Author’s response to reviews

Title: A randomized controlled trial of cognitive remediation for a national cohort of forensic patients with schizophrenia or schizoaffective disorder.

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Author’s response to reviews:

REVIEWER 1

In general, The manuscript describes a thorough and well-executed study, and the field methods are suited to addressing the questions,

Many thanks for these positive comments.
Although the use of controls is not considered which allow clinicians to capture the value of specific intervention benefits.

Thank you. This is a randomised controlled trial in which there is a formal control group with treatment as usual. The characteristics of the control group (TAU) are described in table 2 and we believe these are well matched with the intervention group.

Background In this study, the authors address Cognitive Remediation Training (CRT) for forensic Patients with schizophrenia or schizoaffective disorder by conducting a blind randomized controlled trial;

Thank you for this succinct account of the study protocol.

Whereas they have not been narrated about schizoaffective disorder and lifted unjustified

Methods

We believe our methods are conventional. We used SCID-I diagnostic inventory rated by a consultant forensic psychiatrist. We have also analysed whether there were significant differences between the diagnostic groups at baseline. There were no significant differences – see supplementary table -

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We could if need be add this table to the article or include it as supplementary material. We have added a sentence to summarise this finding in the description of the groups at baseline -

“A further sensitivity analysis showed that two groups defined by diagnosis (schizophrenia and schizoaffective disorder) did not differ significantly in any of the variables shown in table 2”
According to DSM-IV, schizophrenia or schizoaffective disorders are classified as Axis I psychiatric disorders (SCID-I), which perhaps be preferable to mention.

Thank you – we have now done so.

With respect to Criteria of allocated participants, some points have not been clear enough as:

- Duration of mental illness –

It is not possible to identify this with sufficient clarity, and this was not a part of our published study protocol. We have given the age, and we have now added the length of stay prior to the commencement of the study (TABLE 2) – there were no statistical differences between the randomised groups.

- Type, frequency and seriousness of the litigation and time elapsed since that –

We have given the numbers found NGRI in each group and we have now added the length of time since admission prior to the study – the time elapsed as requested. These did not differ significantly between randomised groups. From a clinical point of view, it is more important to consider the seriousness of the act itself rather than the legal outcome. This is expressed in the DUNDRUM-1 measure of need for therapeutic security, once again there were no significant differences between the randomised groups (TABLE 2).

There is an argument for clarity of care and treatment approach provided by Ireland's National Forensic Mental Health Service (NFMHS), Inpatient or outpatient? - -

All patients were in-patients in the only secure forensic hospital for Ireland, as explained in the Methods section on “Setting”. We have now added references to our recently published description of ‘treatment as usual’ and its outcomes [11], (Richter et al 2018).
No attention given to participant's demographic information that may be key indicators for trial results.

This is described extensively in TABLE 2 (age, gender etc) with no significant differences between randomised groups. We have now added the data for length of stay at baseline and the test of pre-morbid functioning (TOPF-UK).

REVIEWER 2

In this study, 65 patients with schizophrenia or schizoaffective disorder within a national forensic cohort were enrolled in a single blind randomized controlled trial of CRT versus treatment as usual (TAU). The primary outcome measure was the composite score of the MATRICS Consensus Cognitive Battery (MCCB) while secondary outcome measures included neurocognitive and social cognitive domains, symptoms, and 'real world' functioning. Significant improvements were observed in visual and working memory in patients receiving CRT as compared to those receiving TAU. Mediation analysis found that those who cognitively benefited from CRT had corresponding improved functioning, and more net positive moves to units with lower security within the hospital. The Authors conclude that CRT may be an acceptable and efficacious intervention for forensic patients with schizophrenia or schizoaffective disorder.

Thank you for this helpful summary.

This is an interesting study, performed in a nationally representative sample of forensic patients, and addressing a clinically relevant question.

Some points should however be considered:

1. The mean MCCB composite score of patients was about 3 SDs below the mean of a nonclinical sample: this raises the question of the representiveness of this sample of the larger population of patients with schizophrenia. Perhaps a general IQ level should have been calculated in order to exclude possible cases showing mental retardation.
We were interested in avoiding the exclusion of the most severely ill and impaired patients with schizophrenia and schizoaffective disorder. We have used the MCCB in accordance with the guidance of the NIMH which we have referenced [5,7]. We referenced this also in the published study protocol [8]. None of the patients had a primary diagnosis of developmental intellectual disability, as set out in the inclusion and exclusion criteria. We have now added a statement to that effect:

“None had a pre-morbid diagnosis of developmental intellectual disability.”

We have in addition added the TOPF measures for baseline to Table 2.

Table 2: sample characteristics at baseline

2. There were no significant differences in social cognition, symptomatology and functioning or net positive moves after the intervention period or at follow up between the CRT and TAU groups, after covarying for baseline values of the specific variable (and there was a difference in favour of TAU for the PANSS excitement factor): these are negative findings that are not highlighted and discussed enough in the paper.

Thank you for drawing this to our attention. We have now added a reference to the PANSS excitement factor in the first paragraph of the discussion as follows

“We were also interested in the acceptability of CRT and patients’ experience of the intervention. Five main outcomes were observed. First, patients who participated in CRT obtained significant improvements in the primary outcome measure, a composite score of the MCCB both at end of treatment and at eight months follow up. Second, there were significant improvements in specific cognitive domains including working and visual memory, but not social cognition. Third, there were no significant differences in symptoms (PANSS) apart from a difference in favour of the control group in the PANSS excitement factor. Fourth, there were no significant differences between CRT and TAU on routine measures of real world functioning ascertained by the multidisciplinary team (SOFAS) or net positive moves.”

We hope this addresses the point with sufficient prominence. We go on to draw attention to the importance of mediation as a means of explaining the improved outcomes for patients who had improved cognition.

3. The fact that the mediation analyses revealed significant associations between cognitive gain and change in functioning in CRT treated patients opens the question of identifying
the characteristics of patients who obtain such gains and of predicting them, while this is not considered in the paper and discussion.

We agree that this is an important point for future study. For the future, we believe that larger studies or meta-analyses may enable dismantling analyses to take place.

It was not the goal of this study to identify the characteristics that predict better outcomes from this treatment. We may be able to address this in further secondary analyses, though we believe that we have at least paved the way for further studies specifically designed for these purposes. By showing that positive moves – a real world measure of functional recovery – were mediated by cognitive improvement, we have provided an explanatory model for the benefits of cognitive remediation. We controlled for baseline cognition and baseline SOFAS and showed non-the-less that improved cognition associated with CRT was associated with improved real world function (SOFAS). We also showed that when controlling for baseline MCCB and for gender, positive moves was non-the-less associated with improved neurocognition associated with CRT. It can be taken from this that baseline MCCB, SOFAS and gender were not predictors of response to CRT. We have now added this to the discussion.

“We controlled for baseline cognition and baseline SOFAS and showed non-the-less that improved cognition associated with CRT was associated with improved real world function (SOFAS). We also showed that when controlling for baseline MCCB and for gender, positive moves was non-the-less associated with improved neurocognition associated with CRT. It may be taken from this that baseline MCCB, SOFAS and gender were not predictors of response to CRT. To clarify the predictors of positive response however would require formal dismantling studies [42, 43].”

4. Also, it would be interesting to know which factors were associated to functional improvement and net positive moves in TAU treated patients.

Please see the previous response and the text and references added regarding the benefits of future dismantling studies.

5. The CRT intervention and its flexible principles are interesting but seem scarcely standardized and hardly replicable by other groups.

We have referenced the most influential reviews of this subject – Wampold [15] and in the published protocol we referenced the importance of multi-modal treatment McGuire; [23] and the APA book on the Principles of Therapeutic Change that work [22]. We have now also referenced these in this article. We have discussed this also at some length in a
recent article on measurement of change (Richter et al 2018 [11]). We have now added detail to the description of CRT and TAU as follows:

“Our cognitive remediation training is a principle driven intervention consisting of nine treatment principles, which are flexibly applied during delivery of the intervention [8; Table1]. Principle driven approaches are in keeping with the recommendations of a task force on Principles of Therapeutic Change that Work, sponsored by the American Psychological Association and the North American Society for Psychotherapy Research [22] and are also in keeping with a review of effectiveness and common factors [15]. Psychotherapy principle driven approaches integrate research concerning empirically supported treatments (EST) with research concerning the moderating influence of the therapeutic relationship [15, 22, 24].

“The system for delivering ‘treatment as usual’ has been described and shown to be effective in reducing a measure of violence proneness, the HCR-20 [26]. This draws on principles of multi-modal treatment [23] and multi-systemic treatment [24].”

6. On the other hand, the feasibility and high acceptability of CRT in this cohort of forensic patients is an important finding that positively addresses an unmet need in a group of patients particularly difficult to treat.

We very much appreciate these positive observations.