

Familial covariation of the subclinical psychosis phenotype and verbal fluency in the general population

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Abstract

Objective: Cognitive impairments may be markers of familial transmission of liability to psychosis. This study examined to what degree the subclinical psychosis phenotype in the general population shows similar familial continuity with cognition, measured with a verbal fluency test, and whether this was similar for men and women.

Methods: Measures of the subclinical psychosis phenotype and verbal fluency were administered to a general population sample of genetically related individuals ($n=425$).

Results: In men but not women, higher levels of the subclinical psychosis phenotype were associated with worse verbal fluency performance both within and across relatives.

Conclusion: Psychosis and verbal fluency may be more strongly linked in men than in women, and this difference is also expressed at the subclinical level of the phenotype.

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1. Introduction

There is evidence that the psychosis phenotype is expressed as a continuous distribution of experiences (Van Os et al., 2001). At levels outside the clinical

disorder, expression may be attenuated and take the form of psychosis proneness or ‘schizotypal’ signs and symptoms (Chapman et al., 1994; Raine et al., 1994). Similar to the substantial level of familial clustering of psychotic disorders, there is evidence that the attenuated expressions of psychosis aggregate within families, both in relatives of patients with schizophrenia (Grove et al., 1991; Kendler et al., 1996) and in the general population (Linney et al., 2003).

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Impaired cognitive functioning is a hallmark of schizophrenia (Goldberg et al., 1990; Nuechterlein et al., 1994). Subtle neurocognitive abnormalities have also been found in relatives of patients with schizophrenia, suggesting that cognitive impairments are markers of familial transmission of liability to psychosis (Faraone et al., 1999; Keefe et al., 1994; Krabbendam et al., 2001). It is not known, however, whether subtle cognitive abnormalities also covary with the subclinical psychosis phenotype the general population. Therefore, in the present study, two approaches were used to examine the relationship between cognition, measured using a verbal fluency test, and the subclinical psychosis phenotype in the general population. First, in a cross-trait within-relative approach, the hypothesis was tested that verbal fluency performance is associated with dimensions of the subclinical psychosis phenotype. Second, in a cross-trait between-relative approach, it was examined whether verbal fluency performance in one relative was associated with the subclinical psychosis phenotype in the other.

2. Materials and methods

2.1. Procedure and sample

The Continuum of Mental Disorders Study (COMED study) is a longitudinal family study in the general population in the city of Sittard, The Netherlands, consisting of two measurement points (hereafter, T_1 and T_2).

In order to recruit a general population sample, 4589 subjects aged 36–65 years were randomly selected and sent a letter in which they and their family members were asked to participate. The total general population sample comprised 768 subjects aged 17–77 years, pertaining to 116 families. Taking into consideration every possible family relationship between subjects, 61.0% of the sample were first-degree relatives, 18.2% second-degree, 6.6% third-degree, and 0.4% were fourth-degree relatives; 13.8% of the subjects were married or partners.

At T_1 , all participants filled in the Community Assessment of Psychic Experiences (CAPE) (Stefanis et al., 2002). The CAPE is a self-report

questionnaire measuring attenuated psychotic experiences in the affective and nonaffective domains. The subjects with a mean (between 40th and 60th percentile) and a high (above 75th percentile) score on the CAPE positive symptom dimension were asked, together with their family members, to participate in the second measurement occasion. At T_2 , trained psychologists administered the Structured Interview for Schizotypy—Revised (SIS-R) (Kendler et al., 1989; Vollema and Ormel, 2000) and a verbal fluency test (naming animals) (Lezak, 1995). Verbal fluency was selected because of its high discriminatory power between controls from the general population on the one hand and people with psychotic disorder and their relatives on the other (Gilvarry et al., 2001), in addition to its short duration and ease of administration.

The mean interval between T_1 and T_2 was 7.7 months (S.D. 4.8 months; range 1–26 months). At T_2 , 496 subjects were interviewed using the SIS-R, and 434 subjects were administered the verbal fluency test. The risk set consisted of all subjects who had completed the CAPE at the T_1 interview and the SIS-R and verbal fluency at the T_2 interview ($n=425$).

2.2. Analyses

All analyses were carried out using STATA version 8 (StataCorp, 2003).

First, cross-trait, within-relative linear regression analyses were conducted to examine, within subjects, the association between each dimension of the subclinical psychosis phenotype on the one hand and verbal fluency on the other. Robust estimates of variance were used, which allow observations that are not independent across groups (i.e., families). All analyses were adjusted for the possible confounding effects of age, sex, level of education and drug use. Sex by psychosis dimension interactions were assessed, as previous studies have shown sex-related differences in both cognition and psychosis symptom dimensions (Leung and Chue, 2000). Effect sizes were expressed as the standardized regression coefficient.

Second, cross-trait, between-relative analyses were conducted to examine the associations between verbal fluency in relative 1 and dimensions of the subclinical psychosis phenotype in relative 2. A data

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