

a lead in the further understanding of the amine hypothesis of affective illness, especially mania.

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Dopamine Hypothesis of Neuroleptic Drug Action

SIR: The October issue (*Journal*, **151**, 455–465) contained three articles discussing the merits of the dopamine hypothesis of neuroleptic drug action. Since it is but a small step from there to a dopamine hypothesis of schizophrenia, and since various theorists and textbook authors have made that step, it seems appropriate to ask whether a better understanding of neuroleptic action is likely to tell us more about the underlying cause or causes of schizophrenia. I think that there are three reasons for pessimism in this regard. Firstly, the positive psychotic symptoms that respond to neuroleptic treatment are non-specific even when they are of the 'first rank', occurring in affective and organic disorders as well as in schizophrenia. Secondly, acute psychotic symptoms seem to be the least heritable component of schizophrenia, suggesting that they are only loosely related to the underlying biological predisposition. Finally, the severity of acute psychotic symptoms is a poor predictor of progressive decline with accumulating negative symptoms—a feature that seems much more distinctive of schizophrenia than the acute psychotic episodes themselves.

In the light of these considerations, it seems possible that a better understanding of neuroleptic drug action may reveal little about the origins of schizophrenia, just as an understanding of the actions of aspirin reveals little about the origins of influenza. A dopamine (or calcium-activated potassium conductance) hypothesis may no more explain schizophrenia than a prostaglandin hypothesis

explains influenza. Of course, the treatment of positive psychotic symptoms is extremely valuable, and a better understanding of drug action may lead to future improvements in symptomatic treatment. At the same time, however, we may need to recognise that the search for better neuroleptics is relatively unlikely to lead to a specific treatment for schizophrenia, just as the search for a better febrifuge is unlikely to lead to a specific treatment for influenza.

Given the need for effective treatments for schizophrenia's relatively distinctive negative symptoms, the most appropriate research strategy may be to concentrate primarily on the correlates and origins of those features that generally distinguish schizophrenia from other psychotic disorders. Positive symptoms are striking and easily recognised, but they may be as much of a distraction to researchers as they are to patients. How intact are the research community's filters in the face of such absorbing noise?

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Lithium, Psoriasis, Abnormal Glucose Tolerance, and Thyroid Dysfunction

SIR: We wish to report a patient exhibiting several unusual effects related to treatment with lithium.

Case report: A fifty-year-old man presented to this unit in February 1974 because of heavy drinking. He was noted to have had psoriasis since his early teenage years, characterised by minimal skin lesions but severe, disfiguring nail changes.

In 1975 he developed a depressive illness, and despite treatment with antidepressants continued to be subject to frequent severe fluctuations of mood. Lithium carbonate was commenced in November 1976. His mood swings became less marked, and he remained euthyroid for five years. In May 1982 he presented complaining of headache. There were no clinical signs, but his free thyroxine index was marginally raised. Three weeks later he was admitted as an emergency to a general hospital with chest pain thought to be cardiac in origin. He was noted to have lost a stone in weight over the preceding month, and complained of thirst. On examination he was flushed and sweating with a marked fine tremor and palpable goitre. His pulse was 136/min and blood pressure 160/80. Reflexes were bilaterally brisk. ECG showed sinus tachycardia but no ischaemia. Elevated serum thyroxine confirmed the clinical diagnosis of thyrotoxicosis.

Throughout the hospital stay, intermittent glycosuria occurred and an oral glucose tolerance test was abnormal. This was thought to be secondary to hyperthyroidism, and glibenclamide was commenced. He remained hyperthyroid