



Research paper

Feasibility and preliminary efficacy of remotely delivering cognitive training to people with schizophrenia using tablets



Bruno Biagianti^{a,b,*}, Melissa Fisher^c, Lisa Howard^a, Abby Rowlands^a, Sophia Vinogradov^{c,1},
Joshua Woolley^{a,1}

^a Department of Psychiatry, University of California, San Francisco, USA

^b Posit Science, Inc., USA

^c Department of Psychiatry, University of Minnesota, USA

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ABSTRACT

Background: Limited access to Cognitive Training (CT) for people with schizophrenia (SZ) prevents widespread adoption of this intervention. Delivering CT remotely via tablets may increase accessibility, improve scheduling flexibility, and diminish patient burden.

Methods: In this reanalysis of data from a larger trial of CT, we compared two samples of individuals with SZ who chose to complete 40 h of CT either on desktop computers in the laboratory ($N = 33$) or remotely via iPads ($N = 41$). We examined attrition rates and adherence to training, and investigated whether remote iPad-based CT and in-person desktop-based CT induced significantly different improvements in cognitive and real-world functioning.

Results: The attrition rate was 36.6%. On average, participants completed 3.06 h of CT per week. There were no significant between-group differences in attrition and adherence to CT requirements. Participants who completed iPad-based CT were significantly younger and had lower symptoms at baseline compared to participants who completed CT on the lab desktops. Controlling for age and symptom severity, rANCOVA showed that iPad-based and desktop-based CT similarly and significantly improved verbal learning and problem solving. Main effects of time, at trend level significance, were evident in global cognition, verbal memory, quality of life, and social functioning. All group by time interactions were non-significant except for verbal memory, where iPad users showed greater gains. Within-group effect sizes for changes in outcomes were in the small range.

Conclusion: Although underpowered and not randomized, this study demonstrates that delivering CT remotely to people with SZ using tablets is feasible and results in retention rates, adherence, and cognitive and functional outcome improvements that are comparable to those observed when CT is delivered in the laboratory. This has important implications in terms of scalability and dissemination of CT. These results require confirmation in larger samples.

1. Introduction

Schizophrenia (SZ) is associated with a wide range of Cognitive Impairments (CIs), including deficits in attention, speed of processing, learning and memory, problem solving, and executive functioning that are present early in the course of illness and are more enduring than psychotic symptoms (Green et al., 2004). These CIs undermine independent living and are associated with decreased lifelong community and occupational functioning even when psychotic symptoms are in remission (Kurtz et al., 2008). As a result, CIs account for 20–60% of the variance in functional outcome of individuals with SZ (Green, 1996).

Discovering methods to treat CIs in SZ early in the course of illness, before functional and psychosocial deterioration has occurred, is a major goal of 21st century psychiatry. New treatment approaches to enhance cognition, both pharmacological and behavioral, have been tested for patients with SZ. To date, none of the pharmacological trials found significant effects on CIs compared to placebo (Keefe et al., 2013). However, there is growing evidence that an intensive computerized neuroplasticity-informed Cognitive Training (CT) program may be an effective treatment for CIs in SZ.

Our research group has demonstrated that CT targeting the auditory system in adults with SZ improves early dynamic imaging responses in

* Corresponding author at: 401 Parnassus Ave, LP-255, San Francisco, CA 94143, USA.

E-mail address: bruno.biagianti@ucsf.edu (B. Biagianti).

¹ Co-senior authors.

auditory and prefrontal cortices, as well as global cognition, speed of processing, verbal learning, and verbal memory, and that such cognitive gains predict enhanced quality of life at 6 month follow-up (Biagiante et al., 2016a; Dale et al., 2010, 2015; Fisher et al., 2010, 2016; Subramaniam et al., 2012). Additionally, a new set of exercises targeting processing speed and working memory in the social cognitive domain was tested in young adults with SZ. Results from the pilot study indicated significant improvements on prosody identification, facial memory, social functioning, motivation and reward sensitivity (Nahum et al., 2014). More recently, a randomized controlled trial found that supplementing CT with these social cognitive exercises in people with psychotic disorders confers greater benefits in prosody identification and reward processing relative to CT alone (Fisher et al., 2017). While preliminary evidence indicates that CT is efficacious, access to and engagement with CT by individuals with SZ remain outstanding challenges. This prevents widespread and optimal utilization of this promising intervention. In our studies, we have asked individuals with SZ to complete, without supervision, one hour of training exercises a day, five times a week, for a period of 8–10 weeks. Therefore, this intervention can place a high scheduling burden and become untenable for those who are in school or employed, have caregiver demands, or other medical appointments to manage. Additionally, CT is currently delivered as an experimental treatment in only a few specialized mental health clinics, and may not be accessible to people who live in rural or under-resourced areas or are without transportation (Kohn et al., 2004). The time spent reaching the clinic may therefore be another barrier to the implementation of this treatment. Lastly, some individuals with SZ hesitate to approach traditional mental health treatment settings because of stigma, which interferes with help-seeking behaviors (Angermeyer et al., 2013). These factors may all account for the high attrition rates found in CT trials, with important implications on the scalability of this intervention (Biagiante et al., 2016a).

Advances in interactive software development and health care delivery provide a unique opportunity to overcome these limitations. The rapid expansion of mobile technology in this population (Gay et al., 2016), with 81.4% of individuals with SZ owning a mobile phone (Firth et al., 2016), has already revolutionized the field of treatment development and delivery, allowing users to engage with innovative interventions, entirely remotely, anytime, anywhere, on their own schedule (Berry et al., 2016). Internet and mobile interventions are acceptable and feasible for individuals with SZ and have the potential to improve clinical and functional outcomes (Alvarez-Jimenez et al., 2014; Biagiante et al., 2016b). Similarly, the remote delivery of CT through mobile platforms enables scheduling flexibility and decreases scheduling burden, which may improve adherence to intervention requirements and ultimately increasing cost-effectiveness (Ventura et al., 2013). Additionally, through mobile platforms, CT can be delivered to individuals with SZ who are unable or unwilling to come in to the clinic. In doing so, mobile platforms may improve access, expand reach, and target underserved vulnerable populations.

Recent evidence suggests that CT can be feasibly delivered using mobile platforms. A 4-week feasibility trial delivering 20 h of iPad-assisted cognitive remediation vs. treatment as usual to 20 first-episode SZ in-patients showed significant improvements in working memory and good acceptability and adherence (Dang et al., 2014). More recently, our group demonstrated that it is feasible and acceptable to engage individuals with SZ in social cognition training entirely remotely using iPads (Biagiante et al., 2016b). Taken together, these findings indicate that delivering treatments including CT via internet and mobile platforms is acceptable and feasible. However, given the early state of current research, no studies have evaluated whether delivering evidence-based treatments like CT using online and mobile platforms is as efficacious as in-person delivery.

In this study, we analyzed data from a cohort of participants with SZ from our parent study (described below) who had a choice of completing 40 h of CT either on desktop computers in the laboratory, or

remotely on iPads. We compared attrition rates and adherence to training requirements. We also investigated whether remote iPad-based CT and in-person desktop-based CT induce significantly different improvements in cognitive and real-world functioning.

2. Methods

2.1. Participants

This is a reanalysis of data from a double-blind Randomized Controlled Trial (RCT, [ClinicalTrials.gov](https://clinicaltrials.gov/ct2/show/study/NCT02105779) NCT02105779) that investigated the effects of supplementing CT with social cognitive exercises, as compared with CT alone (Fisher et al., 2017). From 2010 to February 2013, the CT program was only available on desktop computers in the laboratory. This changed in March 2013 when the CT program also became available on iPad devices that could be used remotely. From that point until the study's completion date (June 2016), participants were given the option to complete CT using desktop computers in the laboratory or to participate in the intervention remotely using provided iPads. There were no differences between the iPad and the desktop versions of CT in terms of the stimulus sets, stimulus progressions, adapting parameters, or logic of each exercise. The platforms only varied with respect to the user interface and exercise graphics.

The total number of participants randomized in the original trial was $N = 111$. In this study, however, post-hoc analyses were only performed on the subset ($N = 74$) of data collected from participants who enrolled in the study from March 2013 to June 2016, to allow for a more accurate comparison among participants who could choose both their device and location of use. This comparison is not based on the randomization criterion used in the parent RCT (CT + social cognitive exercises vs CT alone). Here, we directly contrast participants who freely chose to complete CT on iPads with those who chose to complete CT on desktops. Therefore, both groups include a mix of participants from the two treatment arms of the RCT.

Participants were recruited from the San Francisco VA Medical Center outpatient clinic, other local community mental health centers, and via presentations and online advertisements. Participants were clinically stable at the time of testing (no hospitalization and stable dosages of medication over the past month). Other inclusion criteria included: 1) fluent and proficient in English, 2) WTAR > 70 (Green et al., 2008), 3) sober during assessments and training, 4) no neurological disorder. Participants reported no prior cognitive remediation treatment. This study was approved by local Institutional Review Boards.

2.2. Procedures

All participants gave written informed consent for the study and were compensated for their participation in all assessments. Participants were asked to complete 40 h of the computerized CT program BrainHQ, provided free of charge by Posit Science Inc. After an intake evaluation that determined study eligibility, participants underwent an in-person structured diagnostic clinical interview and a battery of cognitive and clinical in-person assessments, which were administered again after training. For participants who completed CT in the laboratory, staff exposure during the intervention was kept to a minimum: staff aided all subjects to start each session but did not provide any coaching. Participants who opted for iPads were shown how to use the app BrainHQ in the lab before they returned home to engage in CT. Weekly phone calls were used to check in, monitor engagement, and offer technical support. Progress with CT was monitored remotely through the BrainHQ research portal. All participants received the same total number of hours of training and contact with research personnel. Multiple safeguards against loss of property were in place, including GPS tracking of the iPad and the option to remotely lock it, if

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