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Brief executive function training for individuals with severe mental illness: Effects on EEG synchronization and executive functioning

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ABSTRACT

Background: Executive Functioning (EF) is an important factor for community functioning for people with severe mental illness. Cognitive remediation programs often improve EF, but do so by using multiple therapeutic techniques. Little is known regarding how individual treatment elements promote cognitive improvement. Oscillatory brain activity is a potential neurophysiological mechanism that may change as a result of targeted training on computerized exercises. The current study aimed to examine the effects of a brief EF training program on EEG and neurocognitive measures.

Methods: 25 people with severe mental illness were randomized to either 2 weeks of computerized EF training or control training. Training consisted of 1 h training sessions 3 times per week and 40 min of daily home training. Assessments examined EEG theta and alpha band oscillatory power during EF tasks and neurocognitive measures of EF.

Results: EF training resulted in greater frontal theta power and reduced posterior alpha power during computerized EF tasks than control training. Power in the alpha frequency band over frontal electrode sites did not significantly differ between the two groups as a result of training. Additionally, participants in the EF training experienced significantly greater improvement in EF ability as measured by neurocognitive tests than the control condition.

Conclusions: Two weeks of EF training is sufficient to produce neurophysiological and neurocognitive change. Frontal theta power and posterior alpha power may be important neurophysiological markers to consider in cognitive remediation studies, and the addition of a brief executive function training procedure to other psychosocial interventions is worth examining.

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1. Introduction

Cognitive impairment is a persistent and functionally debilitating feature of psychotic disorders (Bowie et al., 2010) that is present before the onset of illness (Lencz et al., 2006), is largely unrelated to positive and negative symptoms (Keefe et al., 2006), and has limited response to pharmacotherapy (Keefe et al., 1999). Impairments span broad domains of cognitive abilities (Heinrichs and Zakzanis, 1998), and are stronger predictors of functional outcomes than either positive or negative symptoms (Bowie et al., 2006). Cognitive remediation (CR) treatments were developed as a behavioural intervention designed to specifically target cognitive impairment. Two recent meta-analyses have suggested that cognitive remediation is efficacious, improving cognition with moderate effect sizes (McGurk et al., 2007; Wykes et al., 2011).

Many CR programs are beginning to incorporate more intensive psychotherapeutic elements (Bowie and Medalia, 2016) and generally employ some combination of three primary components: training exercises, strategy monitoring, and generalization (for a review of approaches to cognitive remediation see Best and Bowie, 2017). Training exercises are often computerized, and designed to train specific cognitive abilities by titrating difficulty levels to provide a level of challenge appropriate to each individual. Strategy monitoring involves a therapist facilitating metacognitive awareness of the strategies one is using during the training exercises and development of novel strategies. Generalization involves different therapist-led techniques (e.g. discussions, role-play scenarios) to support individuals in using the skills and strategies developed in therapy during their everyday lives. Presumably, each of these components should act at neurophysiological, neurocognitive, and community functioning levels of analysis, however, the primary target of each component can be considered to directly map onto one of these levels. Training exercises should remediate an underlying neurophysiological impairment through repetitive activation and training of neural circuits known to subserve cognitive functions, strategy monitoring should help people maximally utilize their neurophysiological ability on cognitive tasks, and generalization should facilitate the use of cognitive abilities in the community to improve community functioning.

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Although the evidence for CR programs is generally convincing, evidence for individual components is limited. When computerized training is administered alone and targets perceptual abilities, neurophysiological change occurs in the mismatch negativity, an EEG component associated with perception of auditory stimuli (Fisher et al., 2009). However, independent training of higher-order cognitive abilities has not been examined at the neurophysiological level. Memory and executive functions, particularly, are among the most functionally relevant cognitive domains (Green, 1996; Velligan et al., 2000) and many CR programs include at least some element of memory or executive function training, however, evidence for using exercises that directly target these abilities is lacking. Most programs that utilize computerized training of higher-order cognitive abilities, either also include a psychotherapeutic element (Eack et al., 2010), or do not examine neurophysiological change (Rodewald et al., 2011). Thus, it is unclear whether computerized training of executive function abilities alone is sufficient to produce neurophysiological and neurocognitive improvement. Additionally, the dose required to produce improvements from CR programs is still unknown. Computerized training programs that target perceptual abilities have used 50 h of laboratory based training (e.g. Fisher et al., 2009), however, it is unknown whether briefer interventions will also produce observable results.

Oscillations in the alpha and theta frequency bands within the human electroencephalogram (EEG) have been associated with attentional and working memory abilities respectively (Klimesch, 1999). The alpha frequency band, generally observed between 8 and 12 Hz with a peak at approximately 10 Hz, demonstrates greatest synchronization (power) during a resting state over posterior electrode sites and is thought to represent activation of the default mode network (Knyazev et al., 2011). Oscillations within the alpha frequency band desynchronize (reduced power) with greater engagement of neural resources. Task-related alpha desynchronization over posterior electrode sites has been associated with attentional engagement in a task (Rowland et al., 1985), whereas alpha desynchronization over frontal electrode sites may be associated with engagement of higher level cognitive resources. Slower oscillations within the theta frequency band over the frontal cortex, generally observed between 4 and 8 Hz, are associated with engagement of neural resources involved in working memory/executive function processes, and greater synchronization (power) within the theta frequency during a working memory task is associated with better performance (Onton et al., 2005). While theta synchronization is often examined in working memory tasks, it has also been found to be associated with other executive functions such as arithmetic strategy use (De Smedt et al., 2009) and complex nonverbal problem solving (Doppelmayr et al., 2005). If targeted computerized training of executive functioning produces neurophysiological change then increased task-related synchronization of the theta frequency band over frontal electrode sites and reduced task-related synchronization of the alpha frequency band over both frontal and posterior electrode sites would be expected.

An additional limitation of many CR studies is the inclusion of either waitlist or computer game control conditions which only provide a control for non-specific temporal or computer-use effects. The current study aimed to examine the effects of computerized training of executive functioning using a true sham condition, with two primary aims: (1) Determine whether independent computerized training of executive functions improves task-related EEG theta synchronization and alpha desynchronization, and (2) Examine whether working memory and executive functioning improve after independent computerized training.

2. Method

2.1. Participants

Clinical participants who met study entry criteria were referred from community outpatient services in Kingston, Ontario for the current trial (ClinicalTrials.gov Identifier: NCT02168166). Inclusion criteria included a psychiatric diagnosis made by the referring clinician of schizophrenia, schizoaffective disorder, bipolar disorder with psychotic features, or major depressive disorder with psychotic features, and age between 18 and 65 years. Exclusion criteria included comorbid active substance abuse or substance dependence, neurological conditions, or cognitive enhancing treatments within the past six months. Participants were reimbursed $40 for each assessment, but no financial reimbursement was provided for attending training sessions or completing home practice. A CONSORT diagram of enrollment, allocation, and analyses is shown in Fig. 1. Healthy comparison subjects were recruited through community advertisements, and were required to have never met criteria for a mental illness, substance abuse, or neurological condition. Healthy comparison subjects served to provide a normative comparison group for the EEG and neurocognitive measures, therefore they only attended one assessment session and did not complete training. The assessment administered to healthy comparison subjects was the same as that administered to clinical participants. Demographic characteristics of the sample are presented in Table 1. Groups differed on years of education, population group composition, and current and highest occupation level.

2.2. Measures

2.2.1. Cognition

Cognitive performance was assessed using a brief cognitive battery focusing on working memory and executive functioning. The following measures were included: Trail-Making Test Parts A and B (TMT-A and TMT-B; Reitan & Wolfson, 1993); Letter-Number Sequencing (LNS) and the Spatial Span Test (WMS-SS) from the MATRICS Consensus Cognitive Battery (Nuechterlein & Green, 2006), and the Tower of London from the Brief Assessment of Cognition in Schizophrenia (ToL; Keefe et al., 2004). T-scores were calculated using normative data stratified by age from the test manuals. A ratio of TMT-B to TMT-A was used as a more valid measure of set-shifting ability (Martin et al., 2003), and t-scores were calculated using normative data from Drane et al. (2002).

2.2.2. EEG tasks

Continuous EEG was recorded during alternating two minute blocks of eyes open and eyes closed resting state for a total of four minutes each. To limit the number of analyses, eyes open and eyes closed resting states were averaged to produce a single resting state recording. Participants then completed two computerized cognitive training exercises (Displaced Characters and Basketball in New York, from sbtpro.com); these exercises were not used during the training sessions. Each exercise had a low and high cognitive load version of the task that participants completed for four minutes each. In Displaced Characters, participants are presented with symbols in different positions on the screen for 8 s. Then the symbols disappear and are immediately replaced by a new set of symbols in different positions. Participants must identify which symbols in the new set were not present in the original set that was memorized. Four symbols were presented per set in the low cognitive load version and 8 symbols were presented per set in the high cognitive load version. Basketball in New York requires participants to mentally rearrange three coloured balls in three basketball nets to match a template and indicate how many moves it would take. In the low cognitive load version of the task, trials required an average of 2.5 moves to solve, and in the high cognitive load version of the task, trials required an average of 4.5 moves to solve. There was no time limit for each trial. For all tasks, participants were engaged in the exercise for the duration of the four minutes, with screens such as performance feedback being skipped. Thus, although participants were engaged in multiple different executive processes during the four minutes, they were continually engaged during that time-period.

2.2.3. EEG recording and analysis

EEG was recorded using a HydroCel 64-channel Geodesic Sensor Net from Electrical Geodesics Incorporated at a sampling rate of 250 samples/s. Impedances for each electrode were kept below 30 kΩ upon

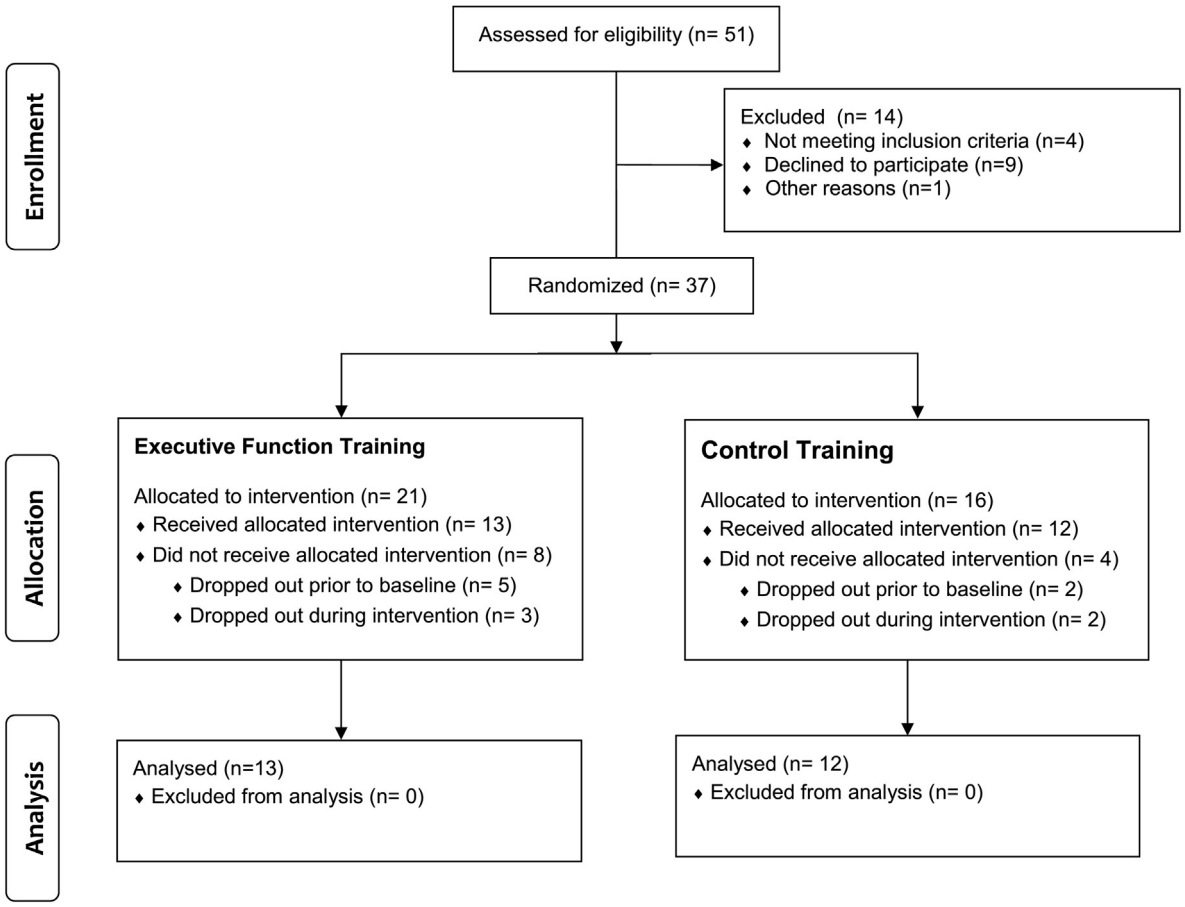

Fig. 1. CONSORT diagram of enrollment in working memory training and control training.

commencement of the study and were not allowed to rise about 70 kΩ throughout the study. EEG data were processed offline using EEGLab (Delorme & Makeig, 2004) and Fully Automated Statistical Thresholding for EEG Artifact Rejection toolbox (FASTER; Nolan et al., 2010). A high pass filter was applied at 0.1 Hz and a low pass filter was applied at 30 Hz. Data were then visually inspected and sections containing movement artifacts or signal discontinuities were removed. The data were then cleaned using FASTER, which uses independent component analysis (ICA) to identify and remove artifactual components from the EEG signal. ICA is effective at correcting for non-neuronal artifacts (Jung et al., 2000),

Table 1
Demographic characteristics of the participant sample by condition and the healthy comparison sample.

	EF training (n = 13)	Control training (n = 12)	Healthy comparison (n = 25)	Test statistic	p	Significant post-hoc comparisons
Age M (SD)	33.18 (11.72)	42.36 (16.18)	35.92 (13.57)	$F = 1.78$	0.178	
Current sex (male:female)	11:2	8:4	20:5	$\chi^2 = 1.28$	0.525	
Years of education M (SD)	14.44 (3.41)	13.54 (1.98)	16.28 (2.99)	$F = 4.46$	**0.016**	HC > EFT = CT
Population group (% Caucasian)	84.6%	100%	72.7%	$\chi^2 = 7.23$	**0.027**	HC > EFT = CT[a]
Independent living (%)	46.2%	50.0%	72.0%	$\chi^2 = 3.03$	0.219	
Hollingshead current occupation level[b] M (SD)	7.69 (0.60)	7.33 (0.98)	3.73 (2.31)	$F = 31.21$	<**0.001**	HC > EFT = CT
Hollingshead highest occupation level M (SD)	5.64 (1.86)	5.15 (1.99)	3.10 (1.92)	$F = 8.49$	**0.001**	HC > EFT = CT
Diagnosis (%)						
Schizophrenia	76.9%	58.3%	-	$\chi^2 = 2.49$	0.287	
Bipolar	23.1%	25.0%	-			
MDD	0.0%	16.7%	-			
Age at first hospitalization M (SD)	23.69 (6.01)	29.60 (13.18)	–	$F = 2.07$	0.165	
Months since last hospitalization M (SD)	95.23 (87.49)	85.50 (80.76)	–	$F = 0.075$	0.787	

Bolded values indicate $p < 0.05$.
[a] Healthy comparison subjects had a larger non-white ethnic background than either of the clinical groups.
[b] Smaller values indicate higher occupation level.

and FASTER has demonstrated good reliability with manual and semi-automatic cleaning procedures (Nolan et al., 2010). After being processed with FASTER, data was visually inspected again to ensure the algorithm was successful at removing artifacts, and re-referenced to an average reference.

Power spectral density was calculated using EEGLAB's spectopo function (Delorme & Makeig, 2004), using Welch's method. Each recording was segmented into 1 s epochs with 50% overlap and Hamming-windowed prior to calculation of the power spectral density. Theta power was examined in the frequency window of 4–8 Hz and alpha power was examined in the frequency window of 8–12 Hz.

Theta power during task engagement tends to be greatest over anterior electrode sites (Jensen and Tesche, 2002), whereas, alpha suppression tends to be greatest over posterior electrode sites (Sauseng et al., 2005; Kelly et al., 2006). Therefore, theta power was examined over the average of 10 anterior electrodes corresponding to Fz, F3, and F4 from the 10–20 system. Alpha power was examined over the average of 6 posterior electrodes corresponding to O1, and O2 from the 10–20 system. Selected electrode sites are depicted in Fig. 2.

2.3. Treatment

Participants were randomized to two weeks of either an executive function (EF) training condition or a control condition. In both conditions, participants attended three one-hour sessions facilitated by a research assistant, who trained participants to login to the exercises and helped with any technical problems, per week. Facilitators did not have a psychotherapeutic role; that is, the treatment did not include components of CR such as strategy monitoring or generalization. Participants were trained how to use the computerized exercises at home and were asked to practice the exercises at home for 40 min each day. Participants were blind regarding which treatment condition they were assigned to and were told that they would be receiving one of two forms of cognitive training. Following the study, participants were debriefed and given access to the other set of exercises for two weeks if they wished to practice them at home.

2.3.1. Executive function training

In the EF training, participants were trained on four computerized exercises that specifically target working memory and executive functions from the program Scientific Brain Training Pro (sbtpro.com). Find Your Way is a spatial working memory task requiring participants to observe a series of rocks that light up, and then to select the rocks either in the same order or in the reverse order. Secret Files requires participants to identify the missing label on filing cabinets, maintain this information in memory, and accurately sort file folders into the cabinets within a time limit. Hurray for Change is a set-shifting task, requiring participants to select items in different sets in alternating order (for example two sets of alphabetical words in different coloured circles). Towers of Hanoi requires participants to manipulate virtual rings on three pegs to make

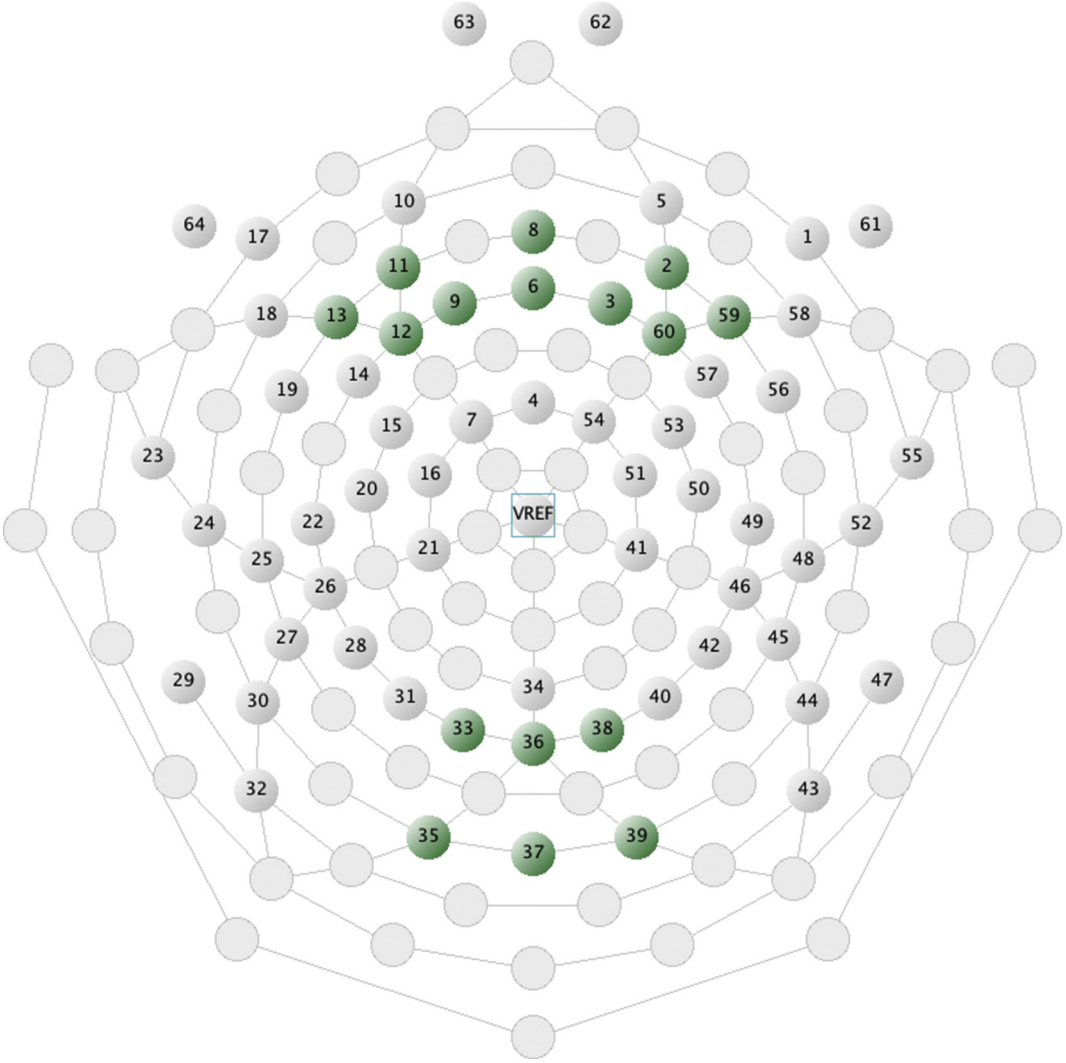

Fig. 2. Frontal and posterior electrode sites selected for analysis from the 64-channel electrode cap.

them match a template in the fewest possible moves within a time limit. These exercises use titrated increases in difficulty to continually challenge participants' cognitive abilities as they improve at the task, and to reward continued effort and improvement with increases in level.

2.3.2. Control training

In the sham intervention, participants were also trained on four computerized exercises from Scientific Brain Training Pro; however, the exercises did not target working memory or executive function. Bird Songs requires participants to learn bird songs and then identify the song. Sound Check requires participants to listen to a series of tones and then answer questions regarding length, loudness, and pitch of the tones. Entangled Figures requires participants to examine two line drawings that have been combined into one, and identify the individual component drawings. Turn Around and Around requires participants to view two geometric shapes at different orientations and decide whether they are identical or different shapes. Of critical importance to the control intervention is the fact that the titrated increase in difficulty was removed from these exercises. The task did not objectively change in difficulty, however, superficial aspects such as the types of figures/sounds, or the number of trials before a break were manipulated to give the illusion of increasing difficulty. Participants were shown an increase in level as they progressed in the training, but the task itself did not actually increase in difficulty.

2.4. Data analysis

2 (Training Condition) × 2 (Time) Mixed Model ANOVAs were conducted to analyze treatment effects across conditions for the EEG and neurocognition measures. Significant ANOVAs were followed-up using paired samples *t*-tests by time within each group. Effect sizes are presented as partial η^2, where 0.01, 0.06, and 0.14 represent a small, medium, and large effect respectively (Cohen, 1988, 1992). Comparisons to the healthy comparison group were conducted using independent samples t-tests. Pearson correlations were conducted to examine the relationship between change in EEG measures and change in the executive functioning composite score. Change scores were calculated as a difference between post-test and pre-test scores.

3. Results

3.1. Treatment adherence

There was no significant difference between groups on the number of minutes of at-home cognitive training completed. On average, participants in the EF training completed 17.84 ($SD = 10.44$) minutes of training per day and participants in the control condition completed 22.52 ($SD = 10.84$) minutes per day, $t(23) = 1.07$, $p = 0.296$, in addition to the laboratory-based training sessions. There was no significant difference in attrition between groups, $\chi^2(1) = 0.71$, $p = 0.399$.

3.2. EEG

3.2.1. Frontal theta power

There were no differences between the EF training condition and the sham group on frontal resting state theta power during the course of training, $F(1, 24) = 0.03$, $p = 0.856$, partial $\eta^2 = 0.001$. Participants in the EF training condition demonstrated a significant increase in frontal theta power during high cognitive load tasks compared to the sham group, $F(1,24) = 7.11$, $p = 0.013$, partial $\eta^2 = 0.209$, but not during the low cognitive load tasks, $F(1,24) = 0.73$, $p = 0.398$, partial $\eta^2 = 0.027$. At baseline, neither participants in the EF training condition ($M = 2.50$, $SE = 1.00$), $t(37) = 0.71$, $p = 0.479$, nor participants in the sham training condition ($M = 1.55$, $SE = 0.75$), $t(36) = 1.68$, $p = 0.10$, differed significantly from healthy comparison subjects ($M = 3.48$, $SE = 0.79$) on theta power during the high cognitive load task. Post-treatment, participants in the EF training showed increased theta power ($M = 4.31$, $SE = 1.20$), not significantly different than healthy comparison subjects, $t(37) = 0.59$, $p = 0.559$, and participants in the sham training condition showed a trend for lower frontal theta power ($M = 1.17$, $SE0.59$), that was significantly lower than healthy comparison subjects, $t(36) = 2.35$, $p = 0.025$. Topographic plots of theta power are presented in Fig. 3.

3.2.2. Frontal alpha power

There were no differences between the EF training group and the sham group on frontal resting state alpha power during the course of training, $F(1,24) = 0.18$, $p = 0.893$, partial $\eta^2 = 0.001$. There were also no differences in frontal alpha power during either the low cognitive load tasks, $F(1,24) = 1.59$, $p = 0.218$, partial $\eta^2 = 0.062$, or high cognitive load tasks, $F(1,24) = 2.12$, $p = 0.158$, partial $\eta^2 = 0.081$, across treatment conditions. Topographic plots of alpha power are presented in Fig. 4.

3.2.3. Posterior alpha power

There were no differences between the EF training group and the sham group on posterior resting state alpha power during the course of training, $F(1,24) = 0.51$, $p = 0.481$, partial $\eta^2 = 0.021$. Individuals in the EF training group demonstrated a significant decrease in posterior alpha power during high cognitive load tasks compared to the sham group, $F(1,24) = 8.26$, $p = 0.008$, partial $\eta^2 = 0.256$, but not during the low cognitive load tasks, $F(1,24) = 1.13$, $p = 0.297$, partial $\eta^2 = 0.045$. At baseline neither individuals in the EF training group ($M = -0.56$, $SE = 0.59$), $t(37) = 0.61$, $p = 0.544$, nor individuals in the sham group ($M = -0.33$, $SE = 0.36$) differed from the healthy comparison sample ($M = -0.20$, $SE = 0.28$), $t(36) = 0.28$, $p = 0.781$, on posterior alpha power during the high cognitive load task. After training there was still no difference between the sham group ($M = 0.65$, $SE = 0.72$) and healthy comparison subjects, $t(36) = 1.33$, $p = 0.189$, however, the EF training group had significantly lower posterior alpha power, ($M = -1.91$, $SE = 0.53$), $t(37) = 3.15$, $p = 0.003$, than the healthy comparison sample. Topographic plots of alpha power are presented in Fig. 4.

3.3. Neurocognition

Participants in the EF Training condition improved significantly more on the EF composite score compared to the sham training condition, and there was a trend for greater improvement on the WMS-SS and ToL tests (Table 2). However, these differences may be at least partially attributed to baseline differences on these tests between the groups, in spite of randomization. Compared to the healthy comparison group, individuals in the sham training group were not significantly different at any time point (Fig. 5). Individuals in the EF training condition performed significantly more poorly on LNS, ToL, and the EF composite before training than healthy controls but were not significantly different after training (Fig. 5). To examine the possibility that the significant interaction was due to baseline differences between groups we excluded participants who scored in the lower 25% ($n = 3$) of the EF training condition and the higher 25% ($n = 3$) of the sham training condition on baseline EF composite score. This resulted in groups with comparable EF functioning at baseline (EF training: $M = 49.51$, $SD = 4.52$; Sham training: $M = 48.31$, $SD = 5.12$). There was a trend level interaction suggesting greater improvement in the EF composite for participants in the EF training condition ($M_{Post} = 53.96$, $SD_{Post} = 4.80$) than in the sham training condition ($M_{Post} = 49.10$, $SD_{Post} = 5.72$), $F(1,17) = 3.46$, $p = 0.08$, partial $\eta^2 = 0.169$. Thus, it appears unlikely that the differential treatment response is due to baseline group differences.

3.4. Correlational analyses

Exploratory correlations were examined between change in EF composite score and change in EEG measures (Table 2). Correlations were

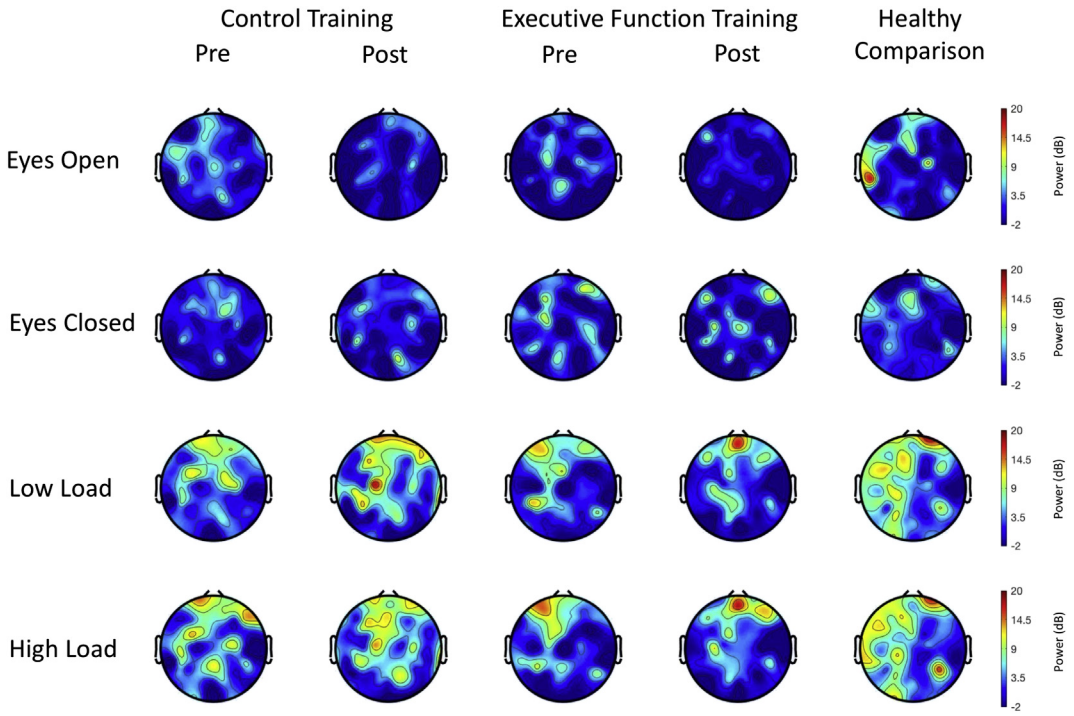

Fig. 3. Topographic plots of theta power by treatment condition and time across resting state, low working memory load task, and high working memory load task.

generally moderate for frontal EEG measures and there was virtually no correlation with change in posterior alpha power.

4. Discussion

Two weeks of independent computerized training of executive functioning was sufficient to increase frontal theta frequency power, reduce posterior alpha frequency power in the EEG, and improve performance on neurocognitive tests of executive functioning. Additionally, training affected EEG power during high cognitive load tasks, but did not produce changes on low cognitive load tasks or resting state EEG power. These effects were observed when compared to a stringent comparison condition of computerized training within the same training environment without titrated increases in difficulty.

These results are the first to examine the neurophysiological effects of independent computerized training of executive functioning. These

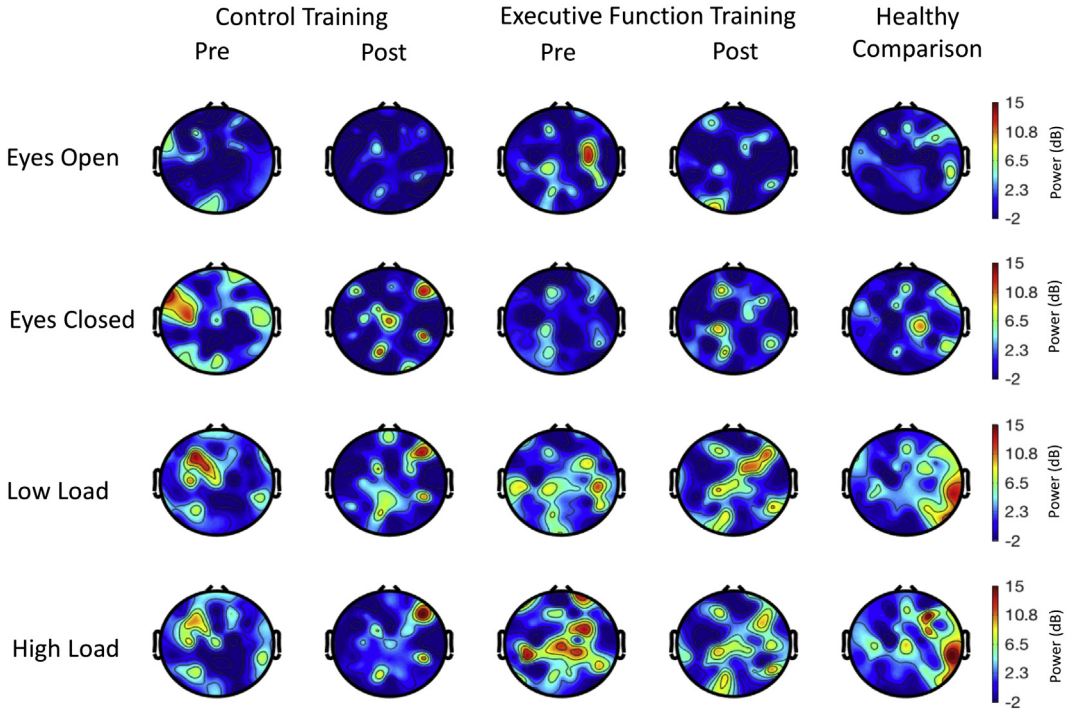

Fig. 4. Topographic maps of alpha power by treatment condition and time across eyes open, eyes closed, low executive function load, and high executive function load recording conditions.

Table 2
Mean (SD) T-Scores on the neurocognitive tasks by treatment condition and time.

	Executive function training (n = 13)		Control training (n = 12)		ANOVA time × condition		
	Pre	Post	Pre	Post	F	p	partial η^2
TMT B/A	49.10 (13.36)	51.14 (10.03)	51.07 (15.02)	52.15 (10.02)	0.055	0.817	0.002
LNS	39.92 (12.88)	44.16 (12.92)	48.33 (5.77)	49.08 (10.51)	1.23	0.279	0.053
WMS-SS	46.69 (10.14)	52.77 (7.47)	49.83 (8.87)	49.41 (8.52)	4.07	0.056	0.150
ToL	44.64 (13.24)	51.83 (4.17)	51.41 (8.75)	51.94 (6.11)	3.71	0.067	0.144
Composite	45.16 (9.14)	50.49 (8.04)	50.26 (5.62)	50.64 (6.00)	7.67	**0.011**	0.250

TMT B/A = Trail Making Test; LNS = MATRICS Letter Number Sequencing; WMS-SS = Weschler Memory Scale – Spatial Span; ToL = BACS Tower of London. Bolded values indicate $p < 0.05$.

findings are similar to findings of "bottom-up" computerized training of perceptual abilities which have demonstrated improvements in neurophysiological markers of perception (Fisher et al., 2009, 2016) and neurocognitive tests of attention (Silverstein et al., 2005; Fisher et al., 2016), but limited transfer to higher-order cognitive domains. The current results suggest that a "top-down" computerized training approach of executive function abilities produces neurophysiological changes in markers of working memory and executive function (frontal theta) and markers of attention and task engagement (posterior alpha), in addition to improvements in neuropsychological measures of executive functioning. Increased power in the theta frequency band over frontal electrode sites suggests greater mobilization of frontal cognitive resources associated with executive functioning, whereas decreased power in the alpha frequency band over posterior electrode sites suggests greater suppression of default mode activation in posterior regions as visual attentional resources engage to meet task demands. After training, posterior alpha power during the high cognitive load tasks in the EF training group was significantly lower than in healthy comparison subjects. Although speculative, it might be the case that EF training facilitates a greater than usual suppression of alpha power in people with psychotic disorders beyond what healthy subjects demonstrate, that is necessary to compensate for other cognitive impairments associated with the illness; this will need confirmation with further work.

Given the improvement in EEG power and executive function ability observed after such a brief course of treatment (2 weeks), such training may serve as an effective adjunctive treatment for other psychosocial interventions such as cognitive behavioural therapy or social skills training, in which participants are required to learn and retain new information. It is possible that a brief course of executive function training prior to, or conducted simultaneously with, engaging in other psychosocial treatments may increase retention from these programs and improve effectiveness. Promising results have been found with the combination of a longer and more comprehensive CR program and functional skills training (Bowie et al., 2012), however, a brief, targeted executive function training may be more feasible to implement in routine clinical settings. Interestingly, even for such a brief intervention we had substantial attrition during the two weeks of training. This may be due to the independent training nature of the program, and perhaps if there had been a more intensive psychotherapeutic element we would have observed less attrition. Treatment engagement is a critical challenge when working with people who have psychotic disorders, and developing methods to promote engagement will be important.

The current findings should be interpreted with consideration of several limitations. The relatively small sample size may limit the generalizability of the current findings. Although the large effect sizes are promising, it is also possible that the small sample size may result in an overestimation of effect size. The lack of a full cognitive assessment battery limits any conclusions we could draw about broad cognitive change. The assessment battery consisted of tests relatively similar to the tasks that were trained during treatment, and so it is unclear whether the improvements observed would generalize to other cognitive or functional domains. Regarding the EEG findings, although changes in

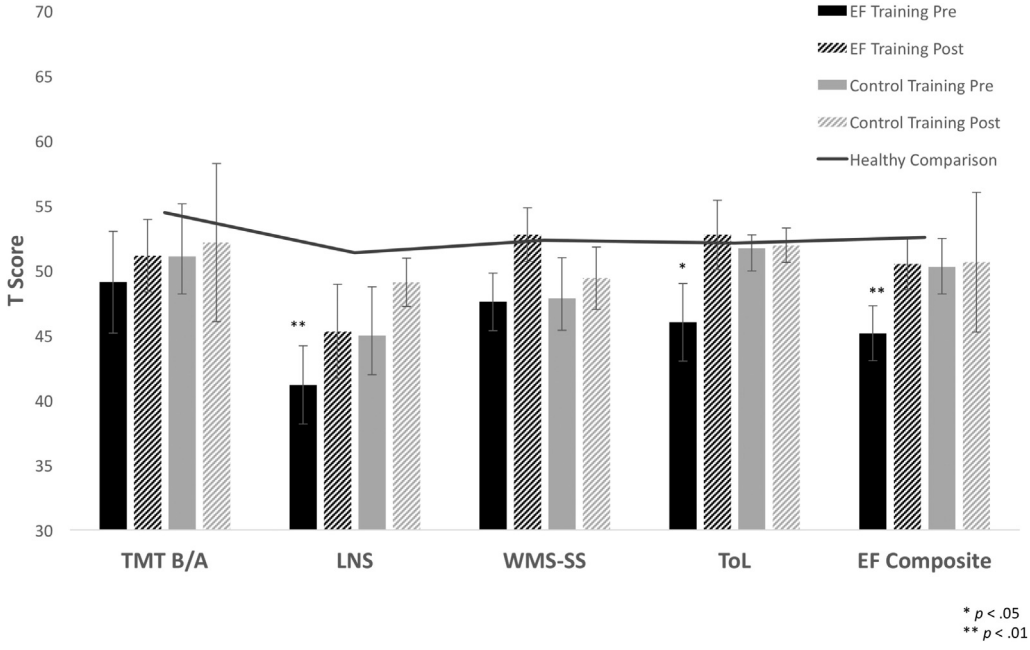

Fig. 5. Mean (SE) T-scores on neurocognitive tasks by condition and time. Healthy comparison scores are presented as a line and asterisks represent significant differences between the clinical and healthy comparison groups at specific time points. TMT B/A = Trail Making Test; LNS = MATRICS Letter Number Sequencing; WMS-SS = Weschler Memory Scale – Spatial Span; ToL = BACS Tower of London; EF Composite = Executive Function Composite.

Table 3
Exploratory correlations between change in EF composite score and change in EEG measures from pre to post training.

	EF training (n = 13)		Control training (n = 12)	
	EF composite change		EF composite change	
	r	p	r	p
Frontal theta power change	0.334	0.288	0.190	0.533
Frontal alpha power change	0.325	0.201	0.466	0.127
Posterior alpha power change	−0.037	0.905	0.083	0.799

EEG power were observed after EF training, we did not include event markers in the EEG recording, so we were unable to parse out whether specific cognitive processes (such as encoding, retrieval, manipulation, problem-solving) were driving the changes in power observed. Lastly, the current clinical sample was performing within the average range on the neurocognitive tests prior to receiving cognitive training, atypical for cognitive remediation studies, which may differentiate the current sample from those typically examined.

It is important to note that the current study only examined a single component of cognitive remediation (CR). While a common misinterpretation of cognitive remediation is that it is simply computerized cognitive training and that this is the only necessary component of cognitive remediation, we view CR as an integrative psychotherapy combining elements of strategy discussion and techniques for generalizing strategies to everyday life in combination with computerized training (see Best and Bowie, 2017, for a review of CR approaches). CR effects are maximized when delivered in a psychotherapeutic environment or when combined with other forms of psychiatric rehabilitation (Wykes et al., 2011), thus it will be important for future research to examine how brief EF training such as the current program fits into broader cognitive remediation programs. Direct comparisons of "bottom-up" and "top-down" approaches will be interesting to consider, as is the potential for CR programs based entirely in facilitating improvement in higher level cognitive abilities without the need to directly target basic perceptual processes. Personalized approaches to CR may be able to utilize both approaches based on the specific cognitive profile of an individual.

4.1. Conclusion

Two weeks of executive functioning training is sufficient to improve EEG frontal theta power and posterior alpha power during executive function tasks, and to improve executive functioning ability on neurocognitive tests. Theta and alpha synchronization may be neurophysiological mechanisms of change during CR requiring further attention, and examination in broader CR programs that include additional therapeutic elements such as strategy monitoring and generalization.

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Conflict of interest
CRB has been a consultant or advisory board member for Takeda, Lundbeck, Otsuka, and Boehringer Ingelheim in the past five years and received grant support from Takeda and Pfizer.User licenses for the cognitive training program were waived for research purposes by Scientific Brain Training Pro.

Contributors
MWB, DG, and CRB designed the study protocol together. MWB and DG performed data collection. TT and MH facilitated training sessions. MWB and CRB contributed to the statistical analyses and MWB wrote the first draft of the manuscript. All authors contributed to, and approve, the final manuscript.

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