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Neuropsychological profiles in individuals at clinical high risk for psychosis: Relationship to psychosis and intelligence

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ABSTRACT

Background: Characterizing neuropsychological (NP) functioning of individuals at clinical high risk (CHR) for psychosis may be useful for prediction of psychosis and understanding functional outcome. The degree to which NP impairments are associated with general cognitive ability and/or later emergence of full psychosis in CHR samples requires study with well-matched controls.

Methods: We assessed NP functioning across eight cognitive domains in a sample of 73 CHR youth, 13 of whom developed psychotic-level symptoms after baseline assessment, and 34 healthy comparison (HC) subjects. Groups were matched on age, sex, ethnicity, handedness, subject and parent grade attainment, and median family income, and were comparable on WRAT-3 Reading, an estimate of premorbid IQ. Profile analysis was used to examine group differences and the role of IQ in profile shape.

Results: The CHR sample demonstrated a significant difference in overall magnitude of NP impairment but only a small and nearly significant difference in profile shape, primarily due to a large impairment in olfactory identification. Individuals who subsequently developed psychotic-level symptoms demonstrated large impairments in verbal IQ, verbal memory and olfactory identification comparable in magnitude to first episode samples.

Conclusions: CHR status may be associated with moderate generalized cognitive impairments marked by some degree of selective impairment in olfaction and verbal memory. Impairments were greatest in those who later developed psychotic symptoms. Future study of olfaction in CHR samples may enhance early detection and specification of neurodevelopmental mechanisms of risk.

1. Introduction

The literature on cognitive functioning during the putative prodrome to psychosis suggests cognitive impairments are generally intermediate between those of healthy comparison (HC) subjects and first episode psychosis (Eastvold et al., 2007; Francey et al., 2005; Keefe et al., 2006; Pukrop et al., 2006; Simon et al., 2007; Jahshan et al., 2010; Seidman et al., 2010). Of particular interest are findings specific to clinical high risk (CHR) individuals who develop psychosis over the course of follow-up, suggesting possible neuropsychological (NP) predictors of psychosis onset (Brewer et al., 2005; Brewer et al., 2003; Keefe et al., 2006; Lencz et al., 2006; Seidman et al., 2010). In the largest published study to date,

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NP function was more impaired at baseline in those who later developed psychosis than in those who did not (Seidman et al., 2010). When placed in the context of clinical factors predicting psychosis (e.g., severity of attenuated positive symptoms, family history, social functioning, and substance abuse), however, NP functioning did not add to the prediction algorithm (Cannon et al., 2008). Just the same, verbal memory may have added value in predicting faster transition to psychosis (Seidman et al., 2010). The relative value of both specific NP measures and general cognitive ability in predicting and understanding psychosis onset warrants additional study.

1.1. "Specific" deficits during the prodrome to psychosis

A number of "specific" deficits (presumably above and beyond any general deficit) have been documented in CHR samples, most reliably spatial working memory (Bartok et al., 2005; Myles-Worsley et al., 2007; Smith et al., 2006; Wood et al., 2003), verbal learning and memory (Brewer et al., 2005; Eastvold et al., 2007; Hawkins et al., 2004; Lencz et al., 2006; Seidman et al., 2010), attention (Francey et al., 2005; Gschwandtner et al., 2006; Hambrecht et al., 2002; Hawkins et al., 2004; Niendam et al., 2006) and processing speed (Seidman et al., 2010). Executive functions such as working memory, verbal fluency, and set-shifting have also been implicated, but less consistently (Eastvold et al., 2007; Gschwandtner et al., 2003; Gschwandtner et al., 2006; Hambrecht et al., 2002; Hawkins et al., 2004; Lencz et al., 2006; Myles-Worsley et al., 2007; Pukrop et al., 2006; Simon et al., 2007). In the few studies with clinical follow-up, poorer baseline verbal memory and olfactory identification have been identified as potential proximate predictors of later psychosis (Brewer et al., 2005; Brewer et al., 2003; Eastvold et al., 2007; Lencz et al., 2006; Seidman et al., 2010).

The possible predictive value of olfactory identification deficits, although measured in only one prior CHR study (Brewer et al., 2005), is intriguing. The ability to name odors is reliably impaired in adults with schizophrenia (SCZ) and in some studies, in individuals at familial high risk (FHR; Mesholam-Gately and Seidman, 2006; Moberg and Turetsky, 2006). In one study of SCZ, this impairment (as measured by the University of Pennsylvania Smell Identification Test, UPSIT) was not significantly associated with performance on measures of attention, executive function, or IQ, suggesting some specific utility (Seidman et al., 1992). Moreover, neurobiological studies have identified abnormalities in the olfactory bulb (Turetsky et al., 2000) and olfactory event related potentials of those with SCZ (Turetsky et al., 2003), suggesting abnormalities in specific neural substrates.

1.2. The role of current and "premorbid" IQ in neuropsychological profiles

In the literature, "specific" deficits are often defined by statistically significant group differences in a single cognitive domain rather than the specificity of the deficit relative to overall functioning. However, it is well established that performance on different NP tests tends to be positively correlated (Spearman, 1927). Furthermore, both degree of inter-test variability and pattern of strengths and weaknesses on a NP battery may vary according to overall cognitive ability or attention, and vary differently for SCZ relative to HC matched on IQ (Diaz-Asper et al., 2004; Dodrill, 1999; Kremen et al., 2008). Because attentional functions have long been hypothesized to be central to schizophrenia and its risk (Seidman, 1983; Nuechterlein and Dawson, 1984; Cornblatt and Keilp, 1994), we also evaluated the role of attentional impairment in the profiles of CHR versus HC.

The role of current global ability in SCZ has also been studied relative to premorbid IQ estimated with measures of single word reading, a function relatively resilient to illness (Dalby and Williams, 1986; Kremen et al., 1996; Weickert et al., 2000). Given its weaker correlation with measures of nonverbal reasoning and processing speed, single word reading may be associated with different patterns of NP performance than Full Scale measures of IQ (FSIQ). Current full scale and premorbid IQ estimates may thus have different relationships to patterns of NP functioning associated with risk and onset of psychosis. These have not yet been adequately investigated in CHR samples.

Finally, potentially important variables such as age, sex, and sociodemographic status have not been controlled routinely and some HC groups are likely to be "supernormal" as reflected by high group mean IQ scores (e.g., 119, Gschwandtner et al., 2006) or have significantly different estimated premorbid IQ relative to CHR groups (Brewer et al., 2005; Pukrop et al., 2006). Thus, there remains a need to characterize NP functioning and profiles within CHR samples relative to well-matched HC, with particular attention to the influential role of premorbid IQ. Matching on premorbid IQ has been strongly recommended in a review of the CHR literature (Brewer et al., 2006).

1.3. Purpose of this study

This study's primary goal was to characterize the overall NP profile of CHR relative to demographically well-matched HC. We predicted that CHR would differ from HC in overall mean NP profile magnitude and shape, with those subsequently developing psychotic-level symptoms showing the greatest level of NP impairment. More specifically, we predicted relatively greater impairment in verbal memory and olfactory functioning after accounting for global abilities estimated by either single word reading or estimated IQ.

2. Methods

2.1. Participants

The CHR sample consisted of participants in a randomized controlled trial (RCT) of family-aided assertive community treatment (FACT, McFarlane, 1997) through the Portland Identification and Early Referral (PIER) program in Portland, ME (McFarlane, et al., 2010). Entry into the study required residence in Greater Portland, estimated IQ $\geq$ 70, and meeting criteria for one of three putatively prodromal syndromes (Criteria of Prodromal Syndromes, COPS) according to the Structured Interview for Prodromal Syndromes (SIPS; Miller et al., 1999). These syndromes are based on the recent onset of brief and intermittent psychotic symptoms (BIPS), recent onset or progression of attenuated positive symptoms (APS),