essential. We hope that our future work attracts similar attention – bad publicity is better than no publicity at all.

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SIR: The article by Dr Brayne (*Journal*, April 1993, **162**, 439–446) concentrates on dementia in the general population but fails to discuss recent findings and recommendations as applied to the largest single group of people who develop Alzheimer's dementia; that is people with Down's syndrome. Difficulties inherent in the application of standard criteria (CAMDEX, DSM–III–R, NINCDS–ADRDA) in people with a learning disability have not been adequately investigated. Such definitions and criteria are difficult to apply to this population when false-positive diagnoses may occur due to difficulty in testing (due to sensory handicap or loss, poor co-operation with testing), confounding illnesses being present (e.g. thyroid disorder), and also due to lack of knowledge of the ageing process in older people with Down's syndrome.

A greater emphasis can be placed on behavioural and neurological changes as these are often valuable in the diagnosis of dementia (Lai & Williams, 1989; Evenhuis, 1990). Serial changes in behaviour over time in people with Down's syndrome may be used to support the clinical diagnosis of dementia (Prasher *et al*, 1993).

The relationship between clinical measurements and post-mortem findings must remain controversial as such findings may not necessarily correlate, as is the case with people with Down's syndrome. Virtually all people over the age of 40 years have neuropathological changes of Alzheimer's dementia, but not all will have changes of clinical dementia (Lai & Williams, 1989).

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Lewy bodies and Alzheimer's disease

SIR: Förstl *et al* (*Journal*, March 1993, **162**, 385–392) have described the clinical characteristics of eight patients meeting NINCDS criteria for Alzheimer's disease but subsequently showing cortical Lewy bodies at autopsy. Although we agree that a significant number of patients meeting existing clinical diagnostic criteria for Alzheimer's disease will have Lewy body pathology, our own experience is that such patients are not representative of the clinical presentations more typically associated with cortical Lewy body disease.

Förstl *et al* report that the "Lewy body variant" patients in their sample were clinically no different from those without Lewy bodies, except for an increase in rigidity developing during the course of illness. This is surely an inevitable consequence of the case selection bias, only patients fulfilling NINCDS clinical criteria having been selected for study and those with other psychiatric presentations excluded. Our experience of 41 autopsy-confirmed cases of Lewy body dementia (McKeith *et al*, 1992*a*, 1992*b*) is that 80% present with a syndrome of fluctuating cognitive impairment associated with hallucinations (usually visual), and with Parkinsonian features which are often precipitated by neuroleptics. A minority (10–15%) of Lewy body patients lack this fluctuating picture and are therefore similar to those described by Förstl *et al*. A further 5–10% present

with either paraphrenic symptoms or delusional depression without any signs of cognitive impairment, at least not in the early stages.

The fact that the clinical classification system has developed without a separate category for these patients should give clinicians considerable cause for concern. In the past, the diagnostic boundaries of Alzheimer's disease have probably been stretched to accommodate these presentations, with concepts such as 'the clinical heterogeneity of Alzheimer's disease' being used to justify such expansions. The more characteristic presentations of Lewy body dementia may now be identified by use of appropriate clinical criteria (McKeith *et al*, 1992*a*).

Förstl *et al* suggest that diffuse Lewy bodies may occur in some cases of Alzheimer's disease as a coincidental phenomena, and cite previous studies which have found a 12–15% "incidental Lewy body" rate in aged normals. The normal populations examined in these studies had either a psychiatric (Forno, 1969) or neurological bias (Gibb *et al*, 1989) and therefore reflect an association between Lewy body pathology and central nervous system disease rather than with normal ageing. A Newcastle study found a 2.3% rate of Lewy body formation in 131 medical and surgical patients with demonstrably normal neurological and mental states (Perry *et al*, 1990). The coincidental occurrence of Lewy bodies in patients with Alzheimer's disease appears then to be an incomplete explanation for the 12% Lewy body rate found by the authors in their sample.

The precise nature of the relationship between Lewy body and Alzheimer-type pathologies, and the different clinical syndromes associated with each remains to be established. Until then, clinicians should be aware of the broad spectrum of clinical presentations of cortical Lewy body disease, ranging from delusional states in the absence of marked cognitive impairment to 'typical' Alzheimer-type dementia. Between these extremes the most frequent clinical presentation appears to involve fluctuating cognitive impairment often associated with psychotic features, Parkinsonism, transient disturbance of consciousness and falls, and sensitivity to neuroleptic medication.

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Human sleep, sleep loss, and behaviour

SIR: I would like to comment on the paper by Horne (*Journal*, March 1993, **162**, 413–419) in which he provided intriguing evidence for a link between prefrontal dysfunction, human slow-wave sleep (hSWS) and depression. One line of argument focused on the neuropsychological effects of total sleep deprivation (TSD) in normal subjects pointing to some reversible dysfunction of the prefrontal cortex (PFC).

However, there is an additional aspect of TSD which was not explicitly mentioned by the author: TSD also has a brief but significant antidepressant effect in about 50% of depressed patients. Hypofrontality in the left dorsolateral PFC measured with the single photon emission computerised tomography (SPECT) method is present in this subset of depressed patients already before TSD, and, different from normal subjects, this hypofrontality is not increased by TSD. There is even a tendency for TSD to reduce hypofrontality, and this trend is more obvious in TSD responders than in non-responders (Ebert *et al*, 1991). This means that TSD may have different effects in normal subjects and depressed patients, but on the other side it strengthens the author's view that hypofrontality may only be a secondary effect of cognitive underactivation in depression.

The effects of TSD in depression, however, do not argue for a proposed theory that a decrease of hSWS in depressed patients (with or without frontal impairment) is part of the aetiology of the disorder because, if an impairment of hSWS was responsible for depression, TSD should not act as an antidepressant, and relapse after TSD should not occur in sleep after TSD with the highest hSWS rebound.

Instead, we may have to look for a theory taking into account that "sleep itself with its related neurobiological mechanisms is the cause of depression and wakefulness is the antidepressant agent". With the