

neuropsychological dysfunction in this French study had cognitive impairments prior to hospital admission. Presumably, a large percentage of them developed neuropsychological dysfunction because of factors related to hospitalisation, such as depressive symptomatology, use of psychotropic medications (e.g. benzodiazepines), or sleep disturbance.

We assessed cognitive functioning with a shortened version of the MMSE (Breakhus *et al*, 1992) in 49 community-dwelling elderly people with fall-related fractures two months after a fall accident. Our sample consisted of 22 patients with ankle or wrist fractures and 27 with a broken hip. They had been admitted to a hospital, but were all discharged at time of testing. Mean (s.d.) age was 73.9 (8.5) years. In contrast with the results of Jabourian *et al* (1994), only 10 patients (20.4%) scored below the cut-off for cognitive impairments on the shortened version of the MMSE (normal value, >9). Sample differences may account for the discrepancy between the two studies (the patients in the French study were somewhat older). However, it might also be that several of the patients studied by Jabourian *et al* suffered from neuropsychological dysfunction due to factors related to hospitalisation.

From reading the letter by Jabourian *et al* (1994) one could (erroneously) get the impression that almost 90% of serious fall incidents are co-determined by cognitive dysfunction. King & Tinetti (1995) published a review of the literature on risk factors for fall injury and identified several risk factors for falls besides cognitive impairments. They made a distinction between intrinsic factors (e.g. medication use, certain chronic diseases, impairments in muscle strength, balance and gait) and extrinsic factors (e.g. poor lighting and slippery floor). According to King & Tinetti older persons are at increased risk for a serious fall when multiple intrinsic and extrinsic factors are present.

Breakhus, A., Laake, K. & Engedal, K. (1992)

The Mini-Mental State Examination: identifying the most efficient variables for detecting impairment in the elderly. *Journal of the American Geriatric Society*, **40**, 1139–1145.

Folstein, M. M. F., Folstein, S. E. & McHugh, B. R. (1975)

'Mini-Mental State'. A practical method for grading the cognitive state of patients for the clinician. *Journal of Psychiatric Research*, **12**, 189–198.

Jabourian, A. P., de Jaeger, C., Findji, G., et al (1994)

Cognitive functions and fall-related fractures (letter). *British Journal of Psychiatry*, **165**, 122.

King, M & Tinetti, M. E. (1995) Falls in community-dwelling older persons. *Journal of the American Geriatrics Society*, **43**, 1146–1154.

M. Jelicic, G. I. J. M. Kempen Department of Health Sciences & Northern Centre for Healthcare Research, University of Groningen, A. Deusinglaan 1, 9713 AV Groningen, The Netherlands

Clozapine-induced hypersalivation

Sir: In a previous letter (Szabadi, 1996), I argued that the troublesome side-effect of increased salivation seen in patients taking clozapine was unlikely to be due to the blockade of alpha-2 adrenoceptors, as had been suggested by others (Corrigan *et al*, 1995). I concluded that "the way in which clozapine causes hypersalivation remains an enigma". Since then, a paper has come to my attention which may shed some light on the mechanism underlying clozapine-induced hypersalivation. Zorn *et al* (1994) have shown that clozapine, in a cellular preparation expressing all five subtypes (M_1 – M_5) of muscarinic cholinergic receptors, has a potent full agonistic effect at M_4 receptors, while having antagonistic properties at the other four subtypes. While M_3 is the predominant muscarinic receptor subtype in salivary glands (Leahy *et al*, 1997), there is evidence that M_4 receptors are also expressed in this tissue (Zorn *et al*, 1994). Therefore, it is possible that the net effect of clozapine on salivation reflects the relationship between M_3 receptor blockade, leading to a decrease in salivation, and M_4 receptor stimulation, leading to an increase in salivary output. In some patients taking clozapine, the effects of M_4 receptor stimulation may exceed those of M_3 receptor blockade, resulting in hypersalivation. Thus, clozapine-induced hypersalivation may reflect the subtype-selective agonistic effect of clozapine at M_4 muscarinic receptors (Zorn *et al*, 1994).

This mechanism may also underlie the clinical effectiveness of the antimuscarinic drug pirenzepine in relieving clozapine-induced hypersalivation (see Szabadi, 1996). Pirenzepine, apart from having the ability to block M_1 receptors, is also a potent antagonist of M_4 receptors (Caulfield, 1993).

Caulfield, M. P. (1993) Muscarinic receptors – characterization, coupling and function. *Pharmacology & Therapeutics*, **58**, 319–379.

Corrigan, F. M., MacDonald, S. & Reynolds, G. P. (1995)

Clozapine-induced hypersalivation and the alpha-2 adrenoceptor (letter). *British Journal of Psychiatry*, **167**, 412.

Leahy, D. J., Newgreen, D. T., Storrs, T. J., et al (1997) Characterisation of functional muscarinic receptors in human submandibular salivary gland. *British Journal of Pharmacology*, **120**, P204.

Szabadi, E. (1996) Clozapine-induced hypersalivation and the alpha-2 adrenoceptor (letter). *British Journal of Psychiatry*, **169**, 380–381.

Zorn, S. H., Jones, S. B., Ward, K. M., et al (1994) Clozapine is a potent and selective muscarinic M_4 receptor agonist. *European Journal of Pharmacology, Molecular Pharmacology Section*, **269**, RI–R2.

E. Szabadi Department of Psychiatry, University of Nottingham, Queen's Medical Centre, Nottingham NG7 2UH

Clozapine, Chinese and blood

Sir: Despite the availability of clozapine and its efficacy in treatment-resistant schizophrenia, it has been difficult to persuade Chinese patients in our practice in Singapore to go on a trial of this drug. The reservation in many instances was often not due to the cost of the drug or the risk of agranulocytosis but the mandatory blood monitoring required. In a review on the experience of using clozapine in China, Potter *et al* (1989) reported that the doctors had to make "considerable effort to overcome many patients' concerns and superstitions about having blood drawn".

The traditional Chinese notion of blood differs very much from that in the West. Blood to the Chinese is an extremely precious commodity, as is summed up by the Chinese saying that "one hundred grains of rice make one drop of blood". This has led to a fear of losing even a small amount of blood – a fear that would seem disproportionate to a Western observer. Reassurance that such monitoring would not have any detrimental effect is usually met with disbelief and scepticism. In their belief in the need to make good the blood loss, many would ask for "tonics", which are a traditional Chinese treatment for anaemia. These tonics are usually in the form of extracts, wines, herbs, food containing high-quality proteins and, in a syncretism of traditional Chinese concepts with Western medicine, vitamin tablets (Koo, 1984). We find that the judicious prescription of vitamin tablets goes a long way in allaying this fear of losing too much of this precious fluid in many of our Chinese patients.

Koo, L. C. (1984) The use of food to treat and prevent diseases in Chinese culture. *Social Science and Medicine*, **187**, 55–66.