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Letter to the Editor

Electrode placement in electroconvulsive therapy – bilateral is still the 'gold standard' for some patients: a reply

We thank Dr Kellner and colleagues for their comments (Kellner *et al*. 2016) on our recent systematic review and meta-analysis of randomized controlled trials of bitemporal *v.* high-dose right unilateral (RUL) electroconvulsive therapy (ECT) (Kolshus *et al*. 2017). We found no significant differences in scores on the Hamilton Depression Rating Scale (seven trials) or in remission rates (six trials) between the two forms of ECT, with some cognitive advantages for high-dose RUL ECT.

Kellner *et al.* raise concerns that these results are misleading at the individual patient level and highlight the important issue of what to do if a patient does not respond sufficiently well to high-dose unilateral, or indeed bitemporal, ECT. It is generally accepted that randomized controlled trials are the preferred method of establishing differences in efficacy between treatments as potential biases are minimized (Sibbald & Roland, 1998). Systematic reviews of randomized controlled trials offer the advantages of single trials with the added benefit of a larger body of evidence and statistical procedures to synthesize the data into a meaningful whole (Borenstein, 2009; OCEBM Levels of Evidence Working Group, 2011). Thus, we feel our results represent the best available evidence at the moment.

This comes with the caveat that the results will be most relevant to patients similar to the ones recruited to the included trials. Indeed, a lack of external validity is a common criticism that may lead to poor take-up of treatments that have been shown to be beneficial in trials (Rothwell, 2005). Of note, one of the included trials included an analysis indicating that study participants did not differ significantly from eligible non-participants or the general population referred for ECT, supporting its generalizability (Semkovska *et al.* 2016). However, as we discussed in our paper, the most severely ill patients are typically excluded or unable to consent to participate in randomized controlled trials. These patients may benefit more, perhaps in terms of a quicker response, from bitemporal ECT but the strength of that evidence is actually quite limited (Kellner *et al.* 2010). With regard to the McCall *et al*. (2000) paper, the low response rates with RUL ECT in that study (39%) was in the group receiving treatment at a relatively low dose of 2.25 × seizure threshold (ST). This would not be considered 'high-dose' RUL ECT (i.e. $\geqslant 5 \times$ ST) and it is not surprising that the response rate was low. In the group receiving fixed-dose RUL ECT (with treatment doses varying from 3.15–12.6 × ST) the response was 67% (McCall *et al.* 2000).

With regard to crossover treatment, we agree with Kellner *et al.* that this is an area lacking empirical evidence (McLoughlin, 2016). The Sackeim *et al.* (1993) study that is cited did not use what is now known as high-dose RUL ECT (but rather 2.5 × ST) and is therefore not relevant here (Sackeim *et al.* 1993). In the Sackeim *et al*. (2000) study, those who did not respond to their randomized treatment (8–10 sessions) were offered an open course of high-dose bitemporal ECT with 69% responding to this treatment. Interestingly, there was no difference in response based on initial randomized group status (including bitemporal ECT), making it difficult to establish whether it was the crossover aspect or merely a function of continuing treatment beyond 8–10 sessions that led to the eventual response (Sackeim *et al.* 2000). As Kellner *et al.* point out, crossover to bilateral electrode placement is a common strategy in clinical practice. However, the evidence-base is weak. Further trials incorporating crossover treatment would be helpful.

We agree that it is currently not possible to predict 'which patient will respond to which technique' and are not advocating that high-dose RUL ECT should necessarily be the 'gold standard' for all patients despite its cognitive advantages. We do, however, believe that the current evidence-base is that high-dose RUL ECT represents an acceptable first line form of ECT and that patients should be provided with this information to help inform their own decisions.

Declaration of Interest

None.

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