

indeed have *statistically* significant antidepressant effects. However, these analyses all agree that the *clinical* significance of these effects is not yet established.

The results of the Martin *et al* review do not suggest at all that rTMS has no antidepressant effects. On the contrary, this methodologically rigorous review identifies statistically (but not clinically) significant, short-term antidepressant effects for 2 weeks of high-frequency, left prefrontal rTMS and recommends further studies to establish efficacy and identify optimal parameters. Even more importantly, numerous studies have shown that rTMS alters brain functioning, with effects ranging from altered gene expression in animals to modified cerebral perfusion in humans; in many cases, these effects are very similar to those seen with established antidepressant treatments.

With these points in mind, we offer the following recommendations to help guide use of rTMS in clinical and research settings.

- (a) Given the small clinical effects seen with rTMS in studies to date, it does not seem that rTMS is appropriate for widespread clinical use at this time.
- (b) Large, multi-site trials are warranted to clarify the antidepressant effects of rTMS.
- (c) Future studies of rTMS should incorporate several improvements in study design, including appropriate (and well-documented) randomisation, adequate blinding of subjects and therapists (probably requiring an improved sham condition), and better assessment of the duration of any antidepressant effects.
- (d) More research should be directed at clarifying which patient and treatment characteristics might lead to greater antidepressant effects with rTMS.
- (e) More research should be directed at identifying and testing potential mechanisms by which rTMS produces antidepressant effects.

Declaration of interest

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Burt, T., Lisanby, S. H. & Sackeim, H. A. (2002) Neuropsychiatric applications of transcranial magnetic stimulation: a meta-analysis. *International Journal of Neuropsychopharmacology*, **5**, 73–103.

Holtzheimer, P., Russo, J. & Avery, D. (2001) A meta-analysis of repetitive transcranial magnetic stimulation in the treatment of depression. *Psychopharmacology Bulletin*, **35**, 149–169.

Martin, J. L. R., Barbanjo, M. J., Schlaepfer, T. E., et al (2003) Repetitive transcranial magnetic stimulation for the treatment of depression: systematic review and meta-analysis. *British Journal of Psychiatry*, **182**, 480–491.

McNamara, B., Ray, J. L., Arthurs, J., et al (2001) Transcranial magnetic stimulation for depression and other psychiatric disorders. *Psychological Medicine*, **31**, 1141–1146.

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Evidence in cannabis research

The article by Coffey *et al* (2003) regarding adolescent precursors of cannabis dependence has a number of substantial problems in the measures used, the analysis of data and the reporting and discussion of their findings. One of the study's major findings is that the 'relationship between cannabis dependence and persistent frequent drinking in adolescence changed direction, from a risk association in the univariate model to a *protective* association in the adjusted model' (Coffey *et al*, 2003: p. 333, emphasis added). The use of the term protective implies causality, rather than the negative correlation which more accurately portrays the statistical relationship. It also tacitly implies a value judgement that heavy drinking is preferable to cannabis dependence.

This study utilises logistic regression for the majority of its statistical analysis without adequately considering some important caveats. First and foremost, as already

mentioned, correlation does not equal causality. This is particularly the case when there are a substantial number of independent variables associated with the dependent variable. In the case of cannabis use, as the authors point out, there are many independent variables related to cannabis use, such as socio-economic status (not discussed), parental drug use patterns (not discussed), antisocial behaviour, cigarette smoking and level of education, to name a few that are known. Statistical texts (e.g. Gravetter & Wallnau, 1996) point out that to gain the best measure from the use of logistic regression, there should be few independent variables that are unrelated to each other and that 'a regression solution is extremely sensitive to the combination of variables that is included in it' (Tabachnick & Fidell, 1996: p. 126).

These issues are particularly concerning when such papers can be reported in the mass media (as this study was) on a topic such as cannabis use, which generates strong public responses and is the forum for a great deal of misinformation and manipulation of research results to suit political and ideological agendas. The simple acknowledgement of study limitations would substantially improve the quality of the debate surrounding such a complex social, psychological and medical problem.

Coffey, C., Carlin, J. B., Lynskey, M., et al (2003) Adolescent precursors of cannabis dependence: findings from the Victorian Adolescent Health Cohort Study. *British Journal of Psychiatry*, **182**, 330–336.

Gravetter, F. J. & Wallnau, L. B. (1996) *Statistics for the Behavioral Sciences: A First Course for Students of Psychology and Education* (4th edn). Minneapolis, MN: West.

Tabachnick, B. G. & Fidell, L. S. (1996) *Using Multivariate Statistics* (3rd edn). New York: HarperCollins.

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The media response to Coffey *et al* (2003) was predictable. 'Anti-drug campaigners say new research, showing one in three teenagers who smokes cannabis weekly becomes hooked by their early 20s, proves that it should not be treated as a "soft" drug. The shocking study found teens who used cannabis every week were at high risk of addiction' (Lawrence, 2003). Coffey is quoted as saying, 'The message here is that