Letters

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Antidepressant prescribing

The two papers by Middleton and Moncrieff,[1] and Anderson and Haddad[2] published in the January edition of the Journal highlight a fundamental fault line that runs under the concept of depression: the current conventional rationale for treatment of depression with antidepressant medication is increasingly untenable. It has been recognised for some time that the serotonin hypothesis that provides the explanatory model for the supposed action of selective-serotonin reuptake inhibitors is not supported by current evidence.[3] Despite this the model remains dominant, largely through the efforts of the pharmaceutical industry to cultivate a profitable sector of the market. As a result we have a pseudoscientific myth that pervades our approach to human distress.[4]

There is now substantial evidence to suggest that antidepressant drugs exert their effects through mechanisms such as an active placebo response[5] and by inducing non-specific abnormal mental states rather than by any specific 'antidepressant' action.[6] Although many clinicians and patients report improvements in depressive symptoms associated with the use of antidepressants, it is ethically questionable to justify treatment based on a naïve and misleading hypothesis.

A critique of the use of antidepressants would necessarily involve a reappraisal of our understanding of the concept of depression itself. There is growing concern that the term is increasingly used inappropriately to medicalise normal human experience.[7,8] Such a strategy, if pursued to its logical conclusion — as currently seems to be the case with the development of DSM-V — would effectively convert much of human experience into overly simplistic technical problems, to be addressed by biomedical solutions that are likely to be ineffective and possibly harmful.[9]

The widespread use of these agents needs to be reconsidered particularly within primary care where they are least likely to be of benefit. It is time for us to rise to Middleton and Moncrieff's challenge and to recognise that antidepressants are 'unlikely to do any good and may do some harm.'

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REFERENCES

1. Middleton H, Moncrieff J. 'They won't do any harm and might do some good': time to think again on the use of antidepressants. *Br J Gen Pract* 2011; **61(582):** 47–49.
2. Anderson IM, Haddad PM. Prescribing antidepressants: time to be dimensional and inclusive. *Br J Gen Pract* 2011; **61(582):** 50–52.
3. Lacasse JR, Leo J. Serotonin and depression: a disconnect between the advertisements and the scientific literature. *PLoS Med* 2005; **2(12):** e392.
4. Ioannidis JPA. Effectiveness of antidepressants: an evidence myth constructed from a thousand randomized trials? *Philos Ethics Humanit Med* 2008; **3:** 14.
5. Moncrieff J, Wessely S, Hardy R. Active placebos versus antidepressants for depression. *Cochrane Database Syst Rev* 2004; **(1):** CD003012.
6. Moncrieff J, Cohen D. How do psychiatric drugs work? *BMJ* 2009; **338:** b1963.
7. Horwitz AV, Wakefield JC. *The loss of sadness: how psychiatry transformed normal sorrow into depressive disorder.* New York: Oxford University Press, 2007.
8. Summerfield D. Depression: epidemic or pseudo-epidemic? *J R Soc Med* 2006; **99(3):** 161–162.
9. Aldous P. Psychiatry's civil war. *New Scientist* 2009; **2738(Dec):** 39–41.

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Antidepressant prescribing

Middleton and Moncrieff[1] make a good case for being cautious about prescribing antidepressants in primary care. The discussion is, however, somewhat one sided. The responsible GP will be aware that there is always a suicide risk if a severely depressed patient is sent away without an antidepressant. Being on the waiting list for cognitive behavioural therapy will not necessarily prevent suicide. Patients who commit suicide have a low concentration of serotonin in the brain.[2] An experienced GP will also know of patients who have been symptom free on antidepressants who experience breakthrough symptoms when they try to wean themselves off the drug.

The old RCGP dictum that every diagnosis should have a physical, social, and psychological component is especially relevant to treatment of depression. The physical component must surely be serotonin deficiency in many cases but it would be wrong to treat this deficiency and ignore the psychological and social components which might be more important.

Recent evidence suggests a link between the physical component of depression and nutritional deficiencies.[3–5] The evidence for omega-3 and antidepressants working synergistically is especially convincing.[6] Recently, when a patient reported breakthrough depression symptoms, I doubled her selective-serotonin reuptake inhibitor dose and added an over-the-counter high dose omega-3. At follow-up, she told me: 'I feel normal for the first time in over 3 years'. Could this be just a placebo effect?

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REFERENCES

1. Middleton H, Moncrieff J. 'They won't do any harm and might do some good': time to think again on the use of antidepressants. *Br J Gen Pract* 2011; **61(582):** 47–49.
2. Gross-Isseroff R, Israeli M, Biegon A. Autoradiographic analysis of tritiated imipramine binding in the human brain post mortem: effects of suicide. *Arch Gen Psychiatry*; **46(3):** 237–241.
3. Cornah D. *Feeding minds — the impact of food on mental health*. The Mental Health Foundation, 2006.

http://www.mentalhealth.org.uk/publications/feeding-minds/ (accessed 9 Feb 2011).
4. Polivy J, Herman CP. Mental health and eating behaviours: a bi-directional relation. *Can J Public Health* 2005; **96 Suppl 3:** S43–46, S49–53.
5. Hallahan B, Hibbeln JR, Davis JM, Garland MR. Omega-3 fatty acid supplementation in patients with recurrent self-harm. Single-centre double-blind randomised controlled trial. *Br J Psychiatry* 2007; **190:** 118–122.
6. Jazayeri S, Tehrani-Doost M, Keshavarz SA, *et al*. Comparison of therapeutic effects of omega-3 fatty acid eicosapentaenoic acid and fluoxetine, separately and in combination, in major depressive disorder. *Aust N Z J Psychiatry* 2008; **42(3):** 192–198.

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Placebo treatment in mild to moderate depression

Most patients with depression seen in primary care have mild to moderate depression. In trials these patients respond equally well to placebo as to pharmacologically active treatment. We discuss the role of placebo treatment in this situation.

An estimated 3 million people in the UK are currently depressed, with winter and the economic situation likely to increase this number. Even without screening for depression in primary care it is likely that more patients with sub-threshold to moderate depressive symptoms will require care.

A recent paper by Fournier and colleagues showed that the pharmacological management of mild and moderate depression is based on poor evidence. They, and others, found that for mild to moderate depression placebo is as effective as antidepressant treatment. Fournier and colleagues concluded that 'there is little evidence to suggest that they produce specific pharmacological benefit for the majority of patients with fewer severe acute depressions.'[1]

Furthermore, in clinical care, patients with mild to moderate depression can be expected to have a better placebo than in clinical trials[2] and the placebo response has been shown to persist over time.[3]

Current NICE guidance[4] recommends sleep hygiene, active monitoring, and low-intensity psychosocial interventions but advises against antidepressants routinely to treat persistent subthreshold depressive symptoms or mild depression because of a poor risk–benefit ratio.

Where to from here: sleep hygiene, active monitoring, and low-intensity psychosocial interventions are first-line treatment but access to psychological therapies remains a problem.

We believe that it should be possible to augment (not replace) these options with a drug that does not carry the risks of antidepressants, is significantly cheaper, and is equally effective for mild to moderate depression — a placebo.

Folic acid is essential for the synthesis of monoamines and may well be the most suitable placebo. It may even have intrinsic activity and is currently the subject of a randomised controlled trial as an augmenting treatment in moderate to severe depression.[5]

We recently recommended an approach to the safe use of placebo treatment[6] and believe that for patients with mild to moderate depression who cannot access psychological therapies immediately, such an approach would be more honest, ethical, evidence-based, safer, and cheaper than the use of selective-serotonin reuptake inhibitors. The period when a patient is receiving sleep hygiene, active monitoring, and low-intensity psychosocial interventions should also be used for placebo treatment.

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REFERENCES

1. Fournier JC, DeRubeis RJ, Hollon SD, *et al*. Antidepressant drug effects and depression severity: a patient-level meta-analysis. *JAMA* 2010; **303(1):** 47–53.
2. Sneed JR, Rutherford BR, Rindskopf D, *et al*. Design makes a difference: a meta-analysis of antidepressant response rates in placebo-controlled versus comparator trials in late-life depression. *Am J Geriatr Psychiatry* 2008; **16(1):** 65–73.
3. Khan A, Redding N, Brown WA. The persistence of the placebo response in antidepressant clinical trials. *J Psychiatr Res* 2008; **42(10):** 791–796.
4. NICE. Depression: the treatment and management of depression in adults. National Clinical Practice Guideline 90. London: National Institute for Clinical Excellence, 2009. http://www.nice.org.uk/nicemedia/pdf/Depression_Update_FULL_GUIDELINE.pdf (accessed 9 Feb 2011).
5. Roberts SH, Bedson E, Hughes D, *et al*. Folate augmentation of treatment — evaluation for depression (FolATED): protocol of a randomised controlled trial. *BMC Psychiatry* 2007; **7:** 65.
6. Pittrof R, Rubenstein I. The thinking doctor's guide to placebos. *BMJ* 2008; **336:** 1020.

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Depression management

We feel the need to raise two key issues regarding the management of depression at a primary care level. First, the importance of recognising occult bipolar II disorder (depression with episodes of hypomania) in a primary care setting. Such patients often present with episodes of major depression and thus screening for symptoms of hypomania may be overlooked. Moreover, there may be a lack of recognition by the patient of their, often quite brief, hypomanic episodes particularly in their depressed state. The treatment for bipolar II disorder, however, differs significantly from that of patients with major depression: mood stabilisers versus antidepressants. Besides, treating bipolar II patients with the standard cocktail of antidepressants runs the risk of driving such individuals into rapid cycling and mixed affective states. Notably, these states are associated with a high risk of suicidality and hence the importance of not missing bipolar II disorder.

Second, there is a growing body of evidence suggesting the adoption of a collaborative (shared care) model in depression management. This involves the introduction of case managers (mental health workers who are responsible for regularly following up patients, offering psychotherapy, and medication management) working with GPs. From our own experience in Luton, we found the deployment of community mental health nurses in both the primary and secondary care settings acting as both case managers and as a liaison between both teams produced high levels of patient satisfaction, and GPs felt a reduced need for referral to specialist services.[1] Such an approach to care would help to better manage potential occult bipolar II patients as well as the risk of patients running into mixed affective or rapid cycling states. Furthermore, there is strong evidence indicating the clinical