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## Review of the literature

# Neuropsychology of subjects with ultra-high risk (UHR) of psychosis: A critical analysis of the literature



## Neuropsychologie des sujets à ultra-haut risque de psychose (UHR) : une analyse critique de la littérature

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## ABSTRACT

Cognitive disorders are currently considered as central components of disorders found in schizophrenia and are a major handicap for patients day to day. These disorders appear before the first psychotic episode, in the prodromal phase, during which time the symptoms are below the threshold for psychosis. People with these symptoms are considered as presenting an at-risk mental state (or at ultra-high risk, UHR of psychosis) and their risk for psychotic transition is between 20% and 40% within one year. Despite a number of studies, the chronology in which cognitive disorders appear in relation to the psychotic symptoms has not clearly been established and the study of the links between cognition and symptoms could improve our understanding of psychotic disorders. The detection of certain cognitive disorders before the onset of psychotic disorders could help improve early detection. We carried out a systematic analysis of the literature exploring cognitive disorders found in subjects with UHR for psychosis. The objective of most studies was to establish the predictive value for psychotic transition. Nevertheless study results have shown little consensus. Faced with this heterogeneity of results from past studies, we carried out a critical analysis of the literature and suggest areas of reflection for future research.

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## R É S U M É

Les troubles cognitifs sont actuellement considérés comme un élément central des troubles présents dans la schizophrénie et comme un handicap majeur ressenti au quotidien par les patients. Ces troubles sont présents en amont du premier épisode psychotique, dès la phase « prodromique » pendant laquelle, les symptômes sont présents à un niveau infraliminaire du seuil de psychose. Les personnes présentant ces signes sont considérés comme ayant un « état mental à risque de psychose » (ou à ultra-haut risque) et leur risque de transition psychotique est de 20 à 40 % à un an. Malgré de nombreuses études, la chronologie d'apparition des troubles cognitifs par rapport aux symptômes psychotiques n'est pas encore clairement établie et l'étude des liens entre cognition et symptômes pourrait améliorer la compréhension des troubles psychotiques. La reconnaissance de certains troubles cognitifs avant l'expression de troubles psychotiques pourrait aussi permettre d'améliorer la détection précoce. Nous avons réalisé une analyse

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systématique de la littérature explorant les troubles cognitifs rapportés chez les sujets à ultra-haut risque de psychose. L'objectif de la plupart des études est d'établir leur valeur prédictive de transition psychotique. Néanmoins, les résultats des études sont peu consensuels. Devant l'hétérogénéité des résultats des études antérieures, nous effectuerons une analyse critique de la littérature et proposerons des pistes de réflexion pour les études futures.

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## 1. Introduction

Schizophrenia can be considered as a neurodevelopmental pathology resulting from cerebral anomalies acquired early with a delayed occurrence [1]. For many years, cognitive disorders have been seen as a central characteristic of this pathology [2]. Cohort studies have evidenced the existence of cognitive anomalies occurring long before the first psychotic episode: a decrease in intellectual abilities [3], or a decline in verbal abilities [4]. Neurosciences, and in particular neuropsychology, have enabled a better characterization of these cognitive impairments, affecting at the same time neurocognition (attention, memory, executive functions, etc.) [5], and social cognition (which includes, according to Pinkham et al. [6], theory of mind, emotional perception, social perception and knowledge, and attributional style) [7]. This second category of functions has significant functional repercussions on autonomy and rehabilitation, and plays a major role in how patients affected feel on a daily basis [8]. However, even though cognitive impairments in schizophrenia are now well documented, the chronology of their appearance and developmental trajectory has not clearly been established. Indeed, the first psychotic episode that signals the onset of the illness is preceded by a prodromal state, during which time clinical symptoms are present at a subliminal level. Patients suffering from these symptoms are said to be at-risk (AR) or ultra-high risk (UHR) and are likely to develop a psychotic disorder in only one third of cases [9].

Studies exploring cognition among AR subjects have aimed to understand the cognitive processes occurring during the evolution of psychosis, and to determine whether certain cognitive disorders are predictive of a psychotic transition, so as to suggest early preventive intervention strategies. Existing studies have however shown little consensus. The objective of this article was to review current knowledge on the cognitive functioning of AR subjects and carry out a critical analysis of the studies involved, in order to understand the heterogeneity of their results. We carried out a systematic search of the articles and a methodological analysis of the studies described. Finally, we make a few suggestions concerning future areas of research.

## 2. Methodology

We carried out a bibliographic search on Medline and Web of Sciences in two steps, first by targeting meta-analyses on cognition in UHR subjects and secondly by searching for recently published articles, not reported in the meta-analyses (see Fig. 1). For the first stage we used the following keywords ((cogniti\* or cognitive impairment or, neurocogniti\* or social cognition) and (ultra-high risk or clinical high risk for psychosis or at-risk mental state or first episode psychosis or prodromal schizophrenia) and (meta-anal\*)). Concerning the meta-analyses, we preselected articles on their title and then screened them on the basis of the abstracts. This bibliographical search led us to study more particularly 7 meta-analyses [10–16]. In the second step, we carried out a similar search excluding the term meta-anal\* and restricting our search to the years 2013 to 2016, in order to target articles subsequent to the meta-analyses selected. Our bibliographical search is summarized in two

tables, the first one showing cognitive impairments in UHR subjects compared to healthy subjects and the second describing potential differences in the cognitive profiles associated with psychotic transition in UHR subjects. For the first table, we excluded: all studies that did not provide effect sizes (16% of articles), those in a language other than English or French (7% of articles) and those that did not provide a comparison between UHR subjects and control groups (6% of articles). Then, for the second table we excluded all articles that did not mention the subjects' performance at baseline (5% of articles).

## 3. Results

### 3.1. Description of the populations at-risk for psychosis

The prodromal state includes an initial phase in which subjects show not very specific signs associated with slight changes in perception and cognition, and a later phase in which attenuated or transitory psychotic symptoms appear.

### 3.2. The early prodromal phase

During the early phase, subjects show non-specific signs associated with slight changes in perception and cognition that can be related to the notion of basic symptoms (BS) suggested by Huber [17] and then Klosterkötter [18]. BSs correspond to subtle experiences relating to emotions, perception and cognition, not yet detected by the clinician but already felt by patients as the first experiences announcing a pre-eminently subjective change in their perceptions of themselves and the environment. These subjective changes occur before the acute symptoms of psychosis [19]. Their assessment has been made easier by the Bonn Scale Assessment for Basic Symptoms (BSABS, [20]) and the Schizophrenia Proneness Instrument, Adult version (SPI-A, [21]). BSs are therefore early prodromes, occurring throughout the course of the pathological process. The conversion rate for these subjects is under 1% after one year, but it is 48% after four years.

### 3.3. The later prodromal phase

During the later phase, subjects are considered as at ultra-high risk for psychosis (UHR) or Clinical high risk (CHR). According to this approach, three non-exclusive sub-groups have been outlined combining a significant decrease in global functioning over the past year with:

- attenuated psychosis, corresponding to a progressive intensification of attenuated positive psychotic symptoms (fleeting hallucinatory perceptions that are more and more intense, ideas of persecution, etc.);
- Brief Limited or Intermittent Psychotic Symptoms (BLIPS) consisting in the occurrence of brief psychotic episodes of fewer than seven days that resolve spontaneously;
- vulnerability for subjects with a first degree relative is affected by the illness or for young people with a schizotypal personality disorder.

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