pyramidal reactions (EPRs) have been reported in the literature. Overall, there at least 28 reports involving a minimum of 42 patients who have experienced an EPR associated with an SSRI.[5] In this body of literature, a full range of EPRs have been reported including what appears to be a reversible (tardive-like) dyskinesia. Important risk factors for developing EPRs after starting an SSRI may include concurrent antipsychotic use, using a rapid SSRI dose escalation strategy, treating with high daily SSRI doses, older patients, female patients and patients with PD. Unfortunately, because the available information is largely from anecdotal reports, definitive risk factor guidelines are unavailable.

From cases like the one published by Farragher and Walsh, it has become clear that there is a real possibility that patients being treated with an SSRI may experience EPRs. The true risk of SSRI-related EPRs and the associated risk factors, however, are presently unclear. One potential risk factor may include the concurrent use of an antipsychotic (including an atypical antipsychotic). If an EPR develops while a patient is receiving both an SSRI and an antipsychotic, it is important to realise that there is a potential pharmacodynamic interaction which may occur in addition to a pharmacokinetic interaction.

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Re: Diogenes syndrome: review and case history

Sir – O'Shea and Falvey report a case of Diogenes Syndrome and in reviewing the literature in the area emphasise the interplay of factors contributory to the presentation, including organic brain disease, psychotic illness, and personality *(Ir J Psych Med 1997; 14(3): 115-6).*[1] We report a case of a 50 year old female patient in which all three factors appeared to contribute to the classic presentation and discuss implications for investigation of the purported syndrome.

A 50 year old woman was admitted to a psychiatric ward in an advanced state of self-neglect. This retired single nurse had a 20 year history of contact with the psychiatric services, initially for peer relationship problems, subsequently being admitted twice for treatment of depressive episodes. Medical history included menorrhagia, hypothyroidism and scoliosis. In the period prior to admission she had stopped all of her regular medication and allowed her home to become extremely dirty. She ate very little, but her cat was well cared for. She agreed to informal admission.

Mental state and physical examination, and blood tests were normal on admission and she improved rapidly without any new treatment. Occupational therapy assessment suggested visuospatial problems, so a MRI scan was performed. This revealed a large sessile meningioma in the left middle cranial fossa, with temporo-parietal mass effect, as well as some cerebral atrophy. Neuropsychological testing showed selective frontal deficits but a high NART-IQ of 122. Spect scan was normal. She had the tumour removed and was discharged home two months later. She had a fluctuating clinical course subsequently, with at least one more admission (with persecutory delusions and self-neglect). Unconcern with her situation was striking throughout.

Our case demonstrated personality features similar to Clark *et al*'s original series,[2] including detachment and poor integration. We felt that organic brain disease had 'released' the behavioural syndrome at an early age. No association of temporo-parietal lobe lesions with neglect has been previously reported. A possible explanation is that the lesion to the parietal lobe led to unawareness of neglect, akin to anosognosia, the unawareness of disease. We feel that organic brain disease should be suspected in all cases of severe neglect, while acknowledging the potential contribution of multiple factors to the phenomenon. Ascription of her neglect to constitutional (personality) factors, or to her previous psychiatric illness, would have been an unfortunate omission.

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Serious hypertensive reaction after switching from clomipramine to moclobemide

Sir – Moclobemide is a selective, reversible inhibitor of monoamine oxidase A (MAO-A) which differs from the classical, irreversible monoamine oxidase inhibitors (MAOIs), both in pharmacodynamic and pharmacokinetic properties and has therefore a low propensity for producing drug interaction.[1] Recently, in a doubleblind

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placebo-controlled study assessing the safety and tolerability of the switch in treatment from the tricyclic antidepressants amitriptyline and clomipramine to moclobemide, no clinically relevant interaction was noted. Therapeutic doses of moclobemide up to 300mg could be given 24hrs after the last dose of amitriptyline or clomipramine without major risks.[2] We report a case of serious hypertension after a previous treatment with clomipramine was washed-out before treatment with moclobemide was started.

A 23 year old woman, with baseline blood pressure of 110/75mm Hg, was suffering from resistant major depression. She had received treatment with clomipramine for more than six months with doses up to 250mg/day, when it was decided to start a trial with moclobemide. Her concomitant treatment was beclomethasone inhaler and oral contraceptives. Clomipramine was gradually withdrawn over six days, and eight days after the last dose of clomipramine, moclobemide was started initially at 150mg/day then increased up to 300mg/day. A rise in blood pressure up to 170/120mm Hg was noted on day 16 of treatment with moclobemide. The patient started also complaining about severe headaches, blurred vision and restlessness. Initially, it was thought that the combination of the oral contraceptives were responsible for the patients headaches and hypertension and therefore, the treatment with oral contraceptives was stopped. Her blood pressure remained high intermittently up to 170/110mm Hg until it was decided to stop the treatment with moclobemide on day 21. By day 28, her blood pressure was still noted to be up to 150/100mm Hg, however this gradually decreased to 120/80mm Hg on day 36. Also, the treatment with the same oral contraceptives was restarted on day 51 without developing a similar hypertensive reaction. Finally, a treatment with sertraline was successfully introduced on which the patient's mental state improved considerably.

Despite the fact, that the United Kingdom recommended drug-free period of a week was kept after clomipramine was withdrawn, this may have been insufficient in our patient. Dingemanse *et al*[2] only used clomipramine for 14 days at a dose of 100mg/day, before it was abruptly changed to moclobemide. Our patient, received clomipramine at doses of 200-250mg/day for more than six months before it was withdrawn. For the irreversible MAOIs the combination with clomipramine seems to require extra caution.[1] Recently the combination of moclobemide and clomipramine has also been associated with a severe hypertensive reaction.[3] Therefore, blood pressure should be monitored when treating patients with moclobemide, especially when combining with or switching from clomipramine.

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Suicide, depression and immunological resignation

Sir – Abed's paper[1] on suicide as altruism reconciles self-destructive behaviour with the 'selfishness' of the gene,[2] thus clearing the way for an evolutionary hypothesis of depression which takes into account the associated increase in mortality. Suicide is but one of the fatal outcomes of depression and it may be through immunological changes that the depressed individual is disposed to illness and death.[3] Depression facilitating death in the face of adversity with which the individual could not cope appeared to be an empirically testable challenge to the selfish gene hypothesis.[3] However, Abed's neat extrapolation of "inclusive fitness" to explain suicide as potentially enhancing the likelihood of survival of the individual's genes, present in his kin, would offer an alternative and more satisfying resolution of the apparent incompatibility of the immunulogical changes with the generally favoured evolutionary perspective.

A theory which does not account for the reduced life expectancy would need to consider depressive illness to be an abnormal or dysfunctional extension of the adaptive emotional response. The social competition hypothesis[4] proposed that depression signals submission, and acceptance of the resulting change in hierarchical ranking, to rivals in agonistic encounters, and that depression thereby facilitates survival. Another suggestion was that depression may originate from the failure to master an environmental threat, when it becomes adaptive to give up, withdraw, and get on with other activities,[5] unless a dysfunctional prolonged deactivation or depression ensues.

In both these theories depression is a functional response which becomes abnormally severe and perhaps spontaneously occurring in major depressive illness. By contrast immunological resignation could involve a spectrum of response such that an individual without a significant predisposition would only develop physiological changes predisposing to death if circumstances were sufficiently severe, while others perhaps those with a genetic predisposition, adverse early experiences, and more recent significant life disruption would develop depression in less exacting circumstances. A major depressive illness would still be the spontaneous and inappropriate manifestation of these changes but depression itself would still be accompanied by adverse effects on health.

Support for the idea of a continuum – illhealth predisposition not only with the spontaneous occurrence of the severe, illness manifestation but also with the appropriate, adaptive response – comes from the observations that subordination in animals is associated with increased cortisol secretion[6,7] and disruption of cortisol secretion is one of the earliest biochemical observations in severe depression.[8] Cytokine changes in depression, especially in interleukin-6 activity[9] and interleukin-Ib activity[10] may be secondary to, or mediators of, the disruption of HPA activity. Maes et al[11] consider that the low serum high density lipoprotein cholesterol (HDLC) seen in major depressive illness may be induced by the immune/inflammatory response in depression. Depression is known to be associated with an increased risk of myocardial infarction[12] as well as reduced survival following myocardial infarction.[13] Although it can be argued that both depression and ischaemic heart disease largely coincide because they both relate to inadequate