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Subjects at Ultra High Risk for psychosis have 'heterogeneous' intellectual functioning profile: A multiple-case study

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ABSTRACT

In Ultra High Risk (UHR) studies, intellectual functioning is commonly assessed using premorbid IQ tools as a covariate. The aim of this study was to show that the use of the Wechsler Adult Intelligence Scale (WAIS) could yield accurate neuropsychological profiling and that an alternative approach such as a multiple-case study could be a more interesting way to isolate discrete cognitive processes in the early stage of illness.
The studied population consisted of 198 adolescents and young adults (16–30 y.o.) referred to our outpatient clinic. After the CAARMS' interview, we defined 3 subgroups: UHR ($N = 104$), First Episode (FE; $N = 30$), and Help-Seekers (HS; $N = 64$) who were neither UHR nor psychotic. Intellectual functioning was assessed by the WAIS-III (9 subtests version) and 'heterogeneous' intellectual profiles were defined based on the existence of a 3-point difference in scoring at subtests constitutive of the same WAIS index.
While UHR did not differ from FE or HS on WAIS' scores and sub-scores, the multiple-case study indicated a higher proportion of 'heterogeneous' profiles in the Verbal Comprehension Index in the UHR sample than in FE and HS ($p = 0.04$).
The disease progression could heterogeneously impact on specific domains, in patterns depending on the stage of the illness. This approach exploring intra-subject WAIS performances might be more relevant than the use of global scores in detecting the subtle cognitive alteration of emerging psychosis.
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1. Introduction

Cognitive impairment in schizophrenia has been well documented and is thought to be an intrinsic feature of the illness (Green et al., 2004; Heinrichs, 2005; Mesholam-Gately et al., 2009). In individuals at Ultra High Risk for psychosis (UHR), very few studies focused specifically on intellectual functioning; usually a premorbid verbal intelligence quotient is estimated and most authors (Gschwandtner et al., 2006; Lencz et al., 2006; Pflueger et al., 2007; Simon et al., 2007) reported no abnormalities (Pukrop and Klosterkotter, 2010).

The Wechsler Adult Intelligence Scale (WAIS) provides a comprehensive assessment of current intellectual functioning, exploring Verbal Comprehension, Perceptual Organization, Working Memory, and Processing Speed. Findings from previous UHR studies are contradictory with reports of lower IQ compared to healthy controls or lower Performance, but not Verbal IQ (Brewer et al., 2005), no significant deviance from norm (Hawkins et al., 2004; Niendam et al., 2006; Chung et al., 2008), or verbal IQ impairments restricted to UHR who will develop psychosis later on (Woodberry et al., 2010; Giuliano et al., 2012).

This lack of consistency suggests that the exploration of intellectual functioning in individuals at UHR needs a different approach than a basic comparison of scores to normative data, or to healthy control global scores. First, mean-based statistics can overlook specific cognitive deteriorations in population with various degrees of cognitive impairment. Second, help-seeking subjects who do not meet criteria for UHR might be a better control population than healthy controls; showing similar confounding factors such as distress, depressive and/or anxiety symptoms, substance use or medication, this clinical population is more relevant when trying to identify specific cognitive deficits related to early psychosis stages. Finally, a quantitative approach with the use of global scores could not be the best way to analyse the intellectual efficiency' assessment provided by the WAIS battery.

Looking at indices rather than global scores has been previously proposed as a more comprehensive way to explore intellectual functioning in schizophrenia (Wilk et al., 2005) and in autism (Minshew et al., 2005; Towgood et al., 2009). This methodology might be more informative since it provides information beyond a crude score and allows exploring the homogeneity of performance, i.e. 'normal'

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intellectual functioning, in the various WAIS' subtests. In UHR population, i.e. before the FE of psychosis, it can be hypothesized that subjects show subtle cognitive impairments, rather than deficits in a whole domain, thus we expect UHR subjects to show heterogeneous scores within indices.

The aim of this study was to compare intellectual functioning in UHR subjects with age-and gender- matched Help-Seeking (HS) and First-Episode psychosis (FE) subjects using the WAIS-III, 9 subtests version (Wechsler, 1997). We first described subjects' intellectual functioning looking at Full-scale, Verbal and Performance IQ, as well as subtests' scores. Then, we looked at the existence of 'heterogeneous' cognitive profiles in the whole sample and compared the distribution of these 'heterogeneous' profiles between groups.

We first hypothesized that there will be no difference on general intelligence scores between UHR and HS subjects while we expected altered processing speed (measured by the Digit Symbol Coding subtest) in the FE group compared to HS and UHR. Second, using a multiple-case study design, we expected to find more 'heterogeneous' profiles in the UHR than in the HS and FE groups.

2. Materials and methods

2.1. Settings

Participants were recruited from the Adolescents and Young Adults Assessment Centre (C'JAAD), a specialized outpatient unit dedicated to adolescents and young adults, in an Academic Mental Health department (SHU), Sainte-Anne Hospital, Paris (see (Magaud et al., 2010) for further details). Fully trained clinical psychologists and psychiatrists conducted the assessments within the Clinical Research Centre (CERC) following standardized procedures. All individuals gave their written informed consent. All the study's procedure fulfilled the recommendations of the Helsinki Declaration and the EU recommendations for Good Clinical Research Practice and followed French ethical regulation.

2.2. Subjects

The sample consisted of 198 young adults (16–30 y.o.) who consecutively sought help at the C'JAAD between 2005 and 2011. The inclusion criteria for this study were (1) a recent alteration in global functioning (GAF < 70 during the last year) associated with (2) psychological distress and/or decline in functioning and/or psychiatric symptoms. We excluded subjects with already diagnosed psychosis (meeting DSM-IV criteria for schizophrenia or schizo-affective disorders), pervasive developmental, or bipolar disorders, as well as patients with well-established diagnosis such as obsessive–compulsive disorders. Other exclusion criteria were: current treatment by antipsychotic for more than 12 weeks, psychoactive substance dependence or abuse (DSM-IV criteria) during the previous year and/or for more than five years; serious or evolutive somatic and neurological disorders; head injury and IQ lower than 70, and non French-native speaking.

2.3. Clinical ratings

An expert psychiatrist (MK) conducted the Comprehensive Assessment of At-Risk Mental State interview — CAARMS (Yung et al., 2005); French translation (Krebs et al., 2006). The CAARMS has been found to have good to excellent reliability (Yung et al., 2005).

Three subgroups of patients were established following the CAARMS criteria: Ultra High Risk, First Episode of Psychosis and Help-seekers individuals. The Help-seekers group corresponds to young help-seekers suffering from psychological distress who do not reach the CAARMS' criteria for UHR or psychosis.

Symptomatology was assessed using the Brief Psychiatric Rating Scale 24 items, extended version with anchor — BPRS-24 EA (Krebs et al., 2006; Mouaffak et al., 2010). Subscales were derived from a factorial solution performed on 202 psychiatric inpatients explaining 66.2% of the total variance. The "positive" component includes items 1, 6, 9, 10, 11, 12, 14, 19, 20, "mania" includes items 7, 8, 21, 22, 23, "negative" includes items 13, 16, 17, 18, and "depressive' includes items 2, 3, 4, 5. Items 15 and 24 had good representation on the negative component and were extracted from the positive component to make a "disorganization" subscale. This factorial solution is similar to Dingemans' methodology (Dingemans et al., 1995) and was used to describe better the "at-risk" profile and psychosis psychopathology considering research concerns.

2.4. Intellectual functioning evaluation

Assessment of intellectual functioning was performed blind to CAARMS categorization.

2.4.1. WAIS scales, sub-scales and indices

The WAIS is the primary clinical instrument used to estimate adult and adolescent intelligence. Ninety minutes are necessary to administrate the 9-subtests version of the WAIS-III including: Vocabulary, Similarities, Information (constituting the Verbal Comprehension Index, VCI), Arithmetic, Digit Span (part of Working Memory Index, WMI), Picture Completion, Block Design, Matrix Reasoning (constituting the Perceptive Organization Index, POI) and Digit Symbol-Coding subscale (part of Processing Speed Index, PSI) (Fig. 1). We used the WAIS-III manual and Wechsler's instruction to obtain age-scaled scores, providing a Verbal IQ (VIQ), a Performance IQ (PIQ), a Full scale IQ (FIQ), as well as indices' scores (VCI, POI). Working Memory and Processing Speed Indices could not be calculated using the 9-subtests version.

2.4.2. WAIS profiles: homogenous, heterogeneous and deteriorated

According to the manual, a 'homogeneous' profile is defined by the absence of significant differences between subtests' scores within each WAIS-III index. The cut-off used to determine 'heterogeneous' profiles is a 3-point discrepancy between the lower and the higher scores on subtests within an index. This difference is equivalent to 1 standard deviation. For example, if *Similarities'* score is 8 and *Information*'s score is 12, the subject is considered as having a 'heterogeneous' profile in the Verbal Comprehension Index.

"Deteriorated" scores are scores lower than 7, corresponding to one standard deviation from normative data.

2.5. Data analysis

ANOVAs and post-hoc tests (Test of Homogeneity of variance Tukey or Games–Howell) were used to compare group scores on VIQ, PIQ and FIQ, as well as on each subtest scores. A chi-square test was used to compare the proportion of individuals with 'heterogeneous' and deteriorated profiles between the 3 groups. SPSS 18 (SPSS, 2010) software was used for statistical analysis.

3. Results

3.1. Demographic and clinical characteristics of the sample

Among our sample, 104 met UHR criteria, 30 met FE criteria, and 64 were HS controls. Table 1 summarizes the sample characteristics.

There was no difference between groups in age, gender, educational level, tobacco and cannabis use (current and age at first time). The only difference was on alcohol use; HS were more often current regular alcohol users, but had a later age of onset than the UHR group ($p < 0.01$).

Groups showed similar scores on depression but significantly differed on other symptomatology level (BPRS subscales), the UHR group showing intermediate scores (Table 1). Post-hoc tests indicated significant differences in mania, positive, negative and disorganization

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