

Pathways to psychosis: A comparison of the pervasive developmental disorder subtype Multiple Complex Developmental Disorder and the “At Risk Mental State”

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Abstract

Background: The comparison of high-risk populations with different developmental pathways to psychosis may lend more insight into the heterogeneity of the manifestation of the psychotic syndrome, and possible differing etiological pathways.

Aim: To compare high-risk traits and symptoms in two populations at risk for psychosis, i.e. (1) help-seeking adolescents presenting with prodromal symptoms meeting the criteria for At Risk Mental State (ARMS), and (2) adolescents with Multiple Complex Developmental Disorder (MCDD), a PDD-NOS subtype characterized by severe, early childhood-onset deficits in affect regulation, anxieties, disturbed social relationships, and thought disorder.

Method: 80 ARMS- and 32 MCDD-adolescents (12–18 years) were compared on prodromal symptoms (Structured Interview of Prodromal Symptoms, and Bonn Scale for the Assessment of Basic Symptoms-Prediction list), and autism traits (Social Communication Questionnaire). In addition, both high-risk groups were compared with 82 healthy controls on schizotypal traits (Schizotypal Personality Questionnaire-Revised).

Results: Although the high-risk groups clearly differed in early developmental and treatment histories as well as autism traits, they did not differ with regard to schizotypal traits and basic symptoms, as well as disorganized and general prodromal symptoms. There were, however, group differences in positive and negative prodromal symptoms. Interestingly, 78% of the adolescents with MCDD met criteria for ARMS.

Conclusion: These findings suggest that children diagnosed with MCDD are at high risk for developing psychosis later in life, and support the notion that there are different developmental pathways to psychosis. Follow-up research is needed to compare the rates of transition to psychosis in both high-risk groups.

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1. Introduction

Psychotic symptoms are not only part of the syndromes of schizophrenia and other psychotic disorders, but may also arise in other psychiatric

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disorders, in particular the affective disorders (American Psychiatric Association, 1994). In addition, certain personality disorders (Benvenuti et al., 2005; Dowson et al., 2002; Rodriguez Solano and Gonzalez, 2000), and genetic syndromes such as Klinefelter (DeLisi et al., 1994; Kunugi et al., 1999; Van Rijn et al., 2006) and 22q11-deletion syndrome (Baker and Skuse, 2005; Debbane et al., 2006; Murphy et al., 1999; Vorstman et al., 2006) have been associated with elevated risks of psychotic symptoms and schizophrenia spectrum disorders.

Retrospective studies have shown that the onset of overt psychosis is often preceded by prodromal signs and symptoms, including functional decline, subtle deviations in thought, emotion and perception, and subthreshold psychotic symptoms (e.g. Häfner et al., 1999; Schothorst et al., 2006). Over the past decade, the focus of attention in schizophrenia research has been widened to also include the prodromal phase. Projects are being set up all over the world to identify and offer treatment to prodromal individuals in the hope of preventing or delaying psychotic outbreak (e.g. Addington, 2004; Bechdolf et al., 2006; Chong et al., 2004; Klosterkötter et al., 2005; McGlashan et al., 2003; McGorry et al., 2002; Ruhrmann et al., 2005). However, because the term “prodrome” can only be used in retrospect, the terms “ultra high-risk” or “clinical high-risk” or “At Risk Mental State” (ARMS) are used. The first results of these projects have indicated that ARMS individuals are indeed at imminent risk of psychosis, with transition rates ranging from 15% to 54% after 6 months to 1 year (e.g. Haroun et al., 2006; Miller et al., 2002).

Another population at risk for psychosis consists of subjects with Multiple Complex Developmental Disorder (MCDD), a subtype of pervasive developmental disorder not otherwise specified (PDD-NOS) which is characterized by early childhood-onset affect dysregulation, high levels of anxiety, social impairment, and thought disorder. This combination of symptoms has received various labels in the past, including borderline syndrome of childhood, multiplex developmental disorder, schizoid disorder, and schizotypal disorder (Ad-Dab'bagh and Greenfield, 2001; Cohen et al., 1986). Cohen et al. (1986, 1994) proposed a set of diagnostic criteria for MCDD (Table 1), which have been refined by Towbin et al. (1993), and Buitelaar and Van der Gaag (1998). Follow-up of 55 children with MCDD revealed a considerably elevated risk of psychosis; 22% that had been followed until adolescence, and 64% that had been followed until young adulthood had developed schizophrenia spectrum disorders (Van Engeland and Van der Gaag, 1994).

Table 1

Diagnostic criteria for Multiple Complex Developmental Disorder (MCDD; Cohen et al., 1994)

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- 1) Regulation of affective state and anxiety is impaired beyond that seen in children of comparable age, as exemplified by several of the following:
 - a. intense generalized anxiety or tension
 - b. fears and phobias (often unusual or peculiar)
 - c. recurrent panic episodes or flooding with anxiety
 - d. episodes of behavioral disorganization punctuated by markedly immature, primitive or violent behaviors
 - e. significant and wide emotional variability with or without environmental precipitants
 - f. frequent idiosyncratic or bizarre anxiety reactions
 - 2) Consistently impaired social behavior/sensitivity, as exemplified by the following types of disturbances:
 - a. social disinterest, detachment, avoidance or withdrawal despite evident competence
 - b. severely impaired peer relationships
 - c. markedly disturbed attachments; high degree of ambivalence to adults (especially parents/caregivers)
 - d. profound limitations in the capacity for empathy or understanding others affects accurately
 - 3) Impaired cognitive processing (thinking disorder), as exemplified by some of the following difficulties:
 - a. irrationality, sudden intrusions on normal thought process, magical thinking, neologism or repetition of nonsense words, desultory thinking, blatantly illogical, and bizarre ideas
 - b. confusion between reality and inner fantasy life
 - c. perplexity and easy confusability (trouble understanding social processes or keeping thoughts 'straight')
 - d. delusions, overvalued ideas including fantasies of omnipotence, paranoid preoccupations, over-engagement with fantasy figures, grandiose fantasies of special powers, and referential ideation
 - 4) The syndrome appears during the first several years of life
 - 5) The child is not suffering from autism or schizophrenia
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The notion that some psychotic patients show premorbid behavioral abnormalities dates back to Bleuler (1911), and since then it has often been confirmed (e.g. Isohanni et al. 2000; Niemi et al. 2003). Furthermore, the fact that subjects with MCDD have severe impairments from early childhood, whereas the ARMS-symptoms are identified in adolescents and young-adults who in most cases have been relatively inconspicuous as a child, suggests that there are different developmental pathways to psychosis. This is supported by a retrospective study in schizophrenia patients by Rossi et al. (2000) who identified two subgroups. The first displayed only minor behavioral abnormalities during childhood, which increased progressively over the years. The other already displayed severe behavioral abnormalities during childhood, which remained relatively stable over time. Corcoran et al. (2003), who retrospectively studied the evolution of symptoms in ARMS-adolescents, also identified two

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