited by Crow supporting the argument that different pathological processes underlie Type 1 and Type 2 syndromes of schizophrenia does not bear close scrutiny.

Kornetsky (1976) reporting the unremarkable effect of amphetamine on the symptomatology of chronic schizophrenics was clearly referring to Type 1 syndrome and not the Type 2 as implied by Crow. Thus Kornetsky stated of his patients 'they all exhibited an active thought disorder, delusional thinking, and in some cases hallucinations were present', and was clearly assessing change in these symptoms. His negative results contradict the unpublished results of Angrist quoted by Crow.

Crow stated "In some chronic schizophrenic patients there is CT scan evidence of increased ventricular size (Johnstone *et al*, 1978a) and in these patients increased ventricular size is correlated with intellectual impairment and the presence of negative symptoms". Yet in the results section of the paper, we are told that apart from correlations between some measures of cognitive function and measures of brain size "All other comparisons between measures of cerebral size and assessment of cognitive function or mental state were not significant".

Crow cites the work of Johnstone *et al* (1978b) that "in patients with acute schizophrenia, positive and not negative symptoms respond to neuroleptic medication". This controversial finding was inherent in the methods of measurement, as change in the positive symptoms was much more likely to be detected than change in negative symptoms. For example, poverty of speech which made up half of the negative symptoms had a mean pre-treatment score of about 0.8 on a 4 point scale. On this scale (Krawiecka *et al*, 1977), a score of 1 for poverty of speech is given when the 'patient only speaks when spoken to, or tends to give brief replies'. This is contrasted with the mean pre-treatment scores of about 3.8 on a 4 point scale for positive symptoms of delusions and about 3.4 for hallucinations.

Acute syndromes with positive symptoms have a variable outcome and may end in complete remission, in recurrent acute episodes or in progression to a defect state. The defect state may be arrested at any stage and acute exacerbations of positive symptoms may be superimposed on the clinical picture at any stage. Defect states rarely occur without evidence of positive symptoms at some stage in the development of the illness and the concept of simple schizophrenia rarely stands up to careful scrutiny. These clinical observations seem to fit the idea of varying manifestations and outcome of a single process rather better than two different pathological processes. Any hypothesis must also take into account other clinical observations, e.g. the occurrence of Schneiderian first rank symptoms in mania and in organic brain disease and also in drug induced psychosis.

The following model is advanced as a possible alternative to those proposed by McKay and Crow.

In the normal individual, dopaminergic activity will vary over a certain range which will never exceed the limits consistent with organized non-psychotic functioning. The pathological variations are possible

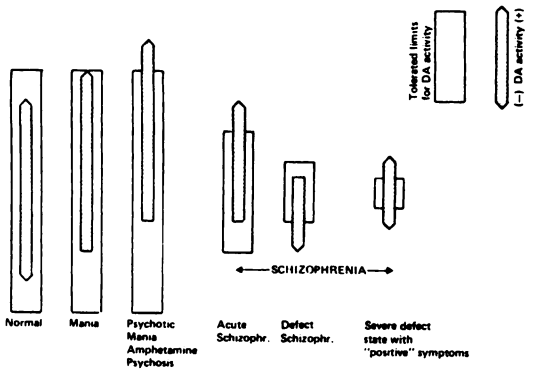

FIG 1.

using the two variables of dopaminergic activity and tolerated limits (Fig 1).

On this model the single abnormality distinguishing the acute schizophrenic syndrome and defect states from other states is a constriction of the tolerated range of dopaminergic activity. Thus situations which increase dopaminergic activity, e.g. stress, may result in psychotic symptoms, acute schizophrenic reaction (reactive schizophrenia, Type 1 schizophrenia).

Further constriction of the range will make attacks of acute symptoms more likely. As the range becomes markedly restricted, dopaminergic activity will fall below the lower limit for normal functioning—this may represent the defect state and in the extreme case there may be no range of dopaminergic activity consistent with normal functioning so that positive and negative symptoms may co-exist at all levels of dopaminergic activity.

Of course this model begs the question as to which neuronal systems are involved in determining the limits of tolerated dopaminergic activity. That these limits exist and show individual variation is demonstrated by the fact that widely different doses of amphetamine are required to precipitate psychotic symptoms in normal individuals.

Constriction of the range might follow selective brain damage as in temporal lobe lesions or Huntington's chorea or some of the cases described by Crow. The possibility, however, exists that there might be two types of constriction—one representing an inherited constriction—the other an acquired constriction.

What practical use is this model? It suggests the possibility that some way might be found to extend the limits of tolerated dopaminergic activity as an alternative to blocking the excess dopaminergic activity in the case of positive symptoms or increasing dopaminergic activity as suggested by McKay in the defect states.

Since we know little of the factors involved in setting these limits, this may seem like looking for a needle in a haystack. However, we do have animal models which may allow us to study the changes of behaviour under dopaminergic stimulation and these may be used to identify means by which the range of dopaminergic stimulation consistent with the preservation of integrated behaviour patterns, may be extended. If the only justification for presenting another model is that it prevents opinions on schizophrenia from being fixed prematurely, then it may be serving a useful purpose.

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DOPAMINE HYPOTHESIS IN ACUTE PSYCHOSIS

DEAR SIR,

Angus Mackay (1980) and Tim Crow (1980) recently discussed in this journal the role of dopamine in schizophrenia, but drew somewhat different conclusions. Both Mackay and Crow favoured dopaminergic overactivity in some region of the brain (possibly in the mesolimbic or mesocortical areas, but probably not in the neostriatum) as important in causing the positive Schneiderian symptoms of the acute psychotic phase of some schizophrenic illnesses (the Type 1 syndrome of Crow). Mackay, in addition, suggested that the defect state of