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Cognitive remediation for people with bipolar disorder: The contribution of session attendance and therapy components to cognitive and functional outcomes

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ABSTRACT

Background: Cognitive remediation (CR) can reduce cognitive and functional difficulties in people with bipolar disorder (BD). To date, there is limited evidence on the contribution of session attendance and therapy components to treatment outcomes. This study explores whether attendance and core CR components contribute to treatment outcomes.

Methods: This is a secondary analysis using data from a randomized controlled trial comparing CR plus treatment-as-usual (TAU; n = 40) to TAU only (n = 40) in euthymic people with BD. Session attendance was measured by number of sessions and by achieving therapy completion, pre-defined as attending ≥ 20 sessions. We used instrumental variable analysis to examine the effect of attendance on treatment outcomes. We then considered the association between core therapy components (i.e., massed practice, errorless learning, strategy use, therapist contact) and post-treatment outcome changes using correlation.

Results: The CR group improved significantly in measure of global cognition, psychosocial functioning, and goal attainment. Therapy recipients attended 27.1 sessions on average, with 32 (80%) completing the minimum number of 20 sessions. Attending more sessions and achieving therapy completion were associated with improved treatment outcomes, but this relationship was not significant within the subgroup of CR completers. Improvement in psychosocial functioning was associated with therapist contact and goal attainment with selecting useful strategies during therapy.

Conclusions: Our findings highlight the relevance of session attendance, specifically the importance of achieving a minimum threshold of CR sessions, for outcome improvement. Strategy use and therapist contact might facilitate improvements in psychosocial functioning and personal recovery goals.

1. Introduction

Clinically significant impairments in cognitive functioning are present in a substantial proportion of people with bipolar disorder (BD) (Douglas et al., 2018; Tsapekos et al., 2021a). Importantly, convincing evidence demonstrate that cognitive deficits are linked to daily-life difficulties in areas such as work and other functional outcomes (Brisson et al., 2008; Tse et al., 2014; Wingo et al., 2009). This association prompted the emergence of interventions targeting cognition to tackle functional difficulties as potential treatment options for people with BD.

A psychological therapy aiming to facilitate long-term functional recovery through the improvement of cognitive deficits is cognitive remediation (CR).

Recent findings from randomized controlled trials indicate that CR can benefit people with BD in terms of ameliorating cognitive difficulties (Bernabei et al., 2020; Lewandowski et al., 2017; Strawbridge et al., 2021), as well as that therapy-induced cognitive gains may translate into functional improvements (Tsapekos et al., 2021b). Despite reporting moderate effect sizes for cognitive and functional outcomes at group level, these trials were characterized by substantial variability in

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response to CR and did not offer an insight in what might have caused this variability. One way to explore this is by identifying characteristics of the therapeutic process associated with outcome improvement (Medalia et al., 2018). This can improve our understanding about the ways the therapy works and inform modifications required to improve the efficacy of CR.

The literature on psychological interventions suggests that a candidate contributor to treatment effects is adherence, as measured by *session attendance*. For example, higher attendance during cognitive behavioural therapy is associated with improved post-treatment outcomes (Glenn et al., 2013). In the field of CR, although trials commonly consider the number of sessions as a measure of intervention feasibility, there has been limited examination of attendance as a factor modifying treatment effects. Medalia and Richardson (Medalia and Richardson, 2005) examined that in patients with schizophrenia diagnosis showing that CR improves in cognitive outcomes had better attendance than non-improvers. Treatment intensity is also considered important and delivering two to three sessions per week has been suggested (Bowie et al., 2019), but a recent meta-analysis did not find an association between session intensity and treatment effects possibly because the majority of analyzed studies examined intensive CR programmes (Vita et al., 2021). Another issue is the minimum “dose” of CR required to achieve meaningful changes. Although a total of 20 hourly sessions tends to be recommended (Bowie et al., 2019), empirical evidence is still warranted to support this threshold.

Session attendance reflects the amount of therapy received (the “dose” of CR), but this will also affect the likelihood of other therapy components being provided (e.g., number of tasks completed). A recent working group of experts described the core components and techniques of CR, including facilitation by a therapist, cognitive training, use of problem-solving strategies, and procedures to facilitate transfer to daily-life functioning (Bowie et al., 2019).

The contribution of a trained *therapist* is a feature differentiating CR from computerized cognitive training (Harvey et al., 2018). Therapists assist CR recipients to formulate cognitive difficulties and link them with recovery goals, while also support the transfer of acquired skills to real-world activities (e.g., by discussion, in-session role-playing, out-of-session tasks). Previous research in people with a schizophrenia diagnosis suggested that the therapist’s contribution may be significant for session attendance and drop-out prevention (Huddy et al., 2012). At the same time, patients reporting a good working alliance with their therapist were more likely to improve more on their primary therapy goals (Cella and Wykes, 2017).

Intensive and repetitive training of cognitive tasks (*massed practice*) is assumed to activate relevant neural networks (Vinogradov et al., 2012). This helps therapy recipients not only improve their performance in certain tasks, but also develop new ways of efficient information processing that can be generalized beyond tasks into various cognitively demanding activities. For most CR programmes, cognitive training is delivered in the context of minimal negative feedback (*errorless learning*), meaning to reduce the likelihood of errors during task practice in order to positively reinforce participants and boost their motivation (Middleton and Schwartz, 2012). Computerized CR approaches often facilitate errorless learning by adjusting task difficulty to previous performance and by progressively increasing the level of difficulty within each task, while at the same time gradually removing support from the therapist.

Strategy use during cognitive training is a technique commonly shared between CR programmes as a method of overcoming or compensating for cognitive deficits (Wykes and Spaulding, 2011). For example, a patient’s capacity to memorize information might be limited and cognitive training alone might not suffice to restore this deficit, but employing relevant strategies (e.g., creating associations between target items) may enhance performance. Although strategy use is embedded in several computerized CR approaches, therapists can also be instrumental in recommending useful strategies, especially at the early stages,

and generalizing strategies for use in real-world activities. For some CR approaches, strategy use is integral for the development of meta-cognitive skills (Cella et al., 2015).

These components represent the active ingredients of CR but exploring their contribution to therapeutic effects has been challenging due to measurement difficulties. However, modern computerized CR programmes, such as CIRCuiTS (Reeder et al., 2016), offer this opportunity by recording various parameters of cognitive training. Using these metrics, a study in people with a schizophrenia diagnosis showed significant associations between CIRCuiTS components and post-treatment improvements: massed practice was correlated with cognitive gains, and therapeutic alliance was associated with both cognitive and functional benefits (Cella and Wykes, 2017). A recent meta-analysis reported greater benefits for cognition and functioning for those programmes that combined the core CR components (Vita et al., 2021). For people with BD though, the relationship of session attendance and therapy components with treatment outcomes remains unexplored.

This study investigates whether different therapy features of CR are associated with improvement in cognitive and functional outcomes for euthymic people with BD. First, we examine the “dose-response” relationship between number of sessions and outcome improvement to test whether the effect of CR changes as a function of session attendance. Then, we consider the association between outcome changes and core CR components: massed practice, errorless learning, strategy use and therapist contact.

2. Methods

2.1. Study design

This is a secondary analysis of longitudinal data from a randomized controlled trial comparing CR to treatment-as-usual (TAU) in euthymic patients with BD (Strawbridge et al., 2021). Compared to the original trial, this analysis includes an extended sample of 20 participants recruited under the same protocol and randomly allocated to CR ($n = 11$) or TAU ($n = 9$). These participants were not included in the primary trial analysis conducted according to the published protocol ($N = 60$) (Strawbridge et al., 2016), but are included in this secondary analysis to increase the power of the study. All participants provided written informed consent prior to study procedures. After the baseline assessment (week 0), participants were randomly allocated to CR or TAU groups for 12 weeks and were assessed again after the intervention period (week 13). The trial was approved by the City Road & Hampstead NHS Research Ethics Committee (reference 15/LO/1557).

2.2. Participants

The trial included participants with a DSM-5 diagnosis of BD, recruited via primary and secondary care services, online advertising and mental health charities. Participants had to be fluent in English and aged between 18 and 65 years. The Mini International Neuropsychiatric Interview (Sheehan et al., 1998) was used to confirm the BD diagnosis. Participants had to be on stable psychiatric medication and free of acute mood symptoms for ≥ 1 month prior to inclusion. Euthymia was defined as a score of ≤ 7 on the *Hamilton Depression Rating Scale 17-item* (HAM-D) (Hamilton, 1960) and *Young Mania Rating Scale* (YMRS) (Young et al., 1978) over the period of one month. Participants were not selected based on the presence or absence of cognitive impairment. Exclusion criteria included a neurological disorder, personality disorder diagnosis, abuse or dependence on alcohol or illicit substances over the past six months.

2.3. Cognitive remediation therapy

CR was delivered by a therapist using the online software ‘Computerized Interactive Remediation of Cognition – Interactive Training for

Schizophrenia' (CIRCuiTS) (Reeder et al., 2016). CIRCuiTS is targeting cognition with simple and complex tasks, as well as metacognition through the use of strategies. Simple tasks are designed to target specific cognitive functions (e.g., attention, working memory), while complex tasks are designed as ecologically valid simulations of real-world activities (e.g., working, travelling, shopping), commonly requiring a combination of cognitive skills. The difficulty of these tasks progressively increases, depending on the individual's performance. This scaffolding approach ensures that individual performance remains consistently at high levels (around 80%) and facilitates errorless learning. For each task, participants are also prompted to select and use strategies which they rate after task completion (on a 1–5 scale of helpfulness). This way participants develop a set of personally useful strategies both for CIRCuiTS tasks and real-world activities.

The role of the therapist is critical in this CR approach. Therapists are responsible for motivating participants and assist them with selecting and applying strategies to develop metacognitive skills: becoming aware of their personal cognitive resources, their strengths and shortcomings, recognizing the difficulties of a task and being able to regulate their resources and use appropriate strategies in order to respond appropriately (Cella et al., 2015). Therapists also facilitate the transfer of newly acquired skills and strategies to daily-life activities and personal goals through examples, role-playing, and in vivo practicing. Such real-world goals are set collaboratively at the beginning, using a cogSMART format (i.e., specific, measurable, attainable, realistic, and timely goals related to cognition) and are monitored throughout the therapy.

CIRCuiTS was offered for 12 weeks, comprising one-on-one hourly sessions, either in person or remotely (e.g., video call), and supplementary independent practice sessions at home flexibly adjusting to participant needs. Therapy was delivered by trained postgraduate psychologists with supervision from an experienced clinical psychologist. The target was attending 2–3 hourly sessions per week, aiming for up to 40 sessions for all participants. Although all participants had the chance to receive the maximum number of sessions, therapy delivery was tailored for each participant individually according to their schedule and session attendance differed between participants according to their availability. A 20-h threshold was predefined as the minimum for therapy completion following evidence from a feasibility study in people with schizophrenia (Reeder et al., 2016). Participants did not receive any compensation for undertaking therapy.

2.4. Measures

Information on sociodemographic and clinical characteristics was collected at baseline using a structured interview, while mood symptoms were assessed using the HAM-D and the YMRS. Premorbid IQ was estimated using the *Test of Premorbid Function* (TOPF) (Wechsler, 2011). Use of psychotropic medications was recorded at baseline and changes were monitored during the study. Post-treatment assessments of cognitive and functional outcomes were blinded to group allocation.

2.4.1. Cognitive outcomes

We used four cognitive tests showing significant between-group improvement for this secondary analysis, in order to minimize problems with multiple comparisons and increase the chance of detecting significant associations with therapy variables. For the full list of cognitive tests, including those excluded from this analysis, please see the main trial publication (Strawbridge et al., 2021). Selected tests assessed four core cognitive domains: processing speed, with the *Digit-symbol coding* (Wechsler, 2014); attention and working memory, with the *Digit span* (Wechsler, 2014); verbal memory, with the *Verbal paired associates II* (Wechsler, 2009); and executive functioning, with the *Hotel test* (Manly et al., 2002). Raw scores from each test were transformed to age- and education-corrected standardized scores (z scores; $Mean = 0$, $SD = 1$) according to the test manuals. For all tests, higher scores reflected better performance. A composite score for global cognition was

computed by averaging individual z scores.

2.4.2. Functional outcomes

Psychosocial functioning was assessed using the *Functional Assessment Short Test* (FAST), a validated scale designed to measure functional difficulties with high internal consistency (Cronbach's $\alpha = 0.91$), high concurrent validity with the Global Assessment of Functioning scale (Pearson's $r = -0.9$), and ability to discriminate between euthymic and depressed or manic patients with BD (Rosa et al., 2007). FAST evaluated six different domains of functioning (i.e., autonomy, occupation, cognition, financial issues, interpersonal relationships, leisure time) with higher scores representing greater levels of functional impairment.

Attainment of personal goals was assessed using the Goal Attainment Scale (GAS) (Turner-Stokes, 2009). GAS provided a standardized way of quantifying the extent to which participants achieved their individual recovery goals (defined at baseline based on their own needs and priorities) following CR, with higher scores indicating greater goal achievement. Systematic evidence from clinical rehabilitation settings suggest that goal attainment scaling is a sound method of evaluating behavioural outcomes, demonstrating excellent inter-rater reliability (Pearson's $r > 0.8$), good convergent validity with established outcome measures (Pearson's $r > 0.6$), and high sensitivity to behavioural changes following rehabilitation (Hurn et al., 2006). GAS has previously been adopted as an outcome measure in a CR trial for people with psychosis (Wykes et al., 2018).

2.5. Session attendance and therapy components

The number of hourly sessions completed per week during the 12-week intervention period represented the "dose" of CR received per participant. Therapy completion (i.e., achieving the minimum threshold of 20 sessions or not) was used as a binary measure of attendance.

We also considered four therapy components of CR:

- *Massed practice*, as the total number of tasks completed throughout therapy and the average number of tasks completed per session
- *Errorless learning*, as the average performance achieved across all tasks completed during therapy (score: 0–100)
- *Strategy use*, as the average number of strategies used per session and the same figure for useful strategies (i.e., those rated with 4 or 5)
- *Therapist contact*, as the amount of time per session spent in contact with the therapist rather than in independent task practice.

2.6. Statistical analysis

Analyses were conducted using Stata (version 15, StataCorp., 2017) and SPSS (version 26; IBM, New York). All outcome measures were checked for normality using the Shapiro-Wilk test and log transformation was applied to normalize non-normally distributed measures.

2.6.1. Effect modification by session attendance

Although our protocol aimed for up to 40 sessions, the number of sessions attended varied between participants in the CR group. Thus, we considered whether session attendance modified the effect of CR. In statistical terms, session attendance is a process variable, a characteristic of the therapeutic process (Dunn et al., 2005). Differences in these characteristics might explain some of the variability in treatment effects. However, examining this "dose-response" effect only for participants in the CR group might lead to biased estimations due to measurement error and hidden confounding potentially affecting the relationship between the process variable and the outcome (Maracy and Dunn, 2008).

A solution is the use of an instrumental variable (IV) which accounts for control group participants receiving no intervention and for measurement error or unmeasured confounding affecting the treatment-outcome relationship. This method can provide a more reliable

estimation of treatment effect modification by a post-randomization process variable and has been previously used to estimate “dose-response” effects for psychological interventions delivered in randomized controlled trials where session attendance differed across participants (Goldsmith et al., 2015).

We conducted the IV analysis using two-stage least squares (2SLS) regression to examine the modifying effect of session attendance on cognition and functioning (Graham Dunn and Bentall, 2007; Maracy and Dunn, 2008). The model included randomization to TAU or CR (coded as 0/1) as the instrumental variable, number of sessions as the instrumented process variable, and a post-treatment measure (week 13) as the outcome, while also controlling for age, education and the baseline score (week 0) of the respective outcome (Fig. 1). We used the *ivregress* command in Stata to fit models for different cognitive and functional outcomes. The estimated coefficient corresponded to the effect of one additional session per week on the outcome. IV analysis was repeated with therapy completion as the process variable to estimate the effect of attending at least 20 sessions on treatment outcomes.

This was a complete-case analysis, restricted to participants with complete data for post-treatment outcomes. Missing data were assumed to be missing at random (MAR) and observed baseline variables were tested as factors of missingness (Jakobsen et al., 2017). Any variables predicting missingness were added in as covariates. Session attendance was recorded for all CR participants, while number of sessions was set at zero for those in the TAU group. Baseline covariates were available for all participants irrespective of group allocation.

2.6.2. Therapy components and outcome changes

We examined the association between CIRCuITS therapy components and changes in cognitive and functional outcomes using correlations. This was an exploratory analysis only considering data from CR group participants who achieved therapy completion (≥ 20 sessions), with findings aiming to guide future research. Given that some of the therapy components were not normally distributed, we used a non-parametric correlation coefficient (Spearman’s *rho*). Therapy components were correlated with outcome change scores (i.e., post-treatment minus baseline score). We also examined correlations between different therapy components to check for potential overlap. There were no missing data in this analysis.

3. Results

A total of 80 participants were randomly allocated to CR ($n = 40$) or TAU ($n = 40$). Baseline characteristics for the two groups are presented in Table 1. There were no missing data for participant characteristics or baseline measures and no significant baseline or medication change differences between groups. Post-treatment data were obtained for 93% and 88% of participants in the CR and TAU groups, respectively. No baseline predictors of missingness were identified.

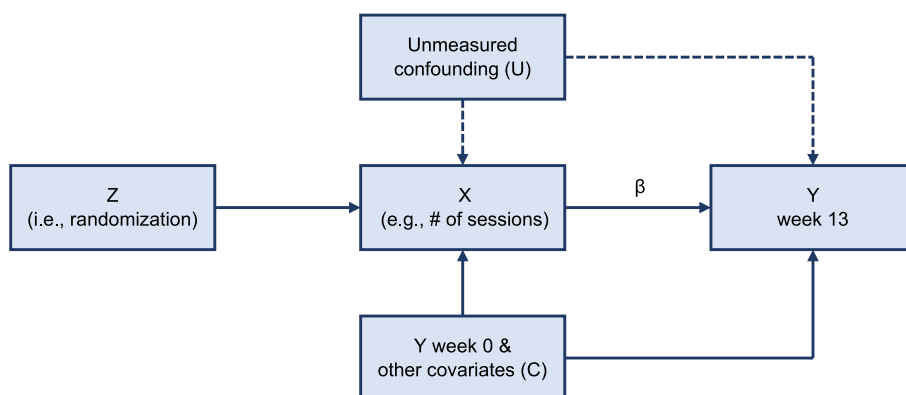


Fig. 1. Example of an instrumental variable model. In this model, the instrument (Z) is related to the outcome (Y) only through exposure to the treatment of interest (X). Both treatment exposure and outcome might be influenced by unmeasured factors (U). Estimating the effect of treatment exposure on outcome without considering these factors might obtain a biased estimate of this effect. The role of the instrument, which is independent of the confounding factors, is to minimize bias introduced by these confounders. This allows a more reliable estimation of the treatment exposure effect on the outcome (β). The model also controls for measured baseline factors (C).

Table 1
Baseline sample characteristics.

	CR group (n = 40)	TAU group (n = 40)	Total sample (N = 80)
<i>Sociodemographic</i>			
Age (years), mean (s.d.)	41.8 (13.9)	42.6 (11.8)	42.2 (12.8)
Gender, n (%)			
Women	30 (75.0)	27 (67.5)	57 (71.3)
Men	10 (25.0)	13 (32.5)	23 (28.7)
Education (years), mean (s.d.)	15.8 (2.7)	15.9 (2.1)	15.9 (2.1)
Premorbid IQ (TOPF), mean (s.d.)	108.9 (7.3)	109.4 (7.3)	109.2 (6.9)
<i>Clinical and illness-history</i>			
BD type, n (%)			
Type I	26 (65.0)	27 (67.5)	53 (66.3)
Type II	14 (35.0)	13 (32.5)	27 (33.7)
Diagnosis duration (years), mean (s.d.)	11.1 (10.2)	10.6 (7.4)	10.8 (8.9)
Number of hospitalizations, mean (s.d.)	2.5 (2.9)	2.4 (2.9)	2.4 (2.9)
History of psychosis, n (%)	23 (57.5)	26 (65.0)	49 (61.3)
HAMD, mean (s.d.)	4.1 (2.6)	3.6 (2.5)	3.8 (2.6)
YMRS, mean (s.d.)	2.4 (2.3)	2.2 (2.4)	2.3 (2.4)
Current euthymia (months), mean (s.d.)	13.6 (27.9)	13.9 (21.2)	13.8 (24.6)
<i>Psychotropic medications</i>			
Number of current medications, mean (s.d.)	2.3 (1.5)	2.6 (1.5)	2.4 (1.5)
Mood stabilizers, n (%)	27 (67.5)	33 (82.5)	60 (75.0)
Antipsychotics, n (%)	29 (72.5)	30 (75.0)	59 (73.8)
Antidepressants, n (%)	17 (42.5)	22 (55.0)	39 (48.8)
Anxiolytics, n (%)	7 (17.5)	6 (15.0)	13 (16.3)
Medication changes, n (%)	14 (35.0)	17 (42.5)	31 (38.8)
<i>Cognitive and functional outcomes</i>			
Global cognition composite, mean (s.d.)	-0.18 (0.63)	-0.27 (0.64)	-0.23 (0.63)
Hotel test, mean (s.d.)	-0.50 (1.07)	-0.40 (1.16)	-0.45 (1.11)
Verbal paired associates II, mean (s.d.)	-0.19 (1.12)	-0.52 (1.08)	-0.31 (1.12)
Digit-symbol coding, mean (s.d.)	-0.21 (0.70)	-0.29 (0.75)	-0.25 (0.72)
Digit span, mean (s.d.)	0.07 (0.66)	0.12 (0.78)	-0.09 (0.72)
FAST total score, mean (s.d.)	23.5 (10.1)	20.2 (9.5)	21.8 (9.8)
GAS total score, mean (s.d.)	33.9 (4.1)	33.9 (4.4)	33.9 (4.2)

Notes: BD: Bipolar Disorder; CR: Cognitive remediation; FAST: Functional Assessment Short Test; GAS: Goal Attainment Scale; HAMD: Hamilton Depression Rating Scale 17 items; TAU: Treatment-as-usual; TOPF: Test of Premorbid Functioning; YMRS: Young Mania Rating Scale.

3.1. Session attendance

Of the 40 participants randomized to CR, 32 (80%) achieved ≥ 20 sessions of CR, five (12.5%) completed less than 20, and three (7.5%) withdrew from therapy without attending any sessions. On average, all CR recipients completed 27.1 sessions (SD = 9.3, range: 5–48) over 12

weeks, with therapy completers attending 29.8 (SD = 6.2, range: 21–48) and non-completers attending 9.2 (SD = 4.9, range: 5–16). Therapy characteristics are presented in Table 2.

3.2. Effect of session attendance on outcomes

Number of sessions had a significant effect on all outcomes (Table 3). For each additional session per week over the course of the therapy, global cognitive performance increased by almost a quarter of an SD on average (0.22, 95% CI: 0.15 to 0.29). This effect was also observed for functional outcome scores in both the FAST (−2.11, 95% CI: −3.07 to −1.16) and the GAS (5.91, 95% CI: 4.25 to 7.57).

Achieving therapy completion (≥ 20 sessions) improved the effect of CR on global cognition by more than half an SD (0.56, 95% CI: 0.38 to 0.75). Therapy completion was also associated with an average reduction of 5.3 points on the FAST (95% CI: −7.72 to −2.96) and an average increase of 14.7 points on the GAS (95% CI: 10.5 to 18.8). Within the subgroup of CR participants who achieved therapy completion though, there were no significant associations between session attendance and post-treatment improvement in global cognition ($\rho = -0.09, p > 0.2$), the FAST ($\rho = 0.08, p > 0.2$) or the GAS ($\rho = 0.22, p > 0.2$).

3.3. Association between therapy components and outcomes

Inter-correlations between therapy components are presented in Supplementary Table 1. Massed practice and strategy use were strongly correlated (i.e., all $\rho > 0.7$). There were no associations between task or strategy components and average task performance or therapist contact.

None of the therapy components was associated with post-treatment changes in cognitive measures (Supplementary Table 2). Reduction of functional difficulties (FAST) was associated with the time per session spent in contact with the therapist ($\rho = -0.52, p = 0.02$) and goal attainment improvement (GAS) was correlated with the number of useful strategies employed per session ($\rho = 0.36, p = 0.04$).

4. Discussion

This is one of the first studies to examine how CR outcomes might be influenced by the characteristics of the therapeutic process for euthymic people with BD. We evaluated a “dose-response” relationship between session attendance and therapy outcomes and showed that higher number of sessions was associated with improved CR effects on

Table 2
Cognitive remediation therapy characteristics considered in the study.

Session attendance and therapy components	All CR recipients $n = 37$		Completers (≥ 20 sessions) $n = 32$	
	Mean (SD)	Min – Max	Mean (SD)	Min – Max
Number of sessions (total)	27.1 (9.3)	5–48	29.8 (6.2)	21–48
Sessions per week	2.3 (0.8)	0.3–4	2.5 (0.5)	1.8–4
Number of tasks (total)	283.5 (145.6)	52–617	306.4 (141.9)	72–617
Tasks per session	11.1 (5.4)	3.1–28.2	10.2 (4.4)	3.2–19.7
Number of strategies (total)	430.8 (230.5)	51–928	467.5 (223.7)	58–928
Strategies used per session	16.3 (7.2)	2.5–34	15.5 (6.9)	2.5–34
Useful strategies (total)	304.6 (191.3)	13–769	337.6 (183.1)	35–769
Useful strategies per session	11.3 (6.2)	1.1–29.7	11.2 (6.1)	1.5–29.7
Average task performance (%)	78.2 (5.6)	65.6–95.2	79.3 (4.6)	69.6–95.2
Therapist contact (minutes per session)	29.7 (7.2)	12–47	30.1 (6.1)	21–47

Notes: CR: Cognitive remediation.

cognitive and functional outcomes. Achieving therapy completion (≥ 20 sessions) had an even more pronounced effect on treatment outcomes. Implementation of CR active components were not associated with cognitive changes but spending more time in contact with the therapist and using more useful strategies were associated with improved functional outcomes.

4.1. Does session attendance modify the effects of CR?

Therapy completion rate in our study was comparable to previous trials offering CIRCuiTS to people with schizophrenia (Reeder et al., 2017), as well as trials testing individual or group-based CR in people with BD (Lewandowski et al., 2017; Ott et al., 2020). The average attendance of 2.5 sessions per week for therapy completers reflects a treatment intensity consistent with a recent, large-scale meta-analysis of CR trials in schizophrenia (Vita et al., 2021). Thus, the initial target “dose” of 40 sessions within 12 weeks may be difficult to achieve in the context of motivational challenges common in people with mental health difficulties (Saperstein and Medalia, 2016). Maintaining an attendance rate of at least two sessions per week is potentially more realistic and attainable for therapist-led CR programmes (Reeder et al., 2017).

Given that study participants did not receive any incentives or compensation to attend sessions and achieve therapy completion, it is likely that higher session attendance reflected greater intrinsic motivation or higher perceived utility of CR (Medalia and Richardson, 2005). These factors have been linked to better therapy engagement and improved treatment outcomes (Medalia and Saperstein, 2011). Similarly, we found that the number of sessions that participants attended during the 12-week intervention period influenced the effect of CR across outcomes, with more pronounced improvements for those receiving a greater “dose” of CR. This is consistent with findings from a randomized trial evaluating the effects of CIRCuiTS in people with schizophrenia (Reeder et al., 2017). A recent CR trial for people with BD did not find an association between cognitive changes and the amount of cognitive training received (Ott et al., 2020). This study only accounted for computer training when estimating the “dose” of CR which is an indication that practice quantity alone may not correspond to therapy quality (e.g., training combined with transfer activities facilitated by the therapist). Pending further replication, higher session attendance may provide the opportunity not only for more extensive cognitive training but also for greater utilization of other therapy aspects underlying treatment effects.

The most clinically relevant finding of this study is the role of therapy completion for treatment outcomes. Twenty hours is a threshold often recommended as the “minimum therapeutic dose” of CR (Bowie et al., 2019). Given the pronounced differences detected in CR effects between therapy completers and non-completers, our analysis suggests that this may be a clinically meaningful threshold to differentiate participants who engaged well and those who did not. Within the subgroup of CR completers though, the association of session attendance with post-treatment improvements was not significant across outcomes. This indicates that additional improvements by higher session attendance are likely to be negligible beyond this threshold. Although more empirical evidence is warranted to support this claim, 20 hourly sessions might represent the minimum “dosing” of therapy time required for the mechanisms of CR to affect the outcomes of interest.

4.2. Do CR therapy components correlate with outcome changes?

Therapy component inter-correlations were largely consistent with previous findings in people with schizophrenia (Cella and Wykes, 2017). The strong association of massed practice with strategy use is in line with the aim of our CR approach to integrate strategy implementation into task practice. In contrast, average task performance and therapist contact were not correlated to any other component metrics, which may

Table 3
Estimates for the effect of session attendance on cognitive and functional outcomes.

Outcomes Attendance measures	2SLS regression statistics				2SLS post-estimation tests	
	Estimate (B)	SE (B)	95% CI	P	First stage ^a (Wald)	Endogeneity ^b (Hausman)
Global cognition composite						
# of sessions per week	0.22	0.04	0.15 to 0.29	<0.001	Yes	No
Therapy completion	0.56	0.09	0.38 to 0.75	<0.001	Yes	No
Hotel test						
# of sessions per week	-0.11	0.03	-0.17 to -0.05	<0.001	Yes	Yes
Therapy completion	-0.28	0.08	-0.43 to -0.13	<0.001	Yes	Yes
Verbal paired associates II						
# of sessions per week	0.46	0.19	0.08 to 0.83	0.02	Yes	No
Therapy completion	1.16	0.49	0.20 to 2.12	0.02	Yes	No
Digit-symbol coding						
# of sessions per week	2.44	0.77	0.95 to 3.95	0.001	Yes	No
Therapy completion	6.26	1.95	2.44 to 10.1	0.001	Yes	No
Digit span						
# of sessions per week	0.88	0.29	0.30 to 1.46	0.003	Yes	No
Therapy completion	2.26	0.75	0.78 to 3.73	0.003	Yes	No
FAST total score						
# of sessions per week	-2.11	0.48	-3.07 to -1.16	<0.001	Yes	Yes
Therapy completion	-5.34	1.21	-7.72 to -2.96	0.004	Yes	Yes
GAS total score						
# of sessions per week	5.91	0.84	4.25 to 7.57	<0.001	Yes	No
Therapy completion	14.7	2.13	10.5 to 18.8	<0.001	Yes	No

Notes: 2SLS: Two-stage least squares regression analysis; FAST: Functional Assessment Short Test; GAS: Goal Attainment Scale. ^a Examines whether an instrumental variable is a strong predictor of the instrumented one (i.e., the strength of randomization as an instrumental variable); ^b Examines whether the instrumented variable is endogenous to the instrumental variable (i.e., the endogeneity of session attendance measures).

indicate that these components represent distinct aspects of CR.

Based on theory, we expected that higher levels of massed practice and more extensive strategy use would be associated with greater improvements in cognition, as previously shown for people with schizophrenia (Cella and Wykes, 2017). However, we did not observe that for people with BD, despite significant variations between participants in these components. Unlike cognition though, achievement of self-defined recovery goals was associated with more useful strategies during task practice. The identification and implementation of helpful strategies is likely more beneficial for patients to pursue their own goals than simply the amount of strategies they use. Emphasizing the development of such strategies during therapy may further improve the attainment of personal goals. In accordance with that, the association between functional improvement and amount of therapist contact supports the importance of contributions by the therapist in facilitating the transfer of cognitive gains to real-world situations (Bowie et al., 2019). Similar to session attendance, it is possible that these associations are explained by differences in baseline motivation levels or even motivational changes emerging over the course of the therapy, as previously shown for people with schizophrenia attending CR (Saperstein et al., 2020).

4.3. Strengths and limitations

This was one of the first studies to examine the modifying effect of session attendance, as well as the impact of achieving therapy completion, on CR outcomes for people with BD. This is important particularly because of the time intensity involved in this treatment. Our findings support a previously proposed “minimum therapeutic dose” for CR using a statistical approach (IV analysis) which accounts for participants either randomized to receive therapy or not. Conversely, associations between CR therapy components and outcome improvement were tested using correlation analysis, given that only one process variable could be examined in the IV analysis. These associations were explored independently of each other, so cannot determine whether therapy components share variance. However, we mitigated that by examining the inter-correlation among the CR components.

Session attendance was considered as an overall variable which does not account for potential differential effects of session types (i.e., in person, remote, independent) on treatment outcomes. Although we

considered the time spent in contact with the therapist during sessions, this does not necessarily reflect the quality of the therapeutic alliance which has been associated with improved adherence (Hargreaves et al., 2018) and outcomes in previous CR studies (Cella and Wykes, 2017; Huddy et al., 2012). As previously shown in patients receiving cognitive behavioural therapy for psychosis, therapeutic alliance can affect the relationship between session attendance and treatment outcomes, with more sessions being beneficial for those having good alliance and detrimental for those with poor alliance (Goldsmith et al., 2015). Considering therapeutic alliance would be important for future studies in order to evaluate the potential interaction between CR session attendance and alliance.

We did not consider participant characteristics (e.g., sociodemographic, clinical) and level of baseline cognitive impairment as factors potentially affecting session attendance and implementation of therapy components. This could provide further explanations of our findings and indicate a profile of those more likely to engage with CR (Hargreaves et al., 2018). We did not control for multiple testing in correlations between therapy components and outcome changes, hence the possibility of false positives cannot be excluded. The generalisability of our findings might be limited by the relatively small size of the study. Finally, this was a complete case analysis not accounting for missing data which, however, were limited (>10%) and without any predictors of missingness.

5. Conclusions

As well as supporting evidence for other psychological therapies and in other populations, this study strengthens the argument for a “minimum therapeutic dose” of CR for people with BD and highlights the importance of the therapist in addition to metacognitive skill development (e.g., identifying and selecting useful strategies) for improving functional outcomes. This is especially important in light of the numerous CR interventions that are entirely computerized or primarily focused on repetitive cognitive training to improve cognitive performance.

Author contributions

DT and MC conceived the study idea and planned this study. DT and RS were involved in data collection. DT carried out the analysis and prepared the first manuscript with support from RS and MC. MC, TW and AHY supervised the project. All authors provided feedback, contributed to the final draft of the paper and approved the manuscript.

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Ethics statement

The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008. All procedures involving human patients were approved by the City Road & Hampstead NHS Research Ethics Committee (reference 15/LO/1557).

Declaration of competing interest

AHY reports paid lectures and advisory boards for the following companies with drugs used in affective and related disorders: AstraZeneca (AZ), Eli Lilly, Lundbeck, Sunovion, Servier, LivaNova, Allegan, Bionomics, Sumitomo, Dainippon Pharma and Janssen; consultant to Johnson & Johnson and LivaNova; principal investigator on the Restore-Life VNS registry study funded by LivaNova, on ESKETINTRD3004 trial funded by Janssen, and the P-TRD trial funded by Compass; no shareholdings in pharmaceutical companies. RS reports a paid lecture from Lundbeck. TW is the creator of CIRCUITS cognitive remediation software. DT and MC report no conflict of interest for this work.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.jpsychores.2022.06.021>.

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