

fully informed in order to be able to make an informed decision on all treatment options. Perhaps partnership with the patient is the most important factor in changing health-related behavior. Finally, from the training perspective, it is important to discuss the patient–doctor relationship with all our trainees under supervision.

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Is there a role for psychostimulants in old age depression and apathy?

Psychostimulants (including dexamphetamine, methylphenidate and modafinil) are a broad class of drugs that reduce fatigue, promote alertness and wakefulness and possess possible mood enhancing properties. A recent Cochrane Review of randomized controlled trials (RCTs) up to June 2006 systematically investigated the effectiveness of psychostimulants in depression (Candy *et al.*, 2008). Most of the 24 RCTs included in the review were of poor quality and did not exclusively involve geriatric patients. In a meta-analysis involving three trials (none having geriatric patients), the authors concluded that oral psychostimulants may have a possible antidepressant effect in the short term (up to four weeks) and appeared to be well tolerated. However, the clinical significance of this effect was unclear and the potential medium or long-term benefits and side effects were virtually unknown (Candy *et al.*, 2008).

Despite the lack of a solid evidence base, psychostimulants have continued to have a role in old age psychiatry in some countries, especially as a monotherapy agent in depression and apathy, or as an augmenting agent to standard antidepressant treatment in major depression. They also have been explored in the treatment of other symptoms, such as fatigue and cognitive complaints (Ng and O'Brien, *in press*).

A possible short-term antidepressant effect for methylphenidate over placebo (as measured by the Hamilton Depression scale, HAM-D) was demonstrated in an eight-day randomized double blind cross-over trial in 16 elderly patients with significant medical comorbidities (Wallace *et al.*, 1995). This was a very short trial with a small

number of patients and a high rate of mortality, making any conclusions tentative. Nevertheless, methylphenidate did demonstrate a short-term antidepressant effect in a very frail and ill population. A recent retrospective chart review at a university hospital investigated the use of methylphenidate in patients over 60 years of age with vascular depression (Mantani *et al.*, 2008). Eleven patients were identified who had been treated with methylphenidate (mean 9.1mg +/- 2.9mg per day; range 5–20mg per day) and 81.8% of them were responders (defined as a decrease of 50% or greater from the baseline scores HAM-D at four weeks). The authors concluded that methylphenidate may be a useful antidepressant in vascular depression. Older studies suggest that psychostimulants as a monotherapy may have a role in treating elderly patients unable to tolerate standard pharmacological treatments, who have significant medical comorbidities such as advanced cancer and stroke, or who are in palliative care settings (Ng and O'Brien, *in press*). However, RCTs are lacking.

Methylphenidate remains a potential augmentation agent in elderly depression. Lavretsky *et al.* (2006) conducted a RCT comparing methylphenidate to placebo augmentation in elderly patients with major depression who were commenced on citalopram. Methylphenidate or placebo was started simultaneously in 16 patients along with citalopram. An accelerated anti-depressant response was noted by week 3 and there was a greater reduction in depression scores on the combination treatment by week 8. There were a number of drop-outs due to side-effects and intolerability of the methylphenidate. The authors concluded that augmentation with methylphenidate at the commencement of anti-depressant treatment may lead to a faster anti-depressant response and a greater reduction in depressive symptoms.

Apathy has been noted to be a very disabling symptom in several neurological and psychiatric disorders, especially dementia. There have been several case reports and one open trial using psychostimulants in the treatment of apathy (Ng and O'Brien, in press). An early RCT in 44 withdrawn and apathetic geriatric patients compared methylphenidate with placebo (Kaplitz, 1975). Methylphenidate was associated with a positive outcome, but, by current standards, there were several methodological shortcomings. Herrmann *et al.* (2008) recently conducted a randomized double blind crossover trial comparing methylphenidate (10 mg b.i.d.) to placebo in 13 patients with significant apathy. There were two phases of two weeks with either drug or placebo separated by a one-week washout. Patients demonstrated a significant improvement on the primary outcome, the Apathy Evaluation Scale, when on methylphenidate but also had a greater proportion of adverse effects. Two patients experienced severe adverse events including agitation, delusions, irritability and insomnia, which ceased when methylphenidate was discontinued.

Whilst the Cochrane Review found no evidence to support the general use of psychostimulants in depression, including the newer medication modafinil, the above studies would suggest that this class of drugs may still have some potential in old age psychiatry. Randomized placebo-controlled studies are still needed as well as the study of longer-term outcomes and potential adverse effects.

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Neurodegeneration and the structure of time: clinical evidence for philosophical reasoning

I enjoyed the recent editorial by Förstl (2008) on time. Here he presents a different way of thinking about what might be happening to people with neurodegenerative diseases and the consequent difficulties for their carers. I was not so sure, however, how the neuropathology was meant to contribute to philosophical discussions about the nature of time.

A general point, which in my view explains why so many discussions about the neurological basis of mental experience simply miss the philosophical concern, is that we can give both causal and constitutive accounts of mental phenomena. We can adapt the distinction made famous by Jaspers (1923) between the explanations of natural science (*Erklären*) and the understandings of human science (*Verstehen*) and talk about causal explanation and

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constitutive understanding. The neuropathology of the dementias does indeed, as Förstl usefully demonstrates, provide a causal explanation of the mental phenomena that underpin the experience of time for people with dementia. There is more to be said, however, about the nature of time. That is, further philosophical concerns relate to the concept of time; and talk of the neuropathology simply passes by such conceptual understanding. Nonetheless, Förstl also gestures at constitutive accounts of time for people with dementia: the loss of the past for those with Alzheimer's disease; the loss of "a laminar flow of consciousness" in dementia with Lewy bodies; or the loss of a sense of the saliency of the future in frontotemporal degeneration. Perhaps it is these accounts, rather than the neuropathology, that give us a better purchase on the conceptual concerns of the philosophers.

As a way to add more detail to such accounts, consider the descriptions given by Sabat (2001) in which people with moderate to severe Alzheimer's