The comments of Dr Aldenhoff are of relevance to all involved in research into the biology of psychiatric illness.

TIMOTHY G. DINAN

Department of Psychiatry
Trinity College Medical School
St James's Hospital
Dublin 8

References

BERNARDO, L. S. & PRINCE, D. A. (1982) Dopamine modulates a calcium-mediated potassium conductance in mammalian hippocampal pyramidal cells. *Nature*, **297**, 76–79.

DINAN, T. G., CRUNELLI, V. & KELLY, J. S. (1987) Neuroleptics decrease calcium-activated potassium conductance in hippocampal pyramidal cells. *Brain Research*, **407**, 159–162.

Late Paraphrenia

SIR: We have followed with interest the debate on aspects of late paraphrenia in your correspondence columns since the publication of an article by Holden (*Journal*, May 1987, **150**, 635–639). Some findings of our recent researches in Salford may be of relevance to the issues discussed.

We cannot agree with Grahame (*Journal*, November 1987, **151**, 702) that the differences between 'late paraphrenia' and other 'persecutory states in the elderly' are now resolved. It may be that paraphrenics show many similarities with schizophrenic patients who have an earlier onset of illness, but there are enough differences to warrant further research so that issues may be resolved. Clinically, the acute illness has a more florid course, affect remains intact, the delusions (sometimes fantastic) are very well organised, and the perceptual dysfunction often also occurs in non-auditory modalities. Even more striking is the almost total absence of thought disorder and the relative rarity of first rank symptoms, even though this aspect has been a subject of much debate recently.

There is a high association of symptoms with the presence of peripheral sensory dysfunction, and in a recent paper (Soni, 1988) we have shown that, in some of these patients at least, there is a close temporal relationship between the onset of peripheral sensory disorder and the development of delusions and perceptual dysfunction. When the more acute disturbances of sensation are relieved by appropriate treatments, some of the related mental symptoms improve even before neuroleptics are prescribed.

Perhaps the course and outcome of the illness, so important for the Kraeplinian concept of schizophrenia, needs to be more intensively investigated. In the earlier follow-up studies this appeared to mirror that seen in schizophrenic patients, although being more insidious and the personality disintegration being minimal, even after many years of follow-up. One avenue of research would be to compare, on various parameters, paraphrenic patients with those schizophrenic patients who 'graduate' into this age group and have no clinical evidence of activity of illness ('deficit state'). In a recent study of a 4-year follow-up (Johnstone *et al*, 1986), the negative symptoms of schizophrenia showed relative stability over time, although there were individual variations. In our survey of chronic schizophrenic in-patients in Salford (in preparation) who had been clinically stable for over 5 years, we noticed that many of these 'graduates' (aged 70 years and above) showed a perceptible fall in performance, even though the underlying schizophrenic process had been dormant for many years. If the deficit state symptoms show relative stability in the younger schizophrenic patients, then one conclusion that could be drawn from these observations is that non-illness factors may be important in determining the course and outcome, especially in the elderly.

It is not unreasonable to assume that ageing, and the physical illnesses and insults that accompany it, may be a contributing factor. There is some evidence to suggest that the ageing process can produce decompensation in many illnesses, and the insidious nature of personality deterioration in paraphrenic patients, which is not dissimilar to that seen in 'graduated' schizophrenic patients, may be the effects of decompensation through ageing and the accompanying physical concommitants rather than the disease process itself.

Finally, many paraphrenic patients show associations which cut across the different 'persecutory states in the elderly' even though the clinical presentations are identical. Thus, many have a paranoid, sensitive, and suspicious personality, over half will have some disorder of peripheral sensory function, and around 40% will show some evidence of organicity; this figure may increase with the use of more refined investigatory techniques than are available at present. Such associations are rare in the non-paraphrenic elderly and practically non-existent in other schizophrenic patients, including the 'graduates', and cannot be overlooked. We feel that the final word on the subject has not yet been spoken, and that intensive research may clarify these issues further. As a start, there is a need for refinement of diagnostic and assessment scales for this age group and for using investigatory techniques such as the neuropsychological battery, computerised tomography scan (Naguib & Levy 1987), and nuclear

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magnetic resonance, so that subtle differences in outcome can be detected.

SOM D. SONI
ATHER MALLIK
JOSEPH MBATIA
J. SHRIMANKAR

Psychiatric Research Department
Hope and Prestwich Hospitals
Eccles Old Road
Salford M6 8HD

References

JOHNSTONE, E. C., OWENS, D. G. C., FRITH, C. D. & CROW, T. J. (1986) The relative stability of positive and negative symptoms in chronic schizophrenia. *British Journal of Psychiatry*, **150**, 60–64.

NAGUIB, M. & LEVY, R. (1987) Late paraphrenia: neuropsychological impairment and structural brain abnormalities on computer tomography. *International Journal of Geriatric Psychiatry*, **2**, 83–90.

SONI, S. D. (1988) The relationship between peripheral sensory disturbance and the onset of symptoms in elderly paraphrenics. *International Journal of Geriatric Psychiatry* (in press).

Lithium, Imipramine and Hydroxytryptophan in Resistant Depression

SIR: Hale *et al* (*Journal*, August 1987, **151**, 213–217) reported "the unique efficacy of the triple combination of lithium, clomipramine, and tryptophan" in seven endogenous depressive patients resistant to several other forms of treatment. One of these patients had previously been treated with imipramine and lithium, and another with imipramine and tryptophan, but without success. I would like to report the case studies of two patients with major depression who did not respond satisfactorily to standard doses of imipramine plus hydroxytryptophan (OH-try), but readily and completely did so when lithium was added.

Case reports: (i) Mr G. L., a 48-year-old married man, was referred to our out-patient service for a 16-month depressive episode. His mother committed suicide during a depressive episode at the age of 39. The patient had a 23-year history of depressive recurrences, with a mean inter-episode interval of 3 years. In his previous episodes he had responded adequately to standard antidepressant treatments. During the present episode, however, he failed to respond to several antidepressants (amitriptyline, nortriptyline, mianserine, amineptine, nomifensine and tranylcypromine) at doses and for periods similar to those of previous episodes. When examined, he was a DST non-suppressor and his Hamilton score was 21. Imipramine (150 mg/day) plus OH-try (300 mg/day) was administered. During the following 6 weeks, a slight but unsatisfactory improvement was evident (Hamilton score = 16). Then, lithium carbonate (900 mg/day) (plasma level 0.41 mEq/l) was added. His mood substantially improved by the following week, with a Hamilton score drop to 5. He recovered completely and returned to his job during the following two weeks.

(ii) Mr D. D., aged 20, was referred to our out-patient service during his military service because of a severe depressive episode and manifest suicidal thoughts. He was a DST non-suppressor, and his Hamilton score was 31. He was administered imipramine (75 mg/day) for two weeks, which was then increased to 150 mg/day plus OH-try (400 mg/day) for the following four weeks. During this time his mood did not change substantially, and the Hamilton score decreased by no more than 20%. Lithium carbonate (900 mg/day) (plasma level 0.52 mEq/l) was added, and an improved mood was immediate. By the following week his Hamilton score had decreased by 80%, and he had a complete recovery during the subsequent two weeks.

These case studies suggest that: (a) the administration of lithium and OH-try is also synergistic with imipramine, and not only with clomipramine as Hale *et al* seem to suggest; (b) the addition of lithium to a tricyclic antidepressant and OH-try show that it is clinically efficacious in a period of time shorter than that of other drug treatments for drug-resistant depressives; (c) the clinical efficacy and rapidity of action of this combined treatment manifests itself even without administration of maximal doses of the tricyclic antidepressant. This might depend on the fact that tryptophan is hydroxylated and thus bypasses the limiting step of tryptophan hydroxylation and is readily metabolised to serotonin by neurons.

This combined treatment might be considered one of first choice in the management of drug-resistant major depressive patients. In fact, the canonical increase of the tricyclic antidepressant dose to the point that intolerable side-effects appear generally does not have clinical efficacy until two to three weeks pass. Moreover, this often may be impractical in elderly patients and those particularly sensitive to side-effects. Finally, it would seem to be good clinical practice to avoid the risks associated with the administration of high tricyclic doses unless such doses are an absolute necessity.

GIOVANNI CONTE

Istituto di Clinica Psichiatrica
Università di Milano
Via F. Sforza, 35
20122 Milano
Italy

Two-Stage Screening

SIR: We read with interest the paper by Sen *et al* (*Journal*, July 1987, **151**, 33–38) which described the success of the two-stage screening procedure for identifying psychiatric morbidity in primary health clinics in Calcutta (India) and Sao Paulo (Brazil).

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