The recognition of antidepressant discontinuation reactions

The recently published clinical guideline on the management of depression from the National Institute for Clinical Excellence contains advice that patients prescribed antidepressants should be given a disclaimer about the risk of discontinuation/withdrawal symptoms.[1] By comparison, not so long ago, a key message of the Defeat Depression Campaign of the Royal Colleges of Psychiatrists and General Practitioners was that patients should be informed clearly when first prescribed antidepressants that discontinuing treatment in due course will not be a problem.[2] Furthermore the general public were criticised in the campaign for believing that antidepressants are addictive.

Although the debate about whether antidepressant discontinuation reactions amount to evidence of dependence may be largely semantic, there is a general perception that withdrawal reactions are indicative of dependence.[3] However, the presence of a withdrawal state is neither sufficient nor necessary for a diagnosis of dependence in the current International Classification of Diseases (ICD-10). Semantic confusion about discontinuation, withdrawal and relapse can be traced to dissatisfaction with the definitions of addiction and habituation, leading to the introduction of the single term 'drug dependence' by a World Health Organisation Expert Committee in 1964.[4] Since then, there have been varying shades of meaning of dependence. Developments, such as the syndromal approach to the diagnosis of drug dependence,[5] and operationalisation of diagnostic criteria to improve diagnostic reliability, have been incorporated into modern classificatory systems. The Diagnostic and Statistical Manual of the American Psychiatric Association made tolerance or withdrawal a required criterion in DSM-III, and in DSM-IIIR dependence was redefined as the antisocial syndrome of clinically significant behaviours and symptoms indicating loss of control of substance use and continued use despite adverse consequences.

Case reports of discontinuation reactions have appeared since antidepressants were first introduced. However, systematic recognition had to wait until a BMJ editorial in 1998.[6] Even then the problems were minimised. A few years later the authors of the editorial updated their views to admit that such reactions are common.[7] Some of the pharmaceutical companies may not have helped scientific debate because of misleading promotion of their products. For example, GlaxoSmithKline eventually dropped its insistence that paroxetine is not addictive.[8] This is at least partly because of confusion about the technical and lay definitions of dependence and addiction. A drug which is thought to improve mood is likely to be habit forming, so however much the medical profession may declare that antidepressants are not primarily reinforcing like psychostimulants, the public understand that there may be problems discontinuing antidepressants.

The earlier distinction between physical and psychological dependence may, therefore, still have some relevance in clinical practice. People may form attachments to their medications more because of what they mean to them than what they do. Psychiatric patients often stay on medications, maybe several at once, even though their actual benefit is questionable. Any change threatens an equilibrium related to a complex set of meanings that their medications have acquired. These issues of reliance on medication should not be minimised, yet commonly compliance with treatment was reinforced by emphasising that antidepressants are not addictive. The

NICE guidelines should eliminate this practice. Antidepressants are often prescribed in life crises reinforcing defensive mechanisms against overwhelming anxiety, and the power of the placebo effect should be recognised. As suggestion can play an important part in initial response to treatment, expectations are as likely to play a role in withdrawal, producing a nocebo reaction.

The relapse rate in randomised controlled trials of discontinuation of antidepressant treatment is substantial.[9] Discontinuation reactions may be confused with relapse, and may also trigger or be a sign of potential relapse. There is also evidence of a loss of benefit emerging with long-term treatment and also on retreatment after discontinuation of antidepressants.[10] There is some naturalistic evidence to support the view that people treated without antidepressants may do better over the long term. The possibility that antidepressants may, therefore, create a vulnerability to relapse needs to be taken seriously.[11]

Even in short-term trials SSRIs do not apparently work that much better than placebo.[12] More evidence is needed from longer-term controlled studies to assess whether patients who work through their difficulties without medication have a better outcome over the longer term. Besides the methodological difficulties of testing this hypothesis, there will be ideological barriers to considering it. However, the lessons of the history of the resistance to the recognition of antidepressant discontinuation reactions should help create a more open attitude to examination of this important issue.

(I declare that the answer to the questions on your competing interest form (http://bmj.com/cgi/content/full/317/7154/291/DC1) are all No and therefore have nothing to declare)

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