Schizophrenia Research 154 (2014) 100–106

Contents lists available at ScienceDirect

Schizophrenia Research

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

Improving the clinical prediction of psychosis by combining ultra-high risk criteria and cognitive basic symptoms

Frauke Schultze-Lutter [a,*], Joachim Klosterkötter [b], Stephan Ruhrmann [b]

[a] University Hospital of Child and Adolescent Psychiatry and Psychotherapy, University of Bern, Bolligenstr. 111, 3000 Bern 60, Switzerland
[b] University of Cologne, Department of Psychiatry and Psychotherapy, Kerpener Str. 62, 50937 Cologne, Germany

ARTICLE INFO

Article history:
Received 1 September 2013
Received in revised form 30 January 2014
Accepted 14 February 2014
Available online 7 March 2014

Keywords:
Ultra-high risk
Attenuated psychotic symptom
Basic symptom
Cognitive disturbances
Prediction
Cognition

ABSTRACT

Objective: Cognitive impairments are regarded as a core component of schizophrenia. However, the cognitive dimension of psychosis is hardly considered by ultra-high risk (UHR) criteria. Therefore, we studied whether the combination of symptomatic UHR criteria and the basic symptom criterion "cognitive disturbances" (COGDIS) is superior in predicting first-episode psychosis.
Method: In a naturalistic 48-month follow-up study, the conversion rate to first-episode psychosis was studied in 246 outpatients of an early detection of psychosis service (FETZ); thereby, the association between conversion, and the combined and singular use of UHR criteria and COGDIS was compared.
Results: Patients that met UHR criteria and COGDIS (n = 127) at baseline had a significantly higher risk of conversion (hr = 0.66 at month 48) and a shorter time to conversion than patients that met only UHR criteria (n = 37; hr = 0.28) or only COGDIS (n = 30; hr = 0.23). Furthermore, the risk of conversion was higher for the combined criteria than for UHR criteria (n = 164; hr = 0.56 at month 48) and COGDIS (n = 158; hr = 0.56 at month 48) when considered irrespective of each other.
Conclusions: Our findings support the merits of considering both COGDIS and UHR criteria in the early detection of persons who are at high risk of developing a first psychotic episode within 48 months. Applying both sets of criteria improves sensitivity and individual risk estimation, and may thereby support the development of stage-targeted interventions. Moreover, since the combined approach enables the identification of considerably more homogeneous at-risk samples, it should support both preventive and basic research.

1. Introduction

Current models of psychoses assume a stepwise process in the formation of positive symptoms: neurobiological changes result in impaired information processing and, consequently, in aberrant experiences (Garety et al., 2001; Kapur, 2003). Thus, cognitive impairment as defined by deficient neurocognitive test performance is integral to the development of psychosis, and "impaired cognition" is one of the eight "dimensions of psychotic symptom severity" proposed in DSM-5 (APA, 2013, p. 743f). Yet, the cognitive dimension is not considered in the ultra-high risk (UHR) criteria of psychosis (Yung et al., 1998; Miller et al., 1999).

1.1. Cognitive impairments in early at-risk stages

Small-to-medium impairments in the neurocognitive test performance of at-risk patients have been repeatedly described, although considerable inter-individual variability exists (Fusar-Poli et al., 2013). These impairments appear to progress during the development of first-episode psychosis: in the very early stages, defined by the presence of cognitive and perceptive basic symptoms (BS; Schultze-Lutter et al., 2007a) and the absence of attenuated (APS) and/or transient psychotic symptoms (BLIPS), cognitive impairments are less pronounced or absent compared to later stages, in which APS and/or BLIPS of the UHR criteria are present (Pukrop et al., 2006, 2007; Frommann et al., 2011). Thus, in the early stage, two problems can occur with detecting emerging cognitive impairments by neurocognitive tests: (1) an early slight decline in test performance might not be detectable when the score is still within the normal range according to the respective test norms, and (2) a deficit below the normal range might not be detected when a person is still able to cope adequately (e.g., by over-focusing).

Thus, with regard to cognitive impairments, the early detection of psychosis resembles that of Alzheimer's dementia (AD; Knopman, 2012; Garcia-Ptacek et al., 2013). Mild cognitive impairments (MCI), as indicated by neurocognitive scores outside the normal range, are preceded by AD-related changes in the brain and by a subtle cognitive decline characterized by test performances that are still within the normal range (Jessen et al., 2010). This subtle cognitive decline shows a temporal association with the occurrence of subjective cognitive

* Corresponding author at: University Hospital of Child and Adolescent Psychiatry and Psychotherapy, Bolligenstr. 111, Haus A, 3000 Bern 60, Switzerland. Tel.: +41 31 932 8564; fax: +41 31 932 8569.
E-mail addresses: frauke.schultze-lutter@kjp.unibe.ch (F. Schultze-Lutter), joachim.klosterkoetter@uk-koeln.de (J. Klosterkötter), stephan.ruhrmann@uk-koeln.de (S. Ruhrmann).

http://dx.doi.org/10.1016/j.schres.2014.02.010
0920-9964/

Table 1
The ultra-high risk criteria according to the Structured Interview of Prodromal Syndromes (SIPS; McGlashan et al., 2001) and the basic symptom criterion 'Cognitive Disturbances' according to the Schizophrenia Proneness Instrument, Adult version (SPI-A; Schultze-Lutter et al., 2007a, 2007b; Fux et al., 2013).

UHR criterion 'Attenuated Psychotic Symptoms' (APS)
➲ At least any 1 of the following 5 symptoms with a SIPS score of '3' to '5'
• Unusual thought content/delusional ideas (P1)
• Suspiciousness/persecutory ideas (P2)
• Grandiosity (P3)
• Perceptual abnormalities/hallucinations (P4)
• Disorganized communication (P5)
➲ First occurrence or worsening within past 12 months
➲ At least weekly occurrence within past month
UHR criterion 'Brief Limited Intermittent Psychotic Symptoms' (BLIPS)
➲ At least any 1 of the above 5 symptoms (P1–P5) with a SIPS score of '6'
➲ Psychotic level of intensity, i.e., a score of '6' was reached within past 3 months
➲ At least present for several minutes per day at a frequency of at least once per month
UHR 'trait-state' criterion
➲ At least any 1 of the following risk criteria
• 1st-degree biological relative with a history of psychotic disorder
• Schizotypal personality disorder in patient[a]
➲ At least a 30% drop in GAF score over the last month as compared to 12 months ago
Basic symptom criterion 'Cognitive Disturbances' (COGDIS)
➲ At least any 2 of the following 9 basic symptoms
• Unstable ideas of reference (B2)
• Disturbances of abstract thinking (D7)
• Inability to divide attention (D8)
• Thought interference (D9)
• Thought pressure (D10)
• Disturbance of receptive speech (D11)
• Disturbance of expressive speech (D12)
• Thought blockages (D15)
• Captivation of attention by details of the visual field (O2)
➲ Occurrence of at least 'several times in a month or weekly' within the past 3 months, i.e. a SPI-A score of at least '3'

GAF: Global Assessment of Functioning scale.
[a] Due to the participation of the FETZ in the German Research Network on Schizophrenia, this criterion was replaced with 'obstetric complications' since July 2000 (Schultze-Lutter et al., 2009).

impairment (SMI) in subjects with subsequent dementia, which suggests that affected individuals experience this initial reduction in cognitive performance (Jessen et al., 2010; Knopman, 2012). Thus, in the detection of the initial subtle decline within the early at-risk stage of AD, SMI might be more reliable than neurocognitive test deficits, whose assessment faces the same two problems as outlined above for the early at-risk stage of psychosis (Stewart, 2012).

In psychosis, the "basic symptoms" (BS) concept is the approach that is most similar to the concept of SMI in AD (Klosterkötter, 1992; Schultze-Lutter, 2009). The term "basic" refers to the idea that subjects may notice subtle changes (i.e., BS), which result from the disturbances in neural information processing that underlie the development of psychosis, at very early stages. Thus, similar to SMI in AD, BS have always been regarded as closely related to neurobiology (Schultze-Lutter, 2009), whereas subsequently occurring APS and/or psychotic symptoms have been considered final psychopathological expressions or "end phenomena", which develop on the basis of dysfunctional or insufficient coping (Klosterkötter, 1992; Schultze-Lutter, 2009). This assumption has recently been revived in the model of aberrant salience for the development of positive symptoms (Kapur, 2003).

1.2. Cognitive basic symptoms in risk assessment

BS criteria are based predominately on cognitive disturbances and the BS criterion "cognitive disturbances" (COGDIS) predicts future psychosis well, independent of UHR (Klosterkötter et al., 2001; Schultze-Lutter et al., 2007a, 2012). COGDIS frequently co-occurs with symptomatic UHR criteria (APS and BLIPS) in help-seeking at-risk samples (Schultze-Lutter et al., 2007a, 2010; Ruhrmann et al., 2010; Ziermans et al., 2011), and this co-occurrence was suggested to define a more homogeneous sample of clinically and neurocognitively impaired persons (Simon et al., 2006). Therefore, a combined UHR and BS approach may improve the prediction of psychosis and the diagnostic/outcome-related homogeneity of risk groups. Initial support for this assumption over a short-term follow-up period of 18 months has been shown (Ruhrmann et al., 2010).

1.3. Aims

The present study aimed to determine whether the combined use of UHR criteria and COGDIS is superior to the singular use of either in predicting first-episode psychosis over an extended period of 48 months. We expected the combined use to be more effective.

2. Methods

2.1. At-risk criteria

APS, BLIPS, and COGDIS (Table 1) have been employed as risk criteria at the Cologne Early Recognition and Intervention Centre (FETZ; Schultze-Lutter et al., 2009). The selection of risk factors included in the third UHR criterion, the trait-state criterion, had changed throughout the baseline assessment period (Table 1; Schultze-Lutter et al., 2009). A "trait-state" UHR criterion (Yung et al., 1998) would have been met by only two patients and, for the change in definition, was not used as a risk criterion in the present study.

The exclusion criteria were as follows: (1) lifetime diagnosis of psychosis; (2) diagnosis of delirium, dementia, amnestic or other cognitive neurological disorders, mental retardation, psychiatric disorders, or symptoms due to a somatic factor or psychotropic substances; and (3) general medical conditions affecting the central nervous system (for details see Schultze-Lutter et al., 2009).

2.2. Recruitment procedure

The sample consisted of patients who (1) had consulted the FETZ during the first 6 years of service (1998–2003), (2) had not already been diagnosed with past or present psychosis at baseline (for detailed descriptions of the sample and the recruitment/referral procedure see Schultze-Lutter et al., 2009), and (3) had been contacted again between 2004 and 2009.

The FETZ is part of the Department of Psychiatry and Psychotherapy at the University Hospital of Cologne that delivers in- and outpatient treatment. The FETZ operates within a universal multi-payer system, meaning that health care is funded on a service-delivery basis and largely dominated by health insurance plans, in which enrolment is mandatory. Private practitioners, who are economically independent within a statutory framework of the main insurance organization, provide the majority of outpatient service (Salize et al., 2007). Thus, throughout the follow-up period, 83.7% of the initial patients [particularly those not considered at-risk at baseline (100%)] (see also Schultze-Lutter et al., 2009), had not or only temporarily remained in contact with the FETZ, but had been referred (back) to private practitioners for treatment. Contact was re-established with these persons by mail after 53 months, on average (SD = 21; Mdn = 53; range 12–124). The first letter contained a detailed description of the study's aims and was followed by a maximum of 2 reminder letters.

When letters were returned because of an invalid address, the current address was identified by telephone registers and/or with the help of registration offices. All residents of Germany are required to register current addresses and address changes at the local registration