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ECT, cognitive function and neuropsychological testing

Patients are often concerned about possible negative effects of electroconvulsive therapy (ECT) on their cognitive performance, and as a result may sometimes be referred for neuropsychological testing. It can frequently prove difficult to advise patients, not only because of the emotion surrounding ECT, but also because of the complexities involved in interpreting neuropsychological test results in this clinical group, where many variables affect test scores, including of course depression itself. Kirov et al[1] report potentially very important data from their excellent long-term study to inform how we advise our patients about ECT, cognition and neuropsychological testing. These data are largely very reassuring, particularly in view of the number of important known confounds they controlled for in their study, and were mostly in accordance with previous findings. However there remain a few issues pertaining to specifically neuropsychological testing that may need further exploration in future studies.

The first issue relates to the accepted current practice in cognitive assessment, that in order to more meaningfully interpret an individual patient's neuropsychological test performance, and specifically detect likely significant change, patients need to be compared against their own pre-morbid level of general cognitive ability (or 'norm'). To achieve this, clinicians use tools such as language-based tests, demographic formulas or the 'best performance method' described by Lezak et al[2] to determine pre-morbid intellectual function. Although there were baseline assessments as part of the protocol, the present study does not provide any such data regarding the more individual comparison standard of a patient's pre-morbid general cognitive ability. It is acknowledged, however, that these data might be difficult to obtain and interpret for many patients in this clinical population.

Clinically meaningful change on test performance, as opposed to statically significant change, can sometimes be difficult to detect. Furthermore, change on a given test with repeated testing can be more difficult to identify if the baseline scores are already well below average – the well-known 'floor effect' seen when testing patients with widely distributed low performance over different cognitive domains. In Kirov and colleagues' study, their Trail Making Test data, when compared with normative data,[3] seem to be potentially already below average at baseline. Again, this might have been a function of participants' depression or other factors that are known to affect performance on a test with high sensitivity such as the Trail Making Test, rather than an already present cognitive impairment related to brain injury. Nevertheless, this possible difficulty with interpreting test performances that may be below the norm at baseline probably needs consideration in the design of future studies.

Potentially related to the above point, it would be helpful to know a bit more about the cognitive performance of a specific subgroup of participants. How many of the 199 patients in the reported study who had never had ECT prior to baseline cognitive testing were there, and when analysing the data from this subgroup what were the findings? While the paper does report a large number of assessments, of which the highest number (122) were with patients who had never had previous ECT, the actual number of patients with no previous ECT was not entirely clear. Perhaps in future studies it would be possible to assess ECT-naive patients for pre-morbid general intellectual ability as a comparison standard to inform the interpretation of subsequent serial neuropsychological test performances. Finally, ECT-naive patients may also, at baseline testing, potentially be further away from floor-level normative data, which could, if showing no significant change over time, provide further evidence to build on the findings from the current landmark study. Such findings may further reassure patients, their families and clinicians when considering cognition and ECT.

1 Kirov GG, Owen L, Ballard H, Leighton A, Hannigan K, Llewellyn D, et al. Evaluation of cumulative cognitive deficits from electroconvulsive therapy. *Br J Psychiatry* 2016; **208**: 266–70.

2 Lezak MD, Howieson DB, Bigler ED, Tranel D. *Neuropsychological Assessment* (5th edn). Oxford University Press, 2012.

3 Tombaugh TN. Trail Making Test A and B: Normative data stratified by age and education. *Arch Clin Neuropsychol* 2004; **19**: 203–14.

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Authors' reply: We agree with most points Dr Coetzer raised, especially that future studies should include more sensitive tests, as there could be subtle cognitive functions that are affected by ECT, which our tests didn't pick up. We fully support the need to obtain comprehensive baseline assessments with as many cognitive tests as possible. These should be repeated around each new course, or at regular intervals for maintenance ECT. This will serve as a safety measure if deterioration is noticed, and give reassurance if no problems are found. The latest Electroconvulsive Therapy Accreditation Service (ECTAS) guidelines reflect this change in practice and recognise the need for standardised assessment pre- and post-ECT. The current guidelines on cognitive testing are not prescriptive about the assessment tool used. At each revision of the ECTAS guidelines, there is much debate about cognitive assessments and we can only encourage the use of more comprehensive tests.

Regarding Dr Coetzer's suggestion that pre-morbid performance be used as a baseline, this is another excellent suggestion, but the comparison might not always be meaningful. Cognitive performance changes with age, with the development of vascular or degenerative changes in later life, due to the depression and other illness-related factors. We therefore feel that assessments closer to the start of the ECT session would be more meaningful for comparison purposes. Baseline assessments are likely to be performed at a time when the patient is depressed, causing further problems. We can't see an easy way out of this problem, therefore we suggest that repeated assessments after each course (i.e. at times when patients are relatively free from depression) will provide a better picture of any potential effect from repeated ECT courses.

Regarding the question on how many patients who had never had ECT were included for testing, the number is indeed 122, as

stated in the paper (i.e. nearly two-thirds of the patients were tested before their first-ever ECT session). The results from this subgroup were not specifically reported, but we can now report on the most meaningful analysis on these patients (those who were tested before their first-ever ECT and tested again after they had >12 ECT sessions). This applies to 37 of the 55 patients who we reported in the paper as having had >12 ECT sessions (average of 21) between their first and their last tests (Table 2 in the paper). The results are basically indistinguishable from those reported in Table 2, with the only significant change (an improvement) found again for the reaction time.

We welcome further research in this field, but want to reiterate that our results refer to cognitive performance, although retrograde memory problems do exist and can upset some patients. Such patients feel more reassured when they are able to compare their performance on cognitive tests pre- and post-ECT.

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Defining clinically significant change

I congratulate ter Heide *et al* on conducting an extremely timely and important clinical trial.[1] As stated by the authors, there is a conspicuous lack of clinical trials investigating the effect of eye movement desensitisation and reprocessing (EMDR) in treating traumatised refugees.

However, in order to be able to appraise/interpret the results more fully, it would be of great value if the authors could analyse their data with different cut-off points for defining clinically significant change. In their article, the authors define clinically significant change as a decrease of 10 points or more on the Clinician-Administered PTSD Scale (CAPS).[2] The authors report that approximately 40% of patients in both conditions achieved clinically significant improvement (Table 2).

However, there is currently no widely agreed threshold for defining clinically significant change on the CAPS and different clinical trials have used a range of different cut-off scores. For example, in two major publications Schnurr *et al*[3,4] defined clinically significant change as a decrease of at least 10 points in total CAPS scores. Hinton *et al*[5] used the rationally derived 15-point change[2] as a marker of clinically significant change. In line with the method set forth by Jacobson & Truax,[6] Taylor *et al*[7] defined clinically significant change as a reduction in total CAPS score of at least two standard deviations. Hien *et al*[8] used a 30-point or greater improvement on the CAPS to determine clinically significant improvement of PTSD symptoms, whereas Bryant *et al*[9] defined clinically significant change as a cut-off of <45 on the CAPS at follow-up.

It is also important to take into consideration the measurement variability of the instrument.[6] A change of 10 points on the CAPS is not necessarily even reliable. Monson *et al*[10] calculated a reliable change score of 12.22 points on the CAPS, and we previously have calculated a conservative reliable change score of 14.3 points.[11] So a change of 10 points might simply be within the measurement variability of the CAPS.

These issues taken together, it would be very informative if the authors made use of different cut-off scores for defining clinically significant change. The Institute of Medicine[12] notes that common methods to define clinically significant change on the CAPS in the treatment literature are to define it as a ≥10-point decrease, a ≥30 percent decrease, or as two standard deviations below pre-treatment level. Using a 30% decrease in total CAPS score for the present sample entails a cut-off score for clinically significant change of approximately 23 points. Using two standard deviations below pre-treatment level[6] as a marker for clinically significant change entails a cut-off score of approximately 36 points. It would be very informative if the authors re-analysed their data with at least these two thresholds for defining clinically significant change in addition to the 10-point cut-off score reported in their paper.

1 ter Heide FJJ, Mooren TM, van de Schoot R, de Jongh A, Kleber RJ. Eye movement desensitisation and reprocessing therapy v. stabilisation as usual for refugees: randomised controlled trial. *Br J Psychiatry* 2016; doi: 10.1192/bjp.bp.115.167775.

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Authors' reply: Dr Halvorsen quite rightly draws attention to the various definitions of clinically significant change, which all have their advantages and disadvantages. We especially agree with the comment that the threshold for clinically significant change should at least coincide with the threshold for reliable change (18.66 in our sample). However, using the threshold of 10 points, as promoted by Schnurr,[1] has specific value in our study. First, the 10-point threshold has been shown to be related to changes in quality of life in several samples.[2,3] Second, clinically significant change refers to both clinical improvement and deterioration. Most clinicians and researchers would agree that a deterioration