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 Clomipramine was gradually withdrawn over six days, and eight days after the last dose of clomipramine, moclobemide was started initially at 150mg/day then increased up to 300mg/day.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Despite the fact, that the United Kingdom recommended drug-free period of a week was kept after clomipramine was withdrawn, this may have been insufficient in our patient.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 Our patient, received clomipramine at doses of 200-250mg/day for more than six months before it was withdrawn.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

intake of omega-3 polyunsaturated fatty acids[14] this would not in itself make redundant an evolutionary hypothesis of depression as these fatty acids have been critically important in the development of the human brain.[15]

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