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Research Paper

Efficacy of cognitive training on cognition, symptoms and functioning: Impact of motivation and attendance

Joanna M. Fiszdon [a,b,*], Kaicheng Wang [c], Karen Lê [a], Lori Parente [a], Jimmy Choi [d]

[a] VA Connecticut Healthcare System, Psychology Service, 116B, 950 Campbell Ave, West Haven, CT 06516, United States of America
[b] Yale University School of Medicine, Department of Psychiatry, New Haven, CT 06511, United States of America
[c] Yale School of Public Health, New Haven, CT 06511, United States of America
[d] Olin Neuropsychiatry Research Center, The Institute of Living at Hartford Hospital, 200 Retreat Avenue, Hartford, CT 06106, United States of America

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ABSTRACT

While cognitive remediation therapy (CRT) and compensatory strategy training both have large literature bases supporting their efficacy on both proximal and distal outcomes, the research base on stand-alone cognitive training (CT) is smaller and less consistent, with little information about factors associated with better outcomes. In this study, we examined the efficacy of CT on training task, cognitive, symptom, and functional ability measures as well as the impact of motivational interviewing (MI), motivation level, and session attendance on treatment outcomes. Adults with psychotic spectrum disorders ($n = 114$) were randomized to MI or a sham control interview (CI), followed by 4 months of computerized CT. In whole sample analyses, participants improved on training tasks, cognitive performance, and psychiatric symptoms, but self-reported cognition, self-reported depression, and functional ability did not change. Compared to CI, MI was associated with greater reductions in self-reported depressive symptoms. Motivation level and session attendance did not significantly influence outcomes. Findings support the efficacy of CT on several key outcomes, and its simplicity may be advantageous in uptake in community clinics with limited staffing. The lack of functional gains underscores the need to incorporate treatment ingredients that promote generalization and real-world implementation of learned skills. We also speculate that engagement during course of training may be a better predictor of training success than baseline task-specific motivation.

1. Introduction

Significant cognitive impairments are present in an overwhelming majority of individuals diagnosed with schizophrenia and other psychotic spectrum disorders (Harvey et al., 2022), and have been shown to predict both progress in psychosocial rehabilitation (Kurtz et al., 2011) as well as overall functioning (Green et al., 2004). As such, cognitive impairments represent an important treatment target.

The three most common approaches to cognitive enhancement are compensatory strategy training, stand-alone cognitive training (CT), and cognitive remediation therapy (CRT). As the name suggests, compensatory strategy training is focused on teaching and implementing strategies to work around cognitive impairments in support of specific functional goals. CT narrowly focuses on repeated, drill-and-practice administration of cognitive exercises, most commonly delivered via computer. CRT subsumes CT but also includes hierarchical, repeated practice of cognitive exercises and is supplemented by trained therapist-guided facilitation, development of problem-solving strategies, and techniques to aid in generalization of skills to everyday function (Bowie et al., 2020). While all three of these approaches have shown some efficacy, there is significant heterogeneity in the types of outcomes assessed and in the efficacy of these approaches (Allott et al., 2020; Best and Bowie, 2017; Vita et al., 2021; Harvey et al., 2018). As far as CT, several large-scale trials have yielded inconsistent results (e.g. (Fisher et al., 2016, Mahncke et al., 2019), with expert consensus that CT does confer some cognitive benefits, though functional gains are more likely when CT is delivered in broader context of CRT (Harvey et al., 2018). Little is known about additional factors that may influence stand-alone CT efficacy, and additional work in these areas is much needed.

We previously reported (Fiszdon et al., 2022) on the efficacy of motivational interviewing (MI) in *improving attendance* in a full course of computerized CT and examined task specific motivation as a potential

* Corresponding author at: Psychology Service 116B, 950 Campbell Ave, VA Connecticut Healthcare System, West Haven, CT 06516, United States of America.
E-mail address: Joanna.fiszdon@yale.edu (J.M. Fiszdon).

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mechanism of action. In the current manuscript, we present secondary analyses from the above RCT, focusing on the *efficacy of the CT itself*. We report on the overall, full sample efficacy of CT on training task, cognitive, symptom, and functional ability measures. As the primary aims of the RCT were to examine the impact of enhancing motivation on session attendance, in the current analyses we also examine whether number of sessions attended and/or degree of motivation for the training impacted outcomes of interest.

2. Methods

2.1. Study design

In the parent RCT examining impact of motivational interviewing on cognitive training attendance, 114 participants were randomized to 2 sessions of motivational interviewing (MI, $n = 56$) focused on potential benefits of cognitive training or 2 sessions of a sham control interview (CI, $n = 58$) focused on providing feedback about learning styles. Both conditions were then followed by a 4-month active phase during which participants could attend up to 50 unpaid computerized cognitive training sessions. Booster MI/CI sessions were administered 1, 2, and 3 months into the cognitive training active phase. The study was approved by the local institutional review board and all participants provided written informed consent. Please refer to Fiszdon et al. (2022) for details of study methods.

2.2. Participants

Participants were 114 adults with DSM-5 (APA, 2013) psychotic spectrum disorders and evidence of cognitive impairment on baseline testing (.5SD or more below healthy control norms). Additional criteria for participation were: no recent hospitalizations or changes in medications, English as primary language, IQ ≥70, no evidence of medical or neurological illness known to impair brain function, not meeting criteria for substance use diagnosis in past 30 days, not currently enrolled in another treatment study targeting cognitive function, and no severe uncorrected auditory/visual impairment.

2.3. Cognitive training

Following baseline assessments and administration of the 2-session motivational or sham control interview, all participants were oriented to the computerized training program and its features by a research assistant and practiced several exercises. They were then invited to complete up to 50, unpaid, 45–60 min training sessions over 4 months. They were given the option of following the program-generated sequence of training tasks or self-selecting which tasks they wanted to practice during each session. A research assistant was available during all training sessions for assistance with any technical issues. For the computerized cognitive training, we purchased licenses for the commercially available BrainHQ program by Posit Science (www.brainhq.com). The program consists of exercises grouped into six different categories: attention, brain speed, people skills, navigation, intelligence, and memory. The training adapts difficulty based on participant performance, with more challenging versions of exercises only unlocked after the trainee has reached a threshold performance level on easier versions of those exercises. The training tasks are presented in a game-like format, with embedded performance rewards (i.e. gold stars), and trainees can monitor their progress and performance throughout the training.

2.4. Measures

Wide Range Achievement Test −3 (WRAT 3, (Wilkinson, 1993) and the 2-subtest version of the Wechsler Abbreviated Scale of Intelligence (WASI, (Wechsler, 1999)) were administered to assess premorbid and current intelligence. Six of the computerized cognitive training tasks, one from each category, were chosen a-priori as proximal measures of training success (Freeze Frame, Hawk Eye, Recognition, Optic Flow, Card Shark, and Memory Grid) and were administered at calibration level during the first CT session, and monthly through the end of the 4-month active phase. For four of these training tasks (Freeze Frame, Hawk Eye, Recognition, Optic Flow), log10-transformed speed in millisecond was the measured outcome, with lower scores representing faster, better performance. For the Card Shark and Memory Grid tasks, percentile correct was the outcome. An additional training task composite score was calculated as the mean of the percentile scores for each of the six tasks. Cognition was assessed at baseline, 2 months, and end of 4-month active phase, using the Matrics Consensus Cognitive Battery (MCCB) (Nuechterlein and Green, 2006), with the seven cognitive domains examined in post-hoc analyses. MCCB was also used at screening to confirm presence of cognitive impairment. Self-reported cognition was assessed using a modified, 3-subscale version of the Patient's Assessment of Own Functioning Inventory (PAOFI) (Richardson-Vejlgaard et al., 2009), assessing perceived performance impairments in areas of Memory, Language and Communication, and Executive Functions. Lower scores on this measure indicate greater perceived impairment. Self-report depression was assessed at baseline and 4 months with the Beck Depression Inventory-2 (BDI-2) (Beck et al., 1996)), with higher scores indicating greater depression. Self-reported task-specific motivation for the cognitive training was assessed using the Intrinsic Motivation Inventory for Schizophrenia Research (IMI-SR) (Choi et al., 2010b), with lower scores representing lower task-specific motivation. IMI was administered before and after the MI or CI sessions, before and after monthly booster sessions, and at 4 months. The clinician rated Positive and Negative Syndrome Scale (PANSS) (Kay et al., 1987) was administered at baseline and 4 months to capture positive, negative and general psychiatric symptoms. Higher scores represent greater psychiatric symptomatology. For post-hoc analyses, we used the 5-factor solution (Bell et al., 1994). Functional ability was assessed at baseline, 2 and 4 months using the Medication Management Ability Assessment (MMAA) (Patterson et al., 2002), with higher scores representing better performance. All assessments were administered by two research associates who were blind to randomization status and had been trained on all measures by the study PI (JMF), with ICC's for PANSS ratings >0.80.

2.5. Data analysis

We applied an intent-to-treat analysis including all participants who were randomized to MI or CI prior to the cognitive training. For the sample as a whole, we compared the differences between post-training (4-month) and baseline performance on training tasks, cognition (MCCB and PAOFI), symptoms (PANSS and BDI-2), and functional ability (MMAA) using univariate mixed-effect models. *P*-values were adjusted using the Bonferroni procedure for multiple comparisons.

Next, mixed-effect models with fixed effects for treatment (MI vs. CI condition) were built using all available repeated measurements on participants to assess the efficacy of the two conditions on outcomes of interest, while adjusting for time as a categorical variable, an interaction between treatment and time, and baseline scores of the measures. The average differences between MI vs. CI condition were estimated using least squares means.

To assess the impact of session attendance and post MI or CI interview motivation on CT efficacy, we performed a moderated mediation analysis (Hayes, 2017). We hypothesized that session attendance mediated the effect of treatment on the desired outcomes. Additionally, we explored how post-interview motivation moderates the relationship between treatment condition and session attendance. The effects were quantified as changes in the desired outcomes between the post-training (4-month) and baseline points, with associated 95 % confidence intervals (CIs) presented. Estimation of the 95 % CIs for indirect effects was calculated using 5000 bootstraps. All analyses were conducted as two-tailed tests with alpha set at 0.05 using SAS, version 9.4 (SAS Institute Inc., 2013). The moderated mediation analysis was performed with the *%process* macro. Visualization was done using R 4.3.0 (R Foundation for Statistical Computing, Austria) and *ggplot2* package.

3. Results

3.1. Efficacy of CT for sample as a whole

See Table 1 for baseline sample characteristics. Participants were on average 55 years old, with mean IQ of 95, mean MCCB composite t-score of 27, and mean PANSS score of 50. The sample was 80 % male, and 44 % white. Full sample analyses revealed significant pre-post training improvements on composite training task performance (mean [SD] 50.23[20.18] vs. 38.34 [19.84], $p < 0.001$), objective cognition (MCCB total: 37.70[6.93] vs. 36.08[6.26], $p = 0.004$), and psychiatric symptoms (PANSS total (38.66[24.19] vs. 50.02[11.33], p < 0.001).

There were no significant changes in self-reported cognition (PAOFI total (122.43[28.51] vs. 118.63[29.14], $p = 0.62$), self-reported depression (BDI-2 (15.43[12.19] vs. 15.61[12.28], $p > 0.99$), or functional ability (MMAA (31.05[14.69] vs. 29.02[8.05], $p = 0.79$) (Fig. 1).

In post-hoc analyses (Fig. 2), we found significant improvements on four of the individual training tasks: Freeze Frame, Hawk Eye, Optic Flow, and Card Shark.

As shown in Fig. 3, there were also significant improvements on two of the MCCB domains: Speed of Processing, and Visual Learning, along with significant improvements on all five PANSS factors.

3.2. Efficacy of CT examining potential contribution of MI administered prior to CT on training outcomes

In between group analyses (Table 2), the MI and CI conditions did not differ in amount of improvement on composite training task performance or individual training tasks. Similarly, there were no significant between-group differences in amount of improvement on the MCCB composite score, MMAA, PAOFI or PANSS total. There was a significantly greater decrease in self-reported depression (BDI-2) favoring the MI condition (13.07 vs. 17.62, $p = 0.01$).

Table 1
Baseline characteristics.

	Condition		
	MI (*N* = 56)	*CI* (*N* = 58)	*Total* (*N* = 114)
Age, Mean (SD), y	56.52 (10.40)	54.34 (12.74)	55.41 (11.65)
Gender, female	13 (23.21 %)	10 (17.24 %)	23 (20.18 %)
Race, White	24 (42.86 %)	26 (44.83 %)	50 (43.86 %)
Ethnicity, Hispanic	3 (5.36 %)	5 (8.62 %)	8 (7.02 %)
GAF, Mean (SD)	42.43 (7.14)	45.16 (11.51)	43.49 (9.07)
N (N Missing)	30 (26)	19 (39)	49 (65)
WRAT, Mean (SD)	47.61 (8.31)	47.10 (7.90)	47.35 (8.07)
WASI, Mean (SD)	94.30 (13.24)	94.95 (12.92)	94.63 (13.02)
PANSS, total, Mean (SD)	49.18 (10.48)	50.83 (12.13)	50.02 (11.33)
BDI-2, Mean (SD)	15.14 (13.32)	16.05 (11.30)	15.61 (12.28)
MMAA, Mean (SD)	30.06 (6.18)	27.99 (9.48)	29.02 (8.05)
N (N Missing)	56 (0)	57 (1)	113 (1)
MCCB, composite t, Mean (SD)	27.77 (9.10)	26.33 (10.61)	27.04 (9.88)
PAOFI, total, Mean (SD)	120.31 (30.80)	117.03 (27.65)	118.63 (29.14)
N (N Missing)	55 (1)	58 (0)	113 (1)
Training Task Performance, Mean (SD)			
N (N Missing)	35 (21)	36 (22)	71 (43)

3.3. Impact of motivation and session attendance on outcomes of interest

Table 3 shows results from the moderated mediation model. The direct effect of MI/CI condition on BDI-2 (point estimation [95 % CI]: −5.01 [−8.52, −1.50]) was significant after controlling for baseline BDI-2. Otherwise, we did not observe significant direct effects on MMAA, MCCB, PANSS or PAOFI, nor significant indirect effects of MI/CI condition on BDI-2, MMAA, MCCB, PANSS or PAOFI through session attendance. The estimated indirect effects (mediation) and bootstrapped 95 % CIs on composite training task performance (3.09 [−1.34, 8.02]) and individual training tasks through session attendance were not significant. We did not observe any significant moderation on session attendance for any outcomes of interest.

4. Discussion

In the current manuscript, we reported on the efficacy of CT and examined potential impact of session attendance and task-specific motivation on outcomes of interest. We found that for the sample as a whole, there were significant improvements on the training tasks, objectively measured cognition, and a broad index of psychiatric symptoms. There were no improvements on self-reported cognition, self-reported depression, or functional ability. Probing for differential efficacy in individuals who received MI vs. CI prior to cognitive training, MI was associated with greater reductions in self-reported symptoms of depression. Neither post-interview motivation nor session attendance significantly impacted any outcomes.

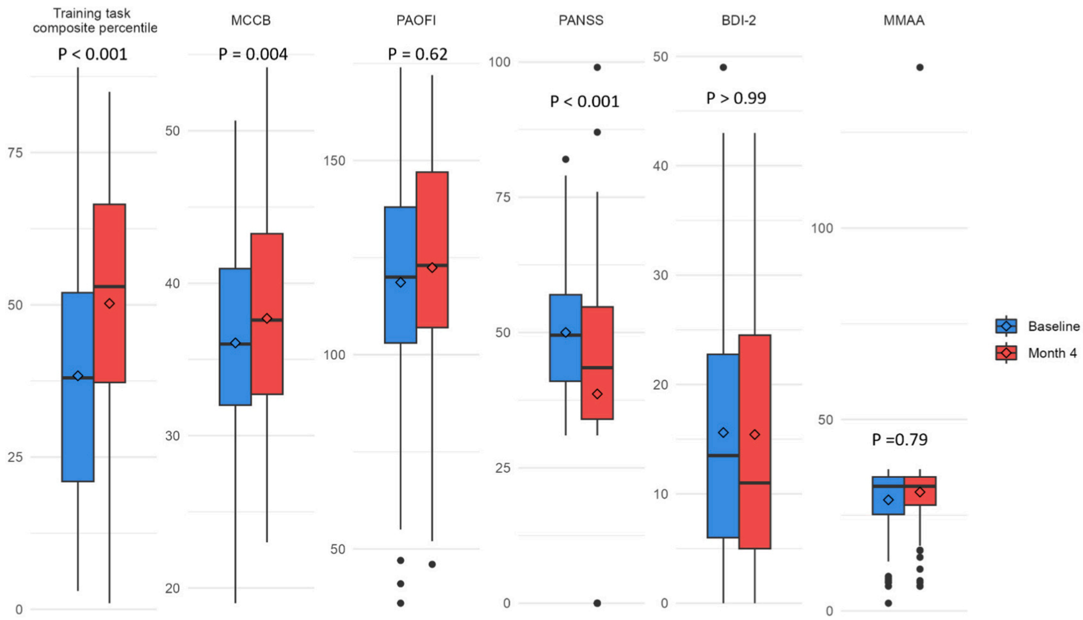
Our findings support the efficacy of CT on proximal training task, cognitive, and psychiatric symptom outcomes. While our findings differ from Mahncke et al. (2019) who examined the efficacy of the same computerized cognitive training program, variability in results might be due to potentially better ‘target engagement’, as indexed by improvements on the cognitive tasks, or reaching some threshold of training task performance. While Mahncke and colleagues also suggested that the older age of their sample may have attenuated any effects of CT on cognition, the average age of our sample was greater than that in the Mahncke and colleagues' trial, suggesting this variable alone is not sufficient to negate positive outcomes of CT.

CT was associated with improvements in objective but not subjective cognition. This is in line with several other studies suggesting a lack of relationship between objective and subjective or self-report measures in not only people with schizophrenia (Elliott and Fiszdon, 2014; Poletti et al., 2012), but also in other populations (Keefe et al., 2022; Mahncke et al., 2021), and highlights the importance of carefully considering what method of measurement is most in line with the construct investigators wish to capture.

In line with expert consensus (Harvey et al., 2018), we did not find CT to have a significant impact on functional ability. As has been suggested previously, in order to observe functional gains CT may need to be delivered within the more comprehensive CRT, and/or the training may need to be incorporated into broader skill training or psychosocial treatment programs (Bowie et al., 2012; Harvey et al., 2018). Modifications to the computerized CT itself to promote transfer of skills and generalization may also be an avenue to pursue.

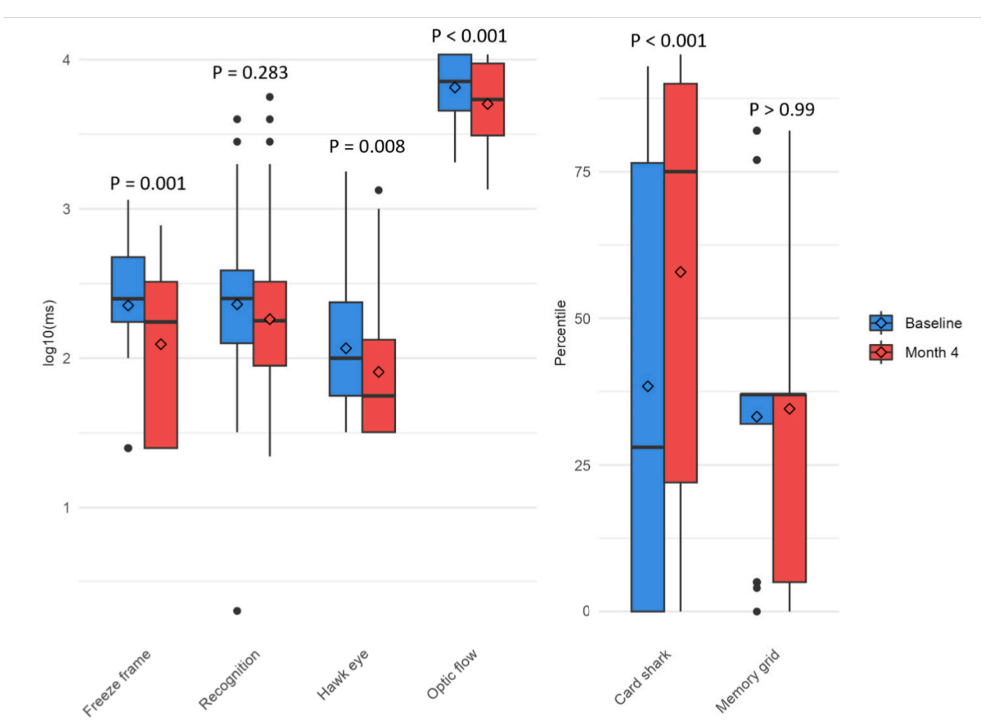
Though our finding of improvements in psychiatric symptoms was somewhat encouraging albeit unexpected, we hesitate to draw any strong conclusions about this given that with our study design we cannot disentangle whether improvements were due to specific or non-specific effects, with the latter presumably related to the added structure of attending training sessions and potential attendant social interactions. We would however like to note that in our prior work, we have observed that a number of variables associated with cognitive change are not specific to CT training itself (Fiszdon et al., 2020).

Also somewhat unexpected is our finding of greater reductions in depression in the MI than in the CI condition. The main difference between the two conditions was the nature and content of the pre-training



Differences between month 4 and baseline were compared with univariate mixed-effect models using all available data. P values were corrected using Bonferroni method for multiple comparison.

Fig. 1. Changes in cognitive training task, objective and subjective cognition, symptoms, and functional ability measures between baseline and month 4. Differences between month 4 and baseline were compared with univariate mixed-effect models using all available data. *P* values were corrected using Bonferroni method for multiple comparison.



Differences between month 4 and baseline were compared with univariate mixed-effect models using all available data. P values were corrected using Bonferroni method for multiple comparison.

Fig. 2. Changes in training task performance between baseline and month 4.
Differences between month 4 and baseline were compared with univariate mixed-effect models using all available data. *P* values were corrected using Bonferroni method for multiple comparison.

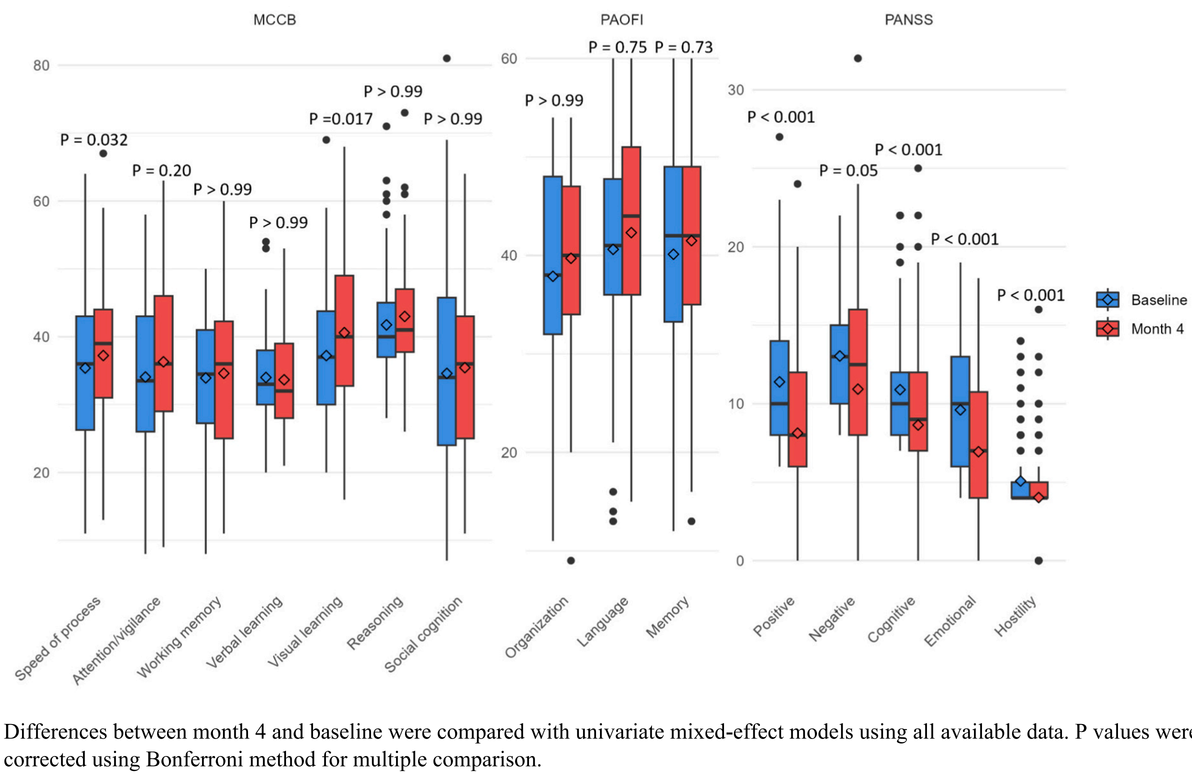


Fig. 3. Changes in MCCB subdomains, PAOFI subscales, and PANSS factors between baseline and month 4.
Differences between month 4 and baseline were compared with univariate mixed-effect models using all available data. *P* values were corrected using Bonferroni method for multiple comparison.

Table 2
Least squares mean estimation of the differences between MI and CI.

	Condition		Diff (95 % CI)	P value[†]
	MI, mean (SE)	CI, mean (SE)		
BDI-2	13.07 (1.23)	17.62 (1.19)	−4.55 (−7.93, −1.17)	0.010
PANSS	36.57 (3.14)	40.67 (3.09)	−4.10 (−12.75, 4.55)	0.355
PAOFI	122.45 (2.37)	119.04 (2.3)	3.42 (−3.1, 9.93)	0.307
MMAA	31.53 (1.27)	30.04 (1.26)	1.48 (−2.03, 5.00)	0.411
MCCB	37.25 (0.55)	37.63 (0.54)	−0.38 (−1.89, 1.13)	0.625
Training Task Performance				
Training Task Composite	50.20 (2.18)	46.84 (2.22)	3.35 (−2.74, 9.44)	0.285
Freeze Frame, $\log_{10}$(ms)	2.15 (0.06)	2.23 (0.06)	−0.08 (−0.24, 0.08)	0.325
Recognition, $\log_{10}$(ms)	2.34 (0.06)	2.33 (0.06)	0.01 (−0.16, 0.17)	0.934
Hawk eye, $\log_{10}$(ms)	1.81 (0.05)	1.91 (0.05)	−0.10 (−0.23, 0.03)	0.142
Optic flow, $\log_{10}$(ms)	3.71 (0.03)	3.74 (0.03)	−0.03 (−0.10, 0.04)	0.444
Card shark, percentile	57.02 (4.84)	52.54 (4.92)	4.48 (−9.06, 18.02)	0.519
Memory grid, percentile	35.90 (3.18)	37.19 (3.20)	−1.29 (−10.21, 7.62)	0.777

[†] Univariate mixed-effect model adjusted for categorical time, interaction between condition and time, and baseline value.

and booster interview sessions. While the MI interviews focused on supporting people as they progressed through the training—revisiting and reinforcing their commitment to improving cognitive function and working collaboratively to address potential barriers to engaging in the training–the CI interviews were more expository, focused on non-evaluative summaries of learning styles and CT task completion rates. Though purely conjecture, it might be the case that the more person-centered, collaborative approach associated with MI led participants to feel more connected and cared for, hence reducing feelings of isolation and depression.

Neither session attendance alone nor in combination with task-specific motivation impacted the degree of training task, cognitive, or symptom improvements. A robust literature does exist on the importance of motivation during the course of learning and the value of incorporating motivational techniques into treatment (Medalia and Saperstein, 2011; Choi and Medalia, 2010). However the relationship between motivation and learning is complex, and several recent studies suggest that it may not simply be motivation level at the beginning of training but instead the degree of motivation and/or engagement during the course of the training itself that impact treatment efficacy. For example, Bryce and colleagues (Bryce et al., 2018) failed to find a relationship between baseline motivation and cognitive improvement. In line with this, both Saperstein and colleagues (Saperstein et al., 2020) as well as Best and colleagues (Best et al., 2020) also did not find a relationship between pre-training motivation and cognitive improvement, though one emerged when they examined end of training motivation levels or treatment engagement as indexed by homework completion, respectively. Relatedly, Harvey and colleagues (Harvey et al., 2020), reported that training engagement, as indexed by training levels achieved per day trained, correlated significantly with cognitive improvements. Furthermore, motivation for learning is greatly impacted by self-efficacy for the task, and Choi and colleagues (Choi et al., 2010a) found perceived competency to be a more robust contributor to better

Table 3
Impact of motivation (moderator) and session attendance (mediator) on outcomes of interest.

	Direct effect from MI vs. CI, Coef. (95 % CI)	Indirect effect through session attendance Coef. (95 % CI)	Moderation of session attendance*motivation, Coef. (95 % CI)
BDI-2	−5.01 (−8.52, −1.50)	0.14 (−0.97, 1.30)	0.06 (−0.17, 0.30)
PANSS	−6.79 (−15.42, 1.84)	1.60 (−0.74, 3.99)	0.05 (−0.15, 0.24)
PAOFI	6.43 (−3.66, 16.52)	−0.35 (−2.35, 1.88)	0.03 (−0.20, 0.26)
MMAA	4.28 (−2.15, 10.70)	0.09 (−0.31, 0.68)	0.08 (−0.16, 0.33)
MCCB	−1.19 (−3.03, 0.65)	0.31 (−0.25, 0.91)	0.04 (−0.22, 0.31)
Training task performance			
Training Task Composite	2.52 (−4.25, 9.29)	3.09 (−1.34, 8.02)	0.04 (−0.33, 0.41)
Freeze frame, $\log_{10}$(ms)	−0.07 (−0.33, 0.18)	−0.06 (−0.17, 0.02)	0.11 (−0.25, 0.48)
Recognition, $\log_{10}$(ms)	0.10 (−0.11, 0.30)	−0.06 (−0.17, 0.03)	0.07 (−0.30, 0.44)
Hawk eye, $\log_{10}$(ms)	−0.09 (−0.27, 0.09)	−0.04 (−0.13, 0.03)	0.03 (−0.34, 0.39)
Optic flow, $\log_{10}$(ms)	0.00 (−0.09, 0.10)	−0.03 (−0.09, 0.01)	0.05 (−0.31, 0.43)
Card shark, percentile	9.08 (−6.64, 24.79)	2.87 (−0.85, 9.35)	0.06 (−0.31, 0.43)
Memory grid, percentile	−2.66 (−16.75, 11.43)	−0.09 (−3.19, 2.96)	0.04 (−0.32, 0.41)

CT outcomes than intrinsic motivation. In fact, perceived self-competency is central to both beginning and sustaining engagement in challenging tasks in various patient populations (Ryan et al., 1995; Williams et al., 1998), and serves as a basic psychological need that ushers in and prolongs motivation during tasks requiring an extended degree of effort and time (Levesque et al., 2007). The in-depth literature on defeatist beliefs and psychosocial treatment outcome in schizophrenia bears out this robust relationship, regardless of motivation (Granholm et al., 2018).

With regard to the impact of session attendance on cognitive improvements, several prior trials have reported that higher treatment dose is associated with better cognitive outcomes (Fisher et al., 2010; Buonocore et al., 2017; Seccomandi et al., 2022). Recent reviews of research in this area however failed to find consistent associations between these variables (Allott et al., 2020; Reser, 2019). Interestingly, both of these recent reviews concluded that progress made on training tasks during the *course* of the training was associated with cognitive gains, pointing again to the importance of motivation and engagement during the training itself.

Study limitations include very limited functional assessment and a lack of a treatment as usual group, the latter making it impossible to disentangle training-specific versus non-specific improvements. Additionally, while the cognitive training provided lacked many of the components of the more comprehensive CRT approach, we did incorporate a research assistant who provided general orientation to the training program and was available to address any technical issues, and also included monthly MI/CI booster sessions. These additional interactions between participants and staff and the perceived support may have led to better outcomes than if participants had only been offered an online training with no instruction or assistance. It should however be pointed out that another study utilizing the same cognitive training package and that also provided orientation to the training and a research assistant for additional support failed to find significant improvements (Mahncke et al., 2019).

In spite of these limitations, our results still provide a meaningful contribution to the literature on cognitive enhancement in schizophrenia. Our study does suggest some value in offering CT even though it lacks the more comprehensive approach of CRT, as this simplified approach may be more scalable to community clinics with limited staffing resources. With that said however, future trials of CT must show improvements in the most important outcome—everyday functioning.

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CRediT authorship contribution statement

Joanna M. Fiszdon: Writing – review & editing, Writing – original draft, Supervision, Methodology, Funding acquisition, Conceptualization. **Kaicheng Wang:** Writing – original draft, Visualization, Formal analysis, Data curation. **Karen Lê:** Writing – review & editing, Writing – original draft. **Lori Parente:** Writing – review & editing, Project administration, Methodology. **Jimmy Choi:** Writing – original draft, Methodology, Conceptualization.

Declaration of competing interest

All authors declare that they have no conflicts to disclose.

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