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Superior memory performance in healthy individuals with subclinical psychotic symptoms but without genetic load for schizophrenia

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1. Introduction

Cognitive deficits are a hallmark core feature of schizophrenia and play a predominant role in determining the functional capacity of an individual (Mohamed et al., 2008; Nuechterlein et al., 2012; Green et al., 2000; Kumar et al., 2016). Cognitive deficits have been reported throughout the psychosis continuum and are seen in unaffected siblings and family members of patients with schizophrenia (Snitz et al., 2006; Sitskoorn et al., 2004; Seidman et al., 2007), individuals with psychosis risk syndrome (Fusar-Poli et al., 2012; Yung et al., 2003) and individuals with subclinical psychotic symptoms with genetic predisposition who are at higher risk of conversion to schizophrenia (Trotman et al., 2006; Walder et al., 2008; Daly et al., 2012; Fusar-Poli et al., 2012; Yung et al., 2003).

These deficits become particularly notable in first episode schizophrenia and persist in patients with chronic schizophrenia (Mesholam-Gately et al., 2009; Siever and Davis, 2004; Nuechterlein et al., 2012; Meehl, 1990). A worsening of cognitive deficits from the preclinical stage of the illness to its first episode stage followed by a relatively stable course is consistent with the widely accepted neurodevelopmental hypothesis of schizophrenia (Lewis and Lieberman, 2000; Lewis and Levitt, 2002).

Cognitive deficits in schizophrenia affect almost all cognitive domains including attention, processing speed, executive function, verbal memory and working memory (Heinrichs and Zakzanis, 1998; Rajji et al., 2009; Fioravanti et al., 2012). Particularly, deficits in verbal memory are well characterized and are known to involve both short term and long term memory and remain stable with age (Heaton et al., 1994, Heaton et al., 2001, Rajji et al., 2009, Rajji et al., 2013, Gur et al., 2007, André Aleman et al., 1999, Brewer et al., 2005). Further, verbal memory deficits in schizophrenia appear to result from poor encoding of information in immediate memory and impaired ability to organize information (Cirillo and Seidman, 2003; Brebion et al., 1997). Integrity of these mechanisms may directly influence the organization of thoughts and may be relevant to precipitation and perpetuation of psychosis in patients with schizophrenia. However, there remains confusion concerning the cognitive characteristics of individuals with subclinical psychotic symptoms who do not have known risk factors to convert to schizophrenia are not well understood (Brewer et al., 2006; Addington and Barbato, 2012). Further, the extent to which different cognitive domains are involved in these individuals is also not clear. Given the known association between subclinical symptoms and cognition in genetically at risk individuals, looking for such an association in non-genetically at-risk individuals might provide a superior understanding of the protective factors and risk factors for psychosis. Numerous studies have investigated this relationship closely. Particularly, a study with 298 female twin pairs youths (mean age 27 \pm 7.5) from the general population, found deficits primarily in processing speed using tests of episodic memory, and simple and complex information processing (Simons et al., 2007). Furthermore, another study found no significant differences in performance on the Wisconsin Card Sorting Test between individuals with high versus low schizotypal traits in a midlife adult sample (mean age 45.9 ± 14.0) (Laurent et al., 2001). Interestingly, one large population-based study (mean age 47.3 ± 11.9) assessed the association between verbal fluency and subclinical psychosis phenotype and found impaired verbal fluency only in men with high level of subclinical psychosis (Krabbendam et al., 2005). In comparison, another study (mean age 38.1 \pm 14.3) reported better performance on verbal memory and working memory tests in individuals with subclinical psychotic symptoms (Korponay et al., 2014). Based upon this conflicting evidence, further investigations must be conducted in this field to truly determine the nature of this association.

A common limitation shared across these studies is the lack of focus in selecting individuals with low genetic risk factors for schizophrenia (ie: low genetic predisposition). This is attributed to the known association between genetic risk for schizophrenia and cognitive impairment. Moreover, these studies did not appropriately assess the impact

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Table 1

Demographic and clinical characteristics.						
	Total Sample	SCPS-Young	SCPS-Old	NPS-Young	NPS-Old	Statistics
N	83	19	14	29	21	Total <i>N</i> = 83
Gender (M:F)	49:34	13:6	8:6	18:11	10:11	Pearson Chi Square: F(3) = 1.955; p = .582
Age	49.96 (18.60)	38 (8.69)	67.14 (7.92)	32.55 (10.12)	64.81 (7.43)	
Education	15,06 (2,03)	15 (1.77)	14.92 (2.87)	15.71 (1.98)	15.05 (1.73)	ANOVA: F(3,76) = 0.51; p = .525
PANSS total	34.76 (3.49)	33.32 (3.48)	36.71 (2.46)	30.45 (0.69)	30.52 (0.87)	ANOVA: $F(3,79) = 36.98; p < .001$
PANSS positive	9.09 (1.29)	8.53 (0.61)	9.86 (1.23)	7.00 (0.00)	7.00 (0.00)	ANOVA: $F(3,79) = 100.74$; p < .001
PANSS negative	7.64 (0.90)	7.42 (0.69)	7.93 (1.07)	7.21 (0.43)	7.29 (0.72)	ANOVA: F(3,79) = 3.421; p = .021

All measures are presented as mean (SD) except for gender.

SCPS: subclinical psychotic symptoms; NPS: no psychotic symptoms; M: male; F: female; PANSS: Positive and Negative Syndrome Scale.

of age or education on cognition. Thus, we performed a study in healthy younger and older adults without genetic vulnerability to schizophrenia as determined by family history. We compared the cognitive profiles of those with subclinical psychotic symptoms (SCPS) to those with no psychotic symptoms (NPS). Furthermore, we controlled for the effect of education on cognition and psychotic symptoms in these four subgroups: younger and older individuals with SCPS along with younger and older individuals with NPS. We hypothesized that individuals with NPS would perform better than individuals with SCPS on selected tests.

2. Methods

2.1. Participants and measures

This study was conducted at the Centre for Addiction and Mental Health (CAMH), a research and teaching hospital affiliated with the University of Toronto, Canada. Adult volunteers were recruited through flyers, existing studies database, and referrals by word of mouth to participate as controls in schizophrenia studies. Eligibility criteria were the following: (1) having no DSM-IV-TR(American Psychiatric et al., 2000) psychiatric diagnosis, except for simple phobias or adjustment disorders; (2) having no first-degree relative with a primary psychotic disorder (i.e. no DSM-IV-TR schizophrenia-spectrum disorder); (3) not suffering from a neurological disorder or sensory deficit that would have impacted neuropsychological testing; (4) not receiving psychotropic medication other than a sedative or a hypnotic at a stable dose for at least 4 weeks; and (5) understanding and speaking English wellenough to complete the neuropsychological assessments. The study was approved by CAMH research ethics board and all participants gave written informed consent to participate in the studies which generates the data we are using for this analysis.

All participants underwent the following assessments: (1) the structured clinical interview (SCID)(First, 2002) for DSM-IV to determine eligibility; (2) the Positive and Negative Syndrome Scale (PANSS) (Kay et al., 1988) to assess clinical symptoms. The PANSS is a 30-item scale containing seven positive symptoms items, seven negative symptoms items, and 16 general psychopathology items. Each item is scored on a seven-point severity scale, yielding a total score between 30 and 210 points, with higher scores indicating increasing severity. The positive and negative symptoms items groups are often reported separately, with a possible range of seven to 49 points; (3) the Repeatable Battery for Assessment of Neuropsychological Status (RBANS) (Pearson INC) and the Trail Making Test A and B (TMT) (Halstead Reitan battery) to assess cognition (the TMT was included as the RBANS does not assess executive functioning). The RBANS, and TMT were administered within one week following the administration of the PANSS. As done in previous studies (Kalache et al., 2015; Rajji et al., 2015), seven main cognitive domains were assessed as follows: (i) immediate recall: RBANS story memory immediate recall (SM-IR); (ii) delayed recall: RBANS story memory delayed recall (SM-DR); (iii) language: RBANS picture naming test; (iv) auditory attention: RBANS digit span; (v) visual attention: TMT-A; (vi) information-processing speed: RBANS digit

symbol coding; and (vii) executive functioning: TMT-B. For all measures, raw scores were used for the analysis.

2.2. Statistical analysis

Participants were divided in four groups based on their age and the absence or presence of SCPS. Since the distribution of age across our sample was bimodal, we divided our participants using a cut-off age of 55 years, congruent with the literature on cognitive aging (Dufouil et al., 2000). Based on the PANSS positive symptoms scores, we distinguished participants with SCPS based on a score of 8 or higher on the PANSS positive symptoms subscale and those with NPS with a score of 7. This cut-off score was chosen because a score of 8 suggests that at least one positive symptom was rated as present and given a severity score of at least 'minimal', whereas a score of 7 suggests that all positive symptoms were rated as 'absent'. We compared the seven cognitive domain scores of the four groups (SCPS-Young, SCPS-Old, NPS-Young, NPS-Old) using Analyses of Covariance (ANCOVAs) controlling for number of years of education. A p value of 0.05 or lower was considered significant and Bonnferroni corrections were used for pos-hoc comparisons among the four groups.

3. Results

3.1. Demographic and clinical characteristics

The demographic and clinical characteristics of the 83 participants are summarized in Table 1. There was no significant difference between the four groups on gender distribution and number of years of educations.

3.2. Cognitive domains scores

There was a group effect on three of the seven cognitive domain scores: immediate recall (RBANS SM-IR), information processing speed (RBANS digit sympbol coding), and executive functioning (TMT-B) (see all results and statistics in Table 2). Post-hoc comparisons revealed that: immediate recall was better in SCPS-Young compared to NPS-Young (Fig. 1); processing speed was significantly lower in SCPS-Old compared to NPS-Young.

4. Discussion

In a sample of young and older healthy adults with no family history of schizophrenia, younger adults with SCPS performed better on immediate recall of a short story (i.e., a verbal learning test from the RBANS) than younger and older adults with NPS. Also, older adults with SCPS performed worse on information processing speed than younger adults with NPS. Finally, we did not find an association between the presence or absence of SCPS and other cognitive domains.

Our findings seem to contradict previous literature which consistently depicts deficits in verbal memory and executive functioning in Download English Version:

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