tiate unipolar from bipolar patients, so that research with improved sampling and methods must continue.

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Reference

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TARDIVE DYSKINESIA AND DEMENTIA

DEAR SIR,

Famuyiwa *et al* (*Journal*, December 1979, **135**, 500–4) discuss two possible explanations of their findings, both of which invoke neuroleptic drugs in the etiology of tardive dyskinesia. Application of Occam's razor suggests a third possibility, namely, that tardive dyskinesia is simply one manifestation of the cerebral degeneration caused by the schizophrenic disease process in these patients.

Although tardive dyskinesia can be suppressed by neuroleptics, until a survey is carried out of its incidence among chronic schizophrenics never exposed to neuroleptics, the etiology of tardive dyskinesia remains uncertain. The finding that the mean dose of fluphenazine decanoate among the tardive dyskinesia patients was higher than among the non-tardive dyskinesia patients could indicate that the former were more brain damaged by their illness and required higher doses of drug to control their symptoms. Had there been more than three patients on oral drugs in the tardive dyskinesia group, a similar difference might have been found between oral dosage means.

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OXYPERTINE FOR TARDIVE DYSKINESIA

DEAR SIR,

We have read with great interest the paper by Drs Mackay and Sheppard on pharmacotherapeutic trials in tardive dyskinesia (*Journal*, December 1979, **135**, 489–499). Brief reference is made there to oxypertine as a possible therapeutic agent and this substance is at present being investigated clinically by us.

Oxypertine is thought to exert its therapeutic effects by depleting pre-synaptic neuronal stores of neurotransmitters. Compared with reserpine and tetrabenazine, it is a more potentent depleter of brain noradrenaline, but has less dopamine depleting activity. It has been shown to be effective as a neuroleptic in controlling the symptoms of schizophrenia, has not been recorded as causing depression, and is thought to be of value in activating patients with marked negative symptoms. It does not show acetylcholine-like properties, nor does it stimulate GABA-systems, both of which may be concerned in the production of TD.

Chien, Jung and Ross-Townsend (1978) carried out a double-blind study to compare the efficacy of oxypertine, sodium valproate and dimethylaminoethanol in the control of TD, using a group of 17 patients. Only oxypertine was found to be significantly superior to placebo, though the number of patients was too small to allow any final conclusion other than that oxypertine shows promise as a therapeutic agent in TD.

In a so far unpublished paper, Kazamatsuri reports an open study of oxypertine in ten chronic mental hospital patients, all showing clear evidence of TD; out of these, seven experienced complete disappearance of their involuntary movements whilst receiving oxypertine. Neuroleptic drugs that were being administered before the trial were continued and no worsening of psychopathology was observed during the trial, nor did new side-effects emerge. Out of a total of 40 patients in four other uncontrolled studies, 22 are said to have shown either disappearance of TD or a marked improvement.

Our study has consisted of a double-blind comparison of oxypertine versus placebo in in-patients, aged between 18 and 70, using the AIMS score. Patients selected for the trial had a drug-free period of two weeks, followed by drug or placebo for a month, another wash-out period and then a month on the other medication. The requirements listed by Mackay and Sheppard for a therapeutic trial in TD were very largely fulfilled.

Only preliminary results are available so far; however, in the first half of the trial, patients receiving oxypertine (N = 10) showed a mean value of 50 per cent improvement, whereas those on placebo (N = 9) showed a mean improvement of 30 per cent. There is thus a significant trend in favour of oxypertine, but certain individual patients showed a dramatic response to the drug. Available information thus suggests that the addition of oxypertine may allow dosages of other neuroleptics to be reduced, thereby diminishing extrapyramidal reactions, treating or preventing TD and possibly improving the treatment