Schizophrenia Research 149 (2013) 48–55

Contents lists available at SciVerse ScienceDirect

Schizophrenia Research

journal homepage: www.elsevier.com/locate/schres

Review

Neurocognition in clinical high risk young adults who did or did not convert to a first schizophrenic psychosis: A meta-analysis

Amber De Herdt [a,*], Martien Wampers [b], Davy Vancampfort [a,b], Marc De Hert [b,c], Luc Vanhees [a], Hella Demunter [c], Ludwina Van Bouwel [c], Emanuel Brunner [a], Michel Probst [a,b]

[a] Department of Rehabilitation Science, KU Leuven, Belgium
[b] University Psychiatric Center, KU Leuven, Campus Kortenberg, Belgium
[c] Department of Psychiatry, KU Leuven, Belgium

ARTICLE INFO

Article history:
Received 31 December 2012
Received in revised form 16 May 2013
Accepted 4 June 2013
Available online 5 July 2013

Keywords:
Cognition
At-risk-mental state
First-episode
Schizophrenia

ABSTRACT

Background: Individuals at clinical high risk (CHR) for psychosis have become a major focus for research designed to explore early predictors of transition to full psychosis. Characterizing differences in neurocognitive (NC) functioning between psychosis converters (CHR-C) and non-converters (CHR-NC) might contribute to the identification of specific NC predictors of psychosis onset. Therefore, the aim of the present meta-analysis was to compare the baseline NC performance between CHR-C and CHR-NC.

Method: PubMed (MEDLINE), Web of Science, Embase and reference lists were searched for studies reporting baseline cognitive data of CHR-C and CHR-NC. Included NC tests were classified within the MATRICS – Measurement and Treatment Research to Improve Cognition in Schizophrenia – cognitive domains.

Results: Of 95 studies assessed for eligibility, 9 studies comprising 583 CHR subjects (N CHR-C = 195, N CHR-NC = 388) met all the inclusion criteria.

CHR-C performed significantly worse compared to CHR-NC on 2 MATRICS domains namely working memory (ES = −0.29, 95% CI = −0.53 to −0.05) and visual learning (ES = −0.40, 95% CI = −0.68 to −0.13). For the remaining 4 domains (processing speed, attention/vigilance, verbal learning, reasoning/problem solving) no significant differences between CHR-C and CHR-NC were observed.

Conclusion: Based on the current meta-analytic data we might conclude that it is possible to differentiate between CHR-C and CHR-NC with respect to working memory and visual learning. The addition of visual learning and working memory tasks to psychosis regression models might contribute to the predictive power of these models.

1. Introduction

Early identification and treatment of subjects at clinical high risk (CHR) for schizophrenia may result in attenuation, delay or even prevention of the onset of first psychosis in some individuals (Yung et al., 2005, 2006; Correll et al., 2010). The CHR state indicates a very high risk of developing psychosis within the first 3 years of clinical presentation, and this risk progressively increases across this period (Fusar-Poli et al., 2012a). Although reported transition rates vary, the best powered studies have observed rates of conversion to full psychosis of about 30–40% over 2–3 years of follow-up (Gee and Cannon, 2010; Fusar-Poli et al., 2012a). The transition risk, the age of the patient, the nature of the treatment provided, and the way the syndrome and transition to psychosis are defined (Fusar-Poli et al., 2012a). The related question about the appropriateness of the inclusion of a "psychosis risk syndrome" in DSM-V is the subject of a lot of controversy. Some authors believe that the available data on both transition rate and the effectiveness of interventions within UHR-samples weighs heavily enough to justify the inclusion of a "psychosis risk syndrome" in DSM-V (Carpenter, 2009; Woods et al., 2009, 2010). However, others oppose the inclusion of such a syndrome in DSM-V because the available study results are found by others to be too limited in number and probative value (Ross, 2010; Yang et al., 2010). Identifying markers of psychosis transition in CHR individuals is a critical step along the pathway to prevention strategies (Sabb et al., 2010). During the past decade, a well-defined set of clinical criteria, the ultra high risk (UHR) criteria, have been developed to detect an imminent risk for conversion to psychosis (Yung et al., 2005; Pukrop et al., 2007). The original UHR criteria required that a young person aged between 14 and 30 being referred for mental health problems met the criteria for 1 or more of the following groups: (1) The *APS group*: those who have experienced subthreshold, positive *attenuated psychotic symptoms* during the past year; (2) the *brief limited intermittent psychotic symptom* (commonly referred to as *BLIPS*) group: those who have experienced episodes of frank psychotic symptoms that have not lasted longer

* Corresponding author at: Department of Rehabilitation Science, KU Leuven, Belgium; Tervuursevest 101 box 1500, B-3001 Heverlee, Belgium. Tel.: +32 468 221223.
E-mail address: amber.deherdt@faber.kuleuven.be (A. De Herdt).

0920-9964/$ – see front matter © 2013 Elsevier B.V. All rights reserved.
http://dx.doi.org/10.1016/j.schres.2013.06.017

than a week and have spontaneously abated (that is, without treatment); and (3) the trait and state risk factor group: those with a first-degree relative with a psychotic disorder or the identified patient has an SPD in addition to a significant decrease in functioning or chronic low functioning during previous year (Yung et al., 2003, 2004; Yung and Nelson, 2013). Across studies, severity of attenuated positive symptoms, poorer social functioning, substance abuse, and genetic risk for schizophrenia appear to be consistent predictors of conversion to psychosis (Gee and Cannon, 2010; Fusar-Poli et al., 2012a). Nevertheless, a substantial fraction of the variance within psychosis conversion remains unexplained, and the detection of additional predictive biomarkers is needed to increase the reliability of identifying individuals in a potential at risk state for developing a psychosis (Pukrop et al., 2007; Correll et al., 2010; Gee and Cannon, 2010). A useful way to explore early psychosis markers is the identification of differences in biopsychosocial baseline functioning between psychosis converters (CHR-C) and non-converters (CHR-NC) (Correll et al., 2010).

Neuropsychological deficits are considered to be core symptoms of schizophrenia (SZ) (Elvevag and Goldberg, 2000; Gold, 2004; Green et al., 2004; Lencz et al., 2006). Impairments manifest themselves prior to the full clinical presentation of the syndrome and are persistent over time (Lencz et al., 2006; O'Donnell, 2007; Giuliano et al., 2012). Neuropsychological deficits in CHR subjects have shown to be intermediate between control and first-episode psychosis samples, with small-to-medium impairments (ES = −0.26 to −0.67) across most neurocognitive domains (Fusar-Poli et al., 2012a,b; Giuliano et al., 2012). Therefore, it is reasonable to assume that cognitive functioning may also be predictive for future psychosis (Cadenhead, 2002) and that prediction of transitions could be improved by introducing neurocognitive tests into a stepwise risk assessment (Riecher-Rössler et al., 2009). In the past few years an increasing number of studies have focused on predictive and/or vulnerability markers in CHR patients by comparing the baseline neurocognitive profile of CHR-C and CHR-NC (Wood et al., 2003; Bartok et al., 2005; Brewer et al., 2005; Francey et al., 2005; Keefe et al., 2006; Lencz et al., 2006; Pukrop et al., 2007; Wood et al., 2007; Hawkins et al., 2008; Walder et al., 2008; Riecher-Rössler et al., 2009; Becker et al., 2010a,b; Jahshan et al., 2010; Koutsouleris et al., 2010; Mittal et al., 2010; Olvet et al., 2010; Sabb et al., 2010; Seidman et al., 2010; Woodberry et al., 2010; Kim et al., 2011; Meijer et al., 2011; Broome et al., 2012). Findings from these follow-up studies suggest that certain cognitive impairments in CHR individuals might display stable vulnerability markers (sustained attention) (Francey et al., 2005; Lencz et al., 2006), while others (verbal IQ, processing speed, verbal memory, working memory) might predict transition to first psychosis (Brewer et al., 2005; Lencz et al., 2006; Pukrop et al., 2007; Jahshan et al., 2010; Seidman et al., 2010). Particular emphasis was placed on both verbal memory and processing speed performance as main neurocognitive predictors for psychosis conversion (Lencz et al., 2006; Pukrop et al., 2007; Riecher-Rössler et al., 2009; Lin et al., 2011). Reported data however remain inconsistent (Keefe et al., 2006). The central aim of this study was to provide a meta-analysis comparing the baseline neurocognitive profile of CHR-C and CHR-NC. We hypothesized that CHR-C subjects would present an overall more impaired neurocognitive functioning compared to CHR-NC subjects.

Another topic of debate in psychosis research is the selection of separable cognitive dimensions to understand, interpret and report domain-specific neurocognitive deficits. To facilitate domain comparisons between CHR-C and CHR-NC subjects, we chose to use the neurocognitive domains that are described in the 'Measurement and Treatment Research to Improve Cognition in Schizophrenia' (MATRICS) cognitive battery (Nuechterlein et al., 2008). The MATRICS is a consensus battery suitable for the assessment of cognitive function in clinical trials of cognition enhancing drugs. Integrating the MATRICS domains might tackle previous inconsistent use of too many different cognitive domains. The separable MATRICS cognitive dimensions also have broader relevance to future research aiming at the understanding of nature and structure of core cognitive deficits in schizophrenia (Nuechterlein et al., 2004).

2. Methods

2.1. Literature search

MEDLINE (PubMed), Embase and Web of Science databases were searched from inception to May 2012 to identify all studies with baseline neurocognitive data of CHR young adults who did or did not convert to a first schizophrenic psychosis. A combination of the following Medical Subject Headings (Mesh) and search terms was used: "at risk mental state" OR "ultra high risk" OR "clinical high risk" OR "prodrome", OR "prodromal" OR " psychosis" – AND " neurocognition"; – AND "neuropsychology"; – AND "processing speed"; – AND "attention"; – AND " vigilance"; – AND "working memory"; – AND short term memory; – AND "verbal memory"; – AND "visual learning"; – AND "reasoning"; – AND "problem solving"; – AND "social recognition ". The systematic review was executed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) standard, including evaluation of bias (confounding, overlapping data, publication bias) (Moher et al., 2009). Title and abstract screening of publications found in the databases was executed by two independent investigators. In the event of disagreement or uncertainty, the full text was read and discussed until conformity was achieved. After database extraction, the next phase of the search strategy involved hand searching for unpublished studies and for studies potentially overlooked or absent from the databases by screening the references of all retrieved articles.

2.2. Inclusion/exclusion criteria

Inclusion criteria for the studies in the current meta-analysis were the following: 1) to be published in an English language peer-reviewed journal, 2) to have a clinical follow-up design 3) to report neurocognitive baseline data of CHR-C and CHR-NC as defined by the UHR-criteria (Yung et al., 2003, 2004; Yung and Nelson, 2013), and 4) the availability of mean (±SD)-, F-, p-, or t-values of baseline neurocognitive data of both groups. Regarding inclusion criteria 3 and 4, the corresponding author was contacted in the case of missing data. Studies in affective psychoses were excluded a priori. There were no inclusion or exclusion criteria for sample-size.

2.3. Neurocognitive domains

To provide a comprehensible frame for the present meta-analysis all included neurocognitive tests were categorized into separate neurocognitive (NC) domains. The selection of the NC domains was based on the MATRICS recommendations: speed of processing (with inclusion of verbal fluency), attention/vigilance, working memory, verbal learning/memory (with inclusion of verbal comprehension), visual learning/memory, reasoning/problem solving, and social cognition (Nuechterlein et al., 2004, 2008). Categorizing the test variables into NC domains was based predominantly on prior summarizing studies in the field of SZ. Table 1 provides an overview of the 7 MATRICS domains and the assigned individual cognitive tests.

2.4. Statistical analysis

For each neurocognitive test result, an effect size was computed. Since the standardized mean difference has been shown to be upwardly biased when based on small sample sizes, Hedges's g, that corrects for this bias, was selected as an unbiased effect size with negative values of Hedges's g reflecting a poorer performance in the CHR-C group