Antipsychotics, cognitive decline and death in Alzheimer's disease

Antipsychotics, cognitive decline and death in Alzheimer's disease: the London and South-East Region Alzheimer's Disease longitudinal study

D Ames

The LASER-AD study provides limited reassurance in relation to the occasional prescription of novel antipsychotics to elderly people with dementia

For psychiatrists in the business of helping old people who exhibit delusions and challenging behaviours related to dementia, it will be a relief to read some good news at last. Apparently, even if we may not be helping old people with dementia very much when we treat them with an atypical antipsychotic,¹ we may after all not be hastening their deaths or irreversibly worsening their cognitive function at the same time. In their paper, Livingston *et al*² (see p 25) report that in an epidemiologically representative cohort of 224 people affected by Alzheimer's disease, the consumption of antipsychotic drugs did not correlate with more rapid cognitive decline over a 6-month period, nor did people taking antipsychotics have a higher death rate than those who were not prescribed such

drugs, once age and severity of dementia were taken into account. The study had robust methods and its results in relation to cognitive decline are based on repeated assessments with a variety of well-accepted cognitive measures.

Of course it is true that too many old people with dementia are treated too often and for too long with antipsychotic drugs,¹ and efforts to diminish the prevalence of such prescriptions is to be greatly applauded, but the merit of the London and South-East Region Alzheimer's Disease study is in examining in an everyday context the potential negative consequences of novel antipsychotic use, which have caused great concern in recent years. As a coauthor of the paper³ that prompted the original panic over novel antipsychotics and the

putative risk of stroke in people with dementia¹ (if we had never conceived our investigator-initiated study, concerns about risk of stroke in people with dementia prescribed antipsychotics might not have surfaced for years to come), I am relieved to find that my inability to manage every single person I see with dementia and distressing ideas, or severe aggression that puts other frail old people at serious risk, without occasional use of a novel antipsychotic drug in an n = 1 trial, may not be wholly irresponsible.

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Symptoms of dementia

Behavioural and psychological symptoms of dementia associated with Parkinson's disease

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Assessment of behavioural and psychological symptoms is important in brain disorders

The recognition that psychiatric symptoms and behavioural disturbances are important in organic brain disorders has grown inexorably over the past 15 years. Their contribution to carer stress and institutionalisation is well recognised.¹ More specifically, in Parkinson's

disease, researchers are becoming increasingly aware of the need to include the assessment of behavioural and psychological symptoms as important outcome measures in clinical trials, and clinicians are starting to recognise the need to identify and manage these

symptoms in addition to focusing on the motor symptoms and their complications.

The study by Aarsland *et al* in this issue² (see p 36) reports the results of a cluster analysis of the symptoms in a larger study in people with dementia associated with Parkinson's disease,³ using the gold standard of the assessment for neuropsychiatric symptoms, the Neuropsychiatric Inventory.⁴ The findings support the fact that these symptoms are common in Parkinson's disease (89% had at least one symptom, and 77% had two or more). The most common symptoms were depression, apathy, anxiety and hallucinations (in this order, all with rates of between 44% and 58% of patients). Five clusters were identified and shown to be related to other aspects of dementia (in particular, psychosis/agitation was associated with carer distress, cognitive impairment and Parkinsonian signs).

The population-based Cache County Study of Memory in Ageing,⁵ focusing

mostly on Alzheimer's disease and also using the Neuropsychiatric Inventory, enables interesting parallels to be drawn between the respective study findings. The behavioural patterns associated with Parkinson's disease seem to differ from those in Alzheimer's disease, underscoring the notion that disparities in underlying pathophysiology drive distinctive clinical neuropsychiatric syndromes. We are in the nascent phases of comprehending these relationships, and high-quality, informative, long-term quantitative surveys and clinical trials of the neuropsychiatric aspects of Parkinson's disease are warranted. Clinical trials are particularly important, as the drugs used to treat the psychiatric aspects of Parkinson's disease often adversely interfere with the management of the motor aspects, leaving the clinician flailing in the midst of the "motion-emotion conundrum".⁶

The findings presented by Aarsland *et al* have implications for the understanding and appreciation of the neuropsychiatric agents of Parkinson's disease. This is highlighted in a recent editorial on care

of patients with Parkinson's disease, where mental health professionals were not specifically mentioned.⁷ Furthermore, the recent publication of the UK's National Institute of Health and Clinical Excellence guidelines on the management of Parkinson's disease accentuated the dearth of reliable evidence in the treatment of mental health aspects. Arguments for the improvement of mental health services and more neuropsychiatric research on people with Parkinson's disease can be made and, as a resultant uplift in service provision, will benefit both patients and their carers.

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Bias of space representations

Investigating the bias of space representations in patients with stroke

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Can mis-orientation of spatial representation re-orient management of patients with stroke?

The analysis of spatial representation biases in patients with hemispheric stroke is the subject of two articles in this issue of the *Journal of Neurology, Neurosurgery and Psychiatry*. This confirms the growing interest for this topic, because it provides data about the brain coding of spatial information and contributes to explaining the behaviour of patients in clinical situations.

In the elaboration of the representation of the egocentred space, it has been suggested that the reference frame constituted by the medial body axis has a strategic influence on the perceptive motor actions in the peripersonal space.¹ The first bias of the representation of this reference was reported in patients with right hemispheric lesions and spatial neglect, and was found in the left-right

dimension (lateral) in relation to the head and body positions. Indeed, the assessment of the subjective straight ahead (SSA), obtained by pointing the index finger or by rod adjustment in front of the medial part of the body and in darkness, showed a deviation ipsilateral to the lesion.^{2–3} But now, the main question is to determine whether these patients also show biases in the other dimensions of the tri-dimensional space. In this issue, Barra *et al*⁴ (see p 43) have shown a contralateral tilt of the representation of the medial body axis in the sagittal plane. Importantly, this deviation was similar when using a visuoverbal or a visuohaptic task, which ruled out the role of an ocular cyclotorsion. In addition, the deviation was more frequent in right hemispheric lesions centred on the

frontoparietal cortex, and it strongly correlated with the severity of spatial neglect, sensory loss and postural disorders. This result provides new evidence for the multidimensional coding of spatial representations by the right hemisphere.

A complementary problem is to determine the relationship of the contralateral tilt with the ipsilateral SSA deviation, because the two phenomena are based on the same representation of the medial body axis. In a recent study,⁵ we showed that the representation of the body axis was at the same time deviated towards the ipsilateral side and tilted contralaterally, especially in patients with spatial neglect. Thus, the classical ipsilateral SSA deviation showed a rostrocaudal gradient. This conception of a pluridimensional misorientation of spatial references can explain some clinical disturbances such as the inclination of writing and the more severe omission rate in the lower or near part of the sheet of paper in cancellation tests.⁶

The subjective visual vertical (SVV) is of a different quality, and is considered to be an allocentric representation. The study by Bonan *et al*⁷ (see p 49) confirms the counterclockwise deviation of the SVV and its predominance in patients with neglect and temporoparietal lesions, which are now well-established facts, but the main interest of that study lies in the fact that the severity of the contralateral