



Effectiveness of cognitive remediation in the ultra-high risk state for psychosis

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were high in EI. Finally, negative self-concept was particularly central for the poly-traumatized sample.

The prominence of sense of threat in the illness group might be suggestive of fear of recurrence. The centrality of avoidance in accidents and assaults might suggest that people are less likely to put themselves in positions where these events can re-occur. Poly-traumatization, especially when occurring in childhood, can lead to a failure to develop age-appropriate competencies, which in turn can lead to a sense of self as defective, helpless, deficient and unlovable.

These results have important implications for the treatment of CPTSD using person-centred approaches. We previously argued⁹ that symptoms of CPTSD can be targeted and prioritized in therapy according to the severity or prominence of a given cluster, alongside the patient's readiness to tackle these symptoms. We now provide evidence that the expression and structure of CPTSD symptoms is associated with the index trauma event. It may be, therefore, beneficial to prioritize different symptom clusters, when planning treatment, depending on the index trauma.

Further research on exploring the salience of different symp-

toms clusters in CPTSD is important and may contribute to effective and efficient treatment planning.

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1. Reed JM, First MB, Kogan CS et al. *World Psychiatry* 2019;18:3-19.
2. Weathers FW, Keane TM. *J Trauma Stress* 2007;20:107-21.
3. Hyland P, Karatzias T, Shevlin M et al. *Psychol Trauma* (in press).
4. Bernstein DP, Fink L. *Childhood Trauma Questionnaire: a retrospective self-report*. San Antonio: Psychological Corporation, 1998.
5. Cloitre M, Shevlin M, Brewin C et al. *Acta Psychiatr Scand* 2018;138:536-46.
6. Epskamp S, Cramer AO, Waldorp LJ et al. *J Stat Softw* 2012;48:1-18.
7. Robinaugh DJ, Millner AJ, McNally RJ. *J Abnorm Psychol* 2016;125:747-57.
8. Van Borkulo CD, Borsboom D, Epskamp S et al. *Sci Rep* 2014;4:5918.
9. Karatzias T, Cloitre M. *J Trauma Stress* 2019;32:870-6.

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Effectiveness of cognitive remediation in the ultra-high risk state for psychosis

Individuals at ultra-high risk (UHR) for psychosis suffer significant cognitive deficits that can hamper functional recovery¹. The beneficial effect of cognitive remediation on cognition and functioning is documented in individuals with established psychosis^{2,3}, but little is known about the effect of this intervention in those at UHR for psychosis.

Cognitive remediation may potentially be more beneficial in the psychosis UHR state than in more advanced illness stages, owing to the potential of greater brain plasticity^{4,5}. For the same reason, reduced doses may be sufficient to produce change.

The randomized, assessor-blinded, parallel-group, superiority clinical trial called FOCUS is the hitherto largest trial to report on the feasibility and efficacy of intensive neurocognitive and social cognitive remediation in the UHR state.

Participants aged 18-40 years who fulfilled the Comprehensive Assessment of At Risk Mental States (CAARMS) UHR criteria were recruited to the FOCUS trial from the psychiatric in- and outpatient facilities in the greater catchment area of Copenhagen, Denmark from April 2014 to December 2017⁶.

On completion of baseline assessments, participants were randomly assigned to either 20 weeks of cognitive remediation as an add-on to treatment as usual (TAU+CR) or to treatment as usual alone (TAU). Randomization was stratified by current use of antipsychotic medication (yes/no) and IQ score (≤ 100 / >100).

The CR intervention comprised two hours of group training (one hour of neurocognitive training, with subsequent 15 min of bridging session, and one hour of social cognitive training)

once a week for a total of 20 weeks. For this group training, we used the Neuropsychological Educational Approach to Cognitive Remediation (NEAR)⁷ and the Social Cognition and Interaction Training (SCIT)⁸ manuals. Additionally, the participants received 12 individual sessions with a cognitive-behavioral format designed to maximize the transfer of the effect of the CR to their daily lives.

The TAU consisted of a regular contact with health professionals in the in- and outpatient facilities, involving monitoring of medication and supportive counselling but not cognitive remediation.

A total of 146 UHR individuals were assigned to either TAU or TAU+CR. Socio-demographic variables were well balanced between the groups. The TAU+CR group attended an average of 10.9 ± 7.6 cognitive remediation sessions and had an average of 11.9 ± 16.4 hours of total neurocognitive training.

The comparisons between the two groups on continuous outcomes at cessation of treatment and at 12-month follow-up were conducted using a generalized linear model adjusted for stratification variables and baseline imbalances, with missing data handled by multiple ($m=100$) imputations.

At cessation of treatment, we found no between-group difference on the primary outcome, i.e. global neurocognition as indexed by the Brief Assessment of Cognition in Schizophrenia (BACS) composite score ($b=-0.125$, 95% CI: -0.423 to 0.172 , $p=0.41$). We also did not find a treatment effect on secondary outcomes, i.e. scores on Personal and Social Performance Scale

(PSP), Brief Psychiatric Rating Scale (BPRS-E), Scale for the Assessment of Negative Symptoms (SANS), and Montgomery-Åsberg Depression Rating Scale (MADRS).

Concerning explorative outcomes, we found a treatment effect on the Emotion Recognition Test (ERT) latency total score and ERT latency happiness, sadness, and fear (b from -152.0 to -226.8 ; p from 0.01 to 0.002), with the TAU+CR group demonstrating faster emotion recognition processing speed.

At the 12-month follow-up, we found a significant between-group difference on the Cambridge Neuropsychological Test Automated Battery (CANTAB) executive functioning Stockings of Cambridge measure and the Paired Associate Learning visual memory measure ($b=0.759$, $p=0.03$ and $b=-1.98$, $p=0.02$, respectively), with the TAU+CR group performing better than the TAU group.

So, the CR intervention did not result in improvements in global measures of cognition, functioning and symptoms in this sample of UHR subjects. The CR may, though, have been underdosed to drive meaningful global improvements, as the TAU+CR group attended an average of 10.9 sessions and had an average of 11.9 hours of neurocognitive training, which is about half the usual dose for people with first-episode schizophrenia.

While the integrative CR format was designed to achieve synergistic benefits of targeting both neurocognition and social cognition, our findings indicate that this may not be a viable approach to the UHR population, that is known to be difficult to engage in treatment⁹.

Our exploratory findings indicate improvements in some areas of social cognition and neurocognition after even a few CR sessions, which points to a potential for cognitive plasticity if UHR individuals can be engaged sufficiently to practice the skills.

In secondary regression analyses, the social cognitive im-

provements (emotion recognition latency total and domain scores) were consistently predicted by better baseline social and role functioning. This finding indicates that UHR individuals with better functioning at ascertainment may be more able to benefit from a CR intervention. On the other hand, greater improvements in executive function and visual memory at 12 months were predicted by worse baseline performance on these neurocognitive measures. If confirmed, these findings support taking baseline patient characteristics into account when implementing CR in the UHR population.

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1. Bolt LK, Amminger GP, Farhall J et al. *Schizophr Res* 2019;206:67-74.
2. Wykes T, Huddy V, Cellard C et al. *Am J Psychiatry* 2011;168:472-85.
3. Bowie CR. *World Psychiatry* 2019;18:274-5.
4. Keshavan MS, Hogarty GE. *Dev Psychopathol* 1999;11:525-43.
5. McGorry PD, Hartmann JA, Spooner R. *World Psychiatry* 2018;17:133-42.
6. Glenthøj LB, Fagerlund B, Randers L et al. *Trials* 2015;16:25.
7. Medalia A, Freilich B. *Am J Psychiatr Rehabil* 2008;11:123-43.
8. Roberts DL, David P, Combs DR. *Social Cognition and Interaction Training (SCIT). Clinician guide*. Oxford: Oxford University Press, 2015.
9. Farris MS, Devoe DJ, Addington J. *Early Interv Psychiatry* 2019;13:169-80.

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