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

P.E.H. and D.A. have received research support from the US National Institute of Mental Health. D.A. has received research support from Philips, Inc., belongs to speakers' bureaux at Cephalon, Wyeth Pharmaceuticals and Pfizer, and is a member of consultancy or advisory boards at Bristol-Myers-Squibb, Cyberonics, Eli Lilly, Inc., Forest Laboratories, Inc., GlaxoSmithKline, Janssen Pharmaceutica Products, Inc., Neuronetics, Inc. and UBC Pharma, Inc. T.E.S. has received research support from NV Organon, USA, Cyberonics, Inc. and Magstim, Inc., UK; belongs to speakers' bureaux at NV Organon, USA, Eli Lilly and Company, Switzerland and Pfizer, Inc., Switzerland; and is a member of advisory boards at Otsuka Pharmaceuticals, USA and Janssen AG, Switzerland.

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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.

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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

https://doi.org/10.1192/bjp.184.6.542-a Published online by Cambridge University Press

cannabis is not as harmless as we had thought earlier' – an amazing conclusion from a study where only 1% of the respondents identified as dependent reported social consequences of their use, while the most prevalent symptom (10%) was persistent desire. In everyday parlance, they smoked because they liked it.

Use of the very broad categorisations of the DSM is especially worrisome. Clinicians using these guidelines apply them to people presenting with problems. The use of such categorisations in research, however, constitutes imprecise criteria to determine a person's dependence, resulting in the phenomenon being grossly overreported.

Researchers have been able to generate dependency by applying these same criteria to behaviours as diverse as jogging, shopping, sex, prayer and mountain climbing. In fact, these activities were found to be as addictive as cannabis (Franklin, 1990).

Problems include the disjunctive nature of the criteria (dependency can be ascribed to two people with absolutely no symptoms in common), and the essentially subjective way in which the characteristics are defined. The lack of specificity in the measurement of cannabis dependence results in subjective measures being presented as objective and an over-reliance on the interpretive framework brought to bear. How did the authors differentiate between 'wants' and what DSM characterises as 'needs'? Was this differentiation communicated to respondents? The study fails to differentiate respondents with no dysfunction associated with their dependence from those with significant cannabis-related problems.

Finally, the only index of consumption employed is frequency of use. This is most unsatisfactory; a 'smoke' is not a standardised measure and the consequent lack of any demonstrable association between tetrahydrocannabinol consumption and the dependence syndrome begs the question, dependent on what? Preparing a joint? Inhaling deeply?

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.

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Authors' reply: In response to Dr Miller we would like to state some general principles, to clarify our methodology and provide some additional results. First, we have no argument with the truism that causality cannot be inferred from correlation. Dr Miller seems to overlook the fact that, despite widespread awareness of the dangers of determining causality, the terms 'risk' and 'protective' are commonly used to describe associations identified in longitudinal studies. Indeed, identifying and interpreting such associations is the primary reason for conducting cohort studies. The reiteration of standard caveats should not be necessary in every article arising from these studies and would make for very tedious reading indeed.

The potential for inadequate control of confounding by unmeasured or omitted confounding factors is always a possibility in any multivariate analysis. Researchers are inevitably constrained by the measures they have at their disposal which, in turn, result from the constraints of research directions, design, responder burden and so on. Dr Miller criticises us for omitting socio-demographic measures while including correlated behavioural measures. In terms of the former, we assessed the influence of both parental education and metropolitan residence on cannabis dependence but as there was no evidence of univariate associations for either measure they were unlikely to be confounders (parental education, reference group 'some tertiary': completed secondary school OR 0.8 (95% CI 0.5–1.3); incomplete secondary OR 1.0 (95% CI 0.6–1.6); school in metropolitan Melbourne: OR 1.0 (95% CI 0.6–1.5)). As they were uninformative, these findings were omitted from the article in the interests of parsimony and conserving space. As the report focused on adolescent behavioural and mental health predictors of cannabis dependence, both parental substance use and peer substance use, although likely to be predictors, were not considered relevant to the question. Indeed, they were omitted from the analysis as their inclusion could have masked the associations of interest, exactly as Dr Miller describes.

We acknowledge that confounding occurred between some of the explanatory measures included in the multivariate analysis. We illustrated and discussed in some detail the confounding that occurred between early-onset cannabis use, cigarette smoking and antisocial behaviour. Furthermore, the interaction between problematic alcohol use and weekly cannabis use to which Dr Miller objects arose as *post hoc* examination of confounding.

Mr Palmer misunderstands the denominator of the reported symptom prevalences: we described overall symptom prevalence in the 1601 participants. Symptom prevalences in participants classified as being cannabis dependent were reported in an earlier publication and were: tolerance 17%, withdrawal 74%, unintentioned use 84%, persistent desire 91%, excessive time spent obtaining, using or recovering from use 74%, social consequences of use 18% and continued use despite acknowledged health problems 63% (Coffey *et al*, 2002). Furthermore, participants classified as dependent cannabis users reported compulsive and out-of-control use more frequently than those classified with dependent alcohol use. That there is gathering evidence of social, physical and mental health harm, including dependence, arising from long-term cannabis use is now beyond debate. For a brief and informative review of the current literature on this topic see Ashton (2002).

Mr Palmer debates what really constitutes cannabis dependence. That young people 'are smoking because they like it' does not preclude the possibility that they may be dependent. Alternatively, they may be using it to stop feeling awful, in the self-medication paradigm. He quotes an assertion that other non-challenging behaviours performed persistently may also fit dependence criteria. This may be so, but the harm that arises from these activities is a moot point. The issue that concerns us, and that we used the current gold standard instrument in population research to identify, is that cannabis dependence inevitably prolongs heavy use. No measure applied at interview can be considered to be completely sensitive and specific for all the reasons that Mr Palmer states but the unreferenced assertion that the 'phenomena [are] grossly overreported' is unsupportable in the light of extensive developmental and confirmatory work performed in treatment and non-treatment settings (e.g. Nelson *et al*, 1999). We do not consider it a problem that individuals can be classified as dependent with different combinations of symptoms – conversely, we need to increase our understanding of symptom combinations and their significance (Nelson *et al*, 1999).

https://doi.org/10.1192/bjp.184.6.542-a Published online by Cambridge University Press