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Pilot study of cognitive remediation therapy on cognition in young people at clinical high risk of psychosis

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ABSTRACT

Individuals at clinical high risk (CHR) of psychosis evidence cognitive deficits. Given suggestions that deficits in cognition are related to poor functional outcome, cognition is a good treatment target. The aim of this study was to test the efficacy of cognitive remediation therapy (CRT) in improving cognition of CHR individuals. Participants were tested at baseline, immediately following CRT and 9 months post-baseline. The mixed effects modelling demonstrated no differences in cognition between the experimental group and the control group at any time point. For the experimental group, however, there was a trend towards improvement in speed of processing between baseline and 9-month follow-up ($t(29) = -2.91$, $P = 0.06$) and at post-CRT compared to 9-month follow-up ($t(29) = -2.99$, $P < 0.05$). In the control group, significant improvements in working memory were observed between post-CRT and 9-month follow-up ($t(29) = -3.06$, $P < 0.05$). Despite significant improvements in social functioning in the intervention group between baseline and 9-month follow-up ($t(28) = -3.26$, $P < 0.05$), these improvements were not correlated with cognition. There were trends towards improvement and no trends of decline in the two groups. While CRT may be valuable for individuals at CHR, the type of intervention employed needs to be carefully considered.

1. Introduction

Onset of psychotic disorders such as schizophrenia, schizophreniform or schizoaffective disorder typically occurs during late adolescence or early adulthood often resulting in chronic social and occupational disability. Recent progress in risk identification methodology has enabled reliable detection of persons who appear to be putatively prodromal for psychosis, that is at clinical high risk (CHR) of developing a psychotic disorder, 35% of whom developed psychosis within 2½ years (Fusar-Poli et al., 2012a). Results from several studies suggest that CHR individuals are distinguished from non-psychiatric controls in several domains, including cognition and functioning (Fusar-Poli et al., 2012b; Carrion et al., 2013; Barbato et al., 2013; Giuliano et al., 2012). In a recent meta-analysis of cognitive functioning of those at CHR Fusar-Poli et al. (2012b) reported small to moderate impairments in those at CHR compared to healthy controls on almost all cognitive domains including general intelligence. According to recent reviews of cognition in CHR cohorts, the most sensitive cognitive domains that discriminated CHR individuals from healthy controls were general cognitive ability, verbal learning and memory and processing speed and attention (Giuliano et al., 2012; Addington and Barbato, 2012).

Deficits in cognition and functional outcome (e.g. social and occupational functioning) often precede the onset of full-blown psychosis (Carrion et al., 2013) although to a lesser degree than observed in schizophrenia (Addington et al., 2006a, 2008). Furthermore, there is evidence, in schizophrenia (Green et al., 2000; Bowie and Harvey 2006; Fett et al., 2011) and to a lesser extent in CHR samples (Carrion et al., 2011, 2013; Niendam et al., 2006b), that deficits in cognition are related to poor functional outcome. It has been suggested that one mechanism for poor functional outcome may be through deterioration in cognition, which adversely affects the rate of learning, understanding and responding to incoming information (Carrion et al., 2013). Since onset of psychosis typically occurs in late adolescence and early adulthood, cognitive deterioration at this time could be particularly disruptive since this is a critical period for learning and establishing new social relationships. This could be an important time for early intervention before the onset of full blown psychosis and further cognitive and functional deterioration.

Since these CHR individuals already evidence cognitive deficits, which increase around the time of conversion (Seidman et al., 2010; Fusar-Poli et al., 2012a), cognition is an excellent treatment target. Furthermore, treatments targeting cognition may consequently

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improve functional outcome. Cognitive remediation therapies tested in schizophrenia populations to date have shown small to moderate improvement in cognition and variable improvements in functional outcome (McGurk et al., 2007). Most of these approaches focus on training subjects with laboratory tasks in order to improve specific abilities in different cognitive domains (e.g. learning, attention, memory). Although these methods have a promising role in schizophrenia treatment, almost all of them involve ongoing administration and monitoring by trained therapists, making them expensive and not readily accessible in most treatment settings.

To the best of our knowledge, there have only been two published studies of CRT in a CHR population to date. In a pilot study of 10 CHR individuals and 16 individuals with schizophrenia by Rauchensteiner et al. (2011), CogPack program was used to provide cognitive training across a broad range of cognitive domains such as attention, speed of processing, executive function and learning and memory. The training was delivered in 10 sessions over a period of 4 weeks. All participants underwent cognitive testing at baseline and immediately following the cognitive training. CHR participants showed significant improvements in verbal learning and memory and on five (out of eight) CogPack exercises compared to those with schizophrenia. In the second published study Bechdolf and associates (Bechdolf et al., 2012) included 12 CogPack training sessions as part of the Integrated Psychological Intervention (IPI) compared to a control treatment consisting of supportive therapy in individuals exhibiting early initial prodromal states (EIPS) or symptoms that precede sub-threshold prodromal symptoms that define CHR. However, given that the focus of the study was on efficacy of IPI as a whole in preventing conversion to psychosis, Bechdolf et al. (2012) did not assess individual contribution of CogPack on the outcome of conversion or its effects on cognition following cognitive training.

Based on the limited evidence for cognitive improvement in individuals at CHR following 10 sessions of CRT and the evidence showing that cognitive dysfunction is present in the prodrome of psychosis, the aim of the current study was to test the effectiveness of an auditory processing CRT, the Brain Fitness Program (BFP) (developed by PositScience), in improving cognition of CHR individuals among youth at CHR. A control treatment consisting of commercially available computer games (Fisher et al., 2009) (CG) was also used. The current methodology was adopted from Fisher et al. (2009) who utilised BFP as a stand-alone treatment in individuals with chronic schizophrenia and reported positive effects of auditory training on cognitive function compared to a control treatment consisting of computer games. In the current study, the primary hypothesis was that the Brain Fitness group (BF) would have improved cognition at post-CRT and 9-month follow-up compared to the CG group. An exploratory hypothesis was that significant improvements in cognition would be associated with improved functioning.

2. Method

2.1. Design and sample

This was a single blind, randomized controlled pilot trial of CRT in 32 persons at CHR. Thirty-two CHR persons between the ages of 14 and 35 years (21 males and 11 females) were recruited into the study (Table 1). All of the participants were recruited as part of a multi-site NIMH funded study, The North American Prodrome Longitudinal Study (NAPLS 2) from the Calgary site (Addington et al., 2012b). The participants met one of the three established criteria for a psychosis risk syndrome, namely: attenuated psychotic symptom state (APSS), brief intermittent psychotic symptom state (BIPS) and genetic risk with deterioration (GRD). Inclusion criteria included (i) between ages 15 and 35; (ii) meet SIPS prodromal criteria, (iii) competent to give written informed consent and exclusion criteria were (i) IQ < 75; (ii) organic central nervous system disorder (e.g., epilepsy, traumatic brain injury);(iii) diagnosis of substance dependence. Participants over the age of 18 provided written informed consent to the study protocol approved by the University of Calgary Ethics Review Committee. Participants under the age of 18 provided assent in addition to parental written informed consent. Detailed descriptions of inclusion and exclusion criteria, as well as the participant recruitment procedures, are provided elsewhere (Addington et al., 2012a, 2012b).

Table 1
Group differences in demographics, symptoms and functioning.

Variable	BF group $n=18$ *M* (S.D)	VG group $n=14$ *M* (S.D)	Test scores
Gender			$\chi^2=0.37$
Male	11	10	
Female	7	4	
Marital status			$\chi^2=0.80$
Never married	17	14	
Married	1	0	
Working			$\chi^2=5.80$**
Competitive	5	9	
Supported	13	5	
Student			$\chi^2=4.23$
Yes	11	13	
No	7	1	
	$n=18$ M (S.D.)	**$n=14$ M (S.D.)**	
Age	19.72 (5.71)	17.5 (3.48)	$t=1.71$
Years of education	10.89 (2.50)	10.28 (2.84)	$t=-0.63$
Global functioning: social and role			
GFS	5.86 (1.70)	7.0 (1.75)	$t=1.68$
GFR SOPS symptoms	5.16 (2.66)	6.57 (1.78)	$t=1.69$
Positive	10.05 (4.73)	8.64 (4.78)	$t=-0.83$
Negative	8.22 (6.10)	7.14 (6.46)	$t=0.48$
Disorganised	4.40 (3.43)	3.0 (2.16)	$t=-1.39$
General	7.94 (3.91)	5.85 (4.63)	$t=-1.38$
Sessions completed	16.28 (13.04)	24.29 (13.17)	$t=1.71$

Note: competitive employment = defined as work in the competitive labour market for which an individual is compensated at or above the minimum wage, but not less than the customary wage and level of benefits paid by the employer for the same or similar work performed by individuals who are not disabled; Supported employment = work in either sheltered or non-sheltered settings that involves some accommodation to the person's disability.

** $p < 0.05$.

2.2. Measures

Basic demographic information including age, gender, education, marital and work/student status was collected. DSM-IV diagnoses were established using the Structured Clinical Interview for DSM-IV (SCID-I). The Structured Interview for Prodromal Syndromes (SIPS) (McGlashan et al., 2010) was used at study entry to determine criteria. Attenuated positive symptoms and negative symptoms were assessed using the Scale of Prodromal Symptoms (SOPS). Quantity and quality of peer relationships, level of peer conflict, age appropriate intimate relationships and involvement with family members was assessed using the Global Functioning: Social Scale (GFS) (Cornblatt et al., 2007). Performance in role functioning such as at school, work or as a home maker, were assessed with the Global Functioning: Role Scale (GFR) (Niendam et al., 2006a).

The MATRICS Consensus Cognitive Battery MCCB was administered in its entirety apart from the Mayer–Salovey Emotional Intelligence Test (MSCEIT) (Mayer, 2002), a test of social cognition. This modified MCCB consisted of nine subtests assessing six different cognitive domains: processing speed, attention/vigilance, working memory, verbal learning, visual learning, and reasoning and problem solving (Nuechterlein et al., 2008).

2.3. Procedure

Participants were randomised to either the BFP or a control treatment consisting of commercial computer games (CG). Participants were not blind to group allocation but all cognitive and symptom raters were. The 40 h of BFP or computer game activity was expected to occur 4 days a week, for an hour each day, over a period of 10–12 weeks. Participants had a choice of accessing training sessions either at the lab or at their own homes. That is, each participant was provided with a unique user login details in order to access their BFT training sessions. In case of the CG group, computer games were installed on either participants' personal computers, or computers at the lab. Training for both groups was delivered online (in case of BFP) or via a computer program (in case of computer games) and all participants