

work is currently underway in the Sheffield programme (e.g. Stiles *et al*, 1988). However, despite the imperfect precision noted by Dr Snaith, comparative evaluation of clinically realistic packages is also required, as a guide for researchers, trainers, and practitioners to the value of investing further effort in the diverse methods currently available.

(b) Patient characteristics. Naturally, it is desirable to define as precisely as we can the nature of the sample in any research. However, the more tight this definition, the narrower the potential range of utility of the findings, and the harder it becomes to recruit patients meeting the criteria and hence to complete the study. Dr Snaith's espousal of what Stiles *et al* (1986) term the 'matrix paradigm' sounds fine in principle, but there is no foreseeable prospect of investigating (say) ten treatments for ten types of patient administered by ten types of therapist in ten different settings, as would be required by sole reliance on this approach to advance the field. In our study PSE-ID-CATEGO diagnoses were obtained, and Firth-Cozens & Brewin (1988) showed that these were unrelated to treatment outcomes. Other analyses are currently considering patient characteristics such as age and initial symptom levels.

(c) Assessment instruments. The assessment of outcome is complex and requires multiple methods, observer perspectives, and degrees of specificity vs generality (Lambert *et al*, 1986). Goal Attainment Scaling has not fulfilled its early promise of overcoming the limitations of other methods. We have reported some of our results from Mulhall's PQRS method elsewhere (Barkham *et al*, 1988). Given the patterns of correlations among psychotherapy change measures that are typically found, Dr Snaith's analogy with cardiac disorder is somewhat misleading.

(d) Design. We chose a crossover design, fully aware of the questions that Dr Snaith rightly says it cannot answer, because it enabled us to answer other questions. By holding therapist and patient variations constant, it provides a more precise and sensitive test of the effects of different methods, albeit over a shorter period of time. The Sheffield Project, of which the outcome report is but a part, was designed to enable detailed study of the elements within each treatment associated with immediate session impact and longer-term change over a series of sessions, and this is enhanced by the crossover's control for large and stable individual differences between participants. Although not designed for long-term comparative evaluation of treatments, the Project did include an as yet unpublished 2-year follow-up, which showed that improvement was maintained over that period.

In the psychotherapy field, no single study can meet all methodological desiderata simultaneously, so that research design is necessarily a matter of considered compromise between conflicting requirements. In this letter, we have tried to account for some of the decisions that informed the design of the Sheffield Psychotherapy Project. Dr Snaith may be a little happier with the design of the Second Sheffield Psychotherapy Project, currently underway (Shapiro *et al*, 1988). Here, patients are restricted to those presenting with major depression, as defined by DSM-III, and the 2 × 2 design evaluates long-term effects and cost-effectiveness by comparing 8 and 16-session versions of prescriptive or exploratory therapies. But this does not make it a 'better' study in any absolute sense; rather, it resolves the conflicting desiderata of the psychotherapy research enterprise somewhat differently, and will have different strengths and limitations.

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Mania in the Early Stages of AIDS

SIR: Fenton (*Journal*, November 1987, **151**, 579–588), in a review of AIDS-related psychiatric disorders, referred to a number of cases of psychosis complicating various stages of human immunodeficiency virus (HIV) infection, and Thomas & Szabadi (*Journal*, November 1987, **151**, 693–695) reported a case of paranoid psychosis as the first presentation of acquired immune deficiency syndrome (AIDS) which

was rapidly fatal. I would like to report a case of a man presenting with mania 6 weeks after the diagnosis of AIDS, which contrasts with the patient described by Thomas & Szabadi (1987) in that he appeared to respond to treatment; in addition, I can report on his condition 6 months later.

Case report: A 37-year-old homosexual man who was known to be HIV-positive presented with *Pneumocystis carinii* pneumonia. AIDS was diagnosed, and he was treated with intravenous co-trimoxazole. Six weeks later his pneumonia had resolved, but he was referred to a liaison psychiatrist because of odd behaviour.

On mental state examination he showed motor over-activity, elated mood, and was grandiose and disinhibited. He had pressure of speech and racing thoughts. He believed himself to have been sent on a mission to warn the world about AIDS, and also had ideas of reference. Cognitive function was normal on clinical testing. He had no personal or family history of psychiatric disorder and drank alcohol only in moderation.

All investigations other than computerised tomography (CT) scan were normal, but the latter showed generalised cerebral atrophy. Hypomania was diagnosed, and central nervous system involvement by HIV was strongly suspected. He improved and was discharged on zidovudine (AZT) only.

In view of the CT scan findings, formal psychometric testing was carried out by a clinical psychologist. This showed a marked reduction in psychomotor speed, perseveration, and some long-term memory loss; deficits consistent with the early stages of AIDS dementia complex (ADC) (Navia *et al.*, 1986).

Following testing he declined psychiatric follow-up, but continued to see a health counsellor from the special clinic. He continues to take AZT, has returned to work, and is coping well 6 months later.

As HIV is believed to be neurotropic and lymphotropic (Levy *et al.*, 1985), psychiatric manifestations may present early in the course of infection. As Drs Thomas & Szabadi pointed out, AIDS or HIV brain involvement must now be among the differential diagnoses of a psychosis in a person from a high-risk group. In the same discussion they also advocated HIV testing on psychotic patients who are intravenous drug abusers who have no previous history or other obvious precipitant. The implication of this is that all patients who are at high risk, who have severe mental illness, should be HIV tested. This raises important ethical issues; many of these patients will not be able to give informed consent, and the position of the Mental Health Act is unclear. Unless a patient is violent or self-harming, which most psychotic patients are not, routine precautions concerning blood contamination are enough to ensure staff safety. A positive HIV result will not alter immediate management, and when the patient is

sufficiently recovered, counselling and possible HIV testing could be considered.

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Time and the Dopamine Hypothesis

SIR: From a neurobiological point of view it appears quite remarkable that the dimension of 'time' has been neglected in nearly all theories which attempt to explain psychic disorder by findings from basic science, including the dopamine-hypothesis questioned recently (*Journal*, October 1987, *151*, 455–459). The methodological reasons for that deficit were focused nearly 20 years ago in a statement by Kety: "It would take many biochemists a long time to find a noisy circuit in a radio receiver if they restricted themselves to chemical techniques" (Kety, 1959). In this respect, Dinan's paper marks a turning point by introducing basic electrophysiology into considerations on the origin of psychic disorder.

Dinan proposed that a electrophysiologically detectable pattern of neuronal activity, caused by a potassium conductance, could be a basic mechanism in information processing which finally could influence psychopathology.

The calcium-dependent potassium conductance (KCa) is activated by the excitation-coupled increase of intracellular calcium concentration (Gorman & Thomas, 1978). As a negative feedback mechanism it represents a functional basis of phasic changes in cellular output between activity and rest. It has been detected in big, often pyramidal neurons in different areas all over the brain, such as cortex, thalamus, hippocampus, hypothalamus, and locus coeruleus. The KCa is one of several potassium conductances which are functional targets for modulatory influences: many neuromediators change the size of KCa and modify thereby the temporal pattern of neuronal activity, such as noradrenaline (Aghajanian & Rogawski, 1983), acetylcholine (McCormick & Prince, 1986), and dopamine (Benardo & Prince, 1982); this is also found with peptides such as corticotropin-releasing factor and drugs such as lithium, caffeine and neuroleptics.