Basic symptoms in offspring of parents with mood and psychotic disorders

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Background

Basic symptoms, defined as subjectively perceived disturbances in thought, perception and other essential mental processes, have been established as a predictor of psychotic disorders. However, the relationship between basic symptoms and family history of a transdiagnostic range of severe mental illness, including major depressive disorder, bipolar disorder and schizophrenia, has not been examined.

Aims

We sought to test whether non-severe mood disorders and severe mood and psychotic disorders in parents is associated with increased basic symptoms in their biological offspring.

Method

We measured basic symptoms using the Schizophrenia Proneness Instrument – Child and Youth Version in 332 youth aged 8–26 years, including 93 offspring of control parents, 92 offspring of a parent with non-severe mood disorders, and 147 offspring of a parent with severe mood and psychotic disorders. We tested the relationships between parent mental illness and offspring basic symptoms in mixed-effects linear regression models.

Results

Offspring of a parent with severe mood and psychotic disorders ($B = 0.69$, 95% CI 0.22–1.16, $P = 0.004$) or illness with psychotic features ($B = 0.68$, 95% CI 0.09–1.27, $P = 0.023$) had significantly higher basic symptom scores than control offspring. Offspring of a parent with non-severe mood disorders reported intermediate levels of basic symptoms, that did not significantly differ from control offspring.

Conclusions

Basic symptoms during childhood are a marker of familial risk of psychopathology that is related to severity and is not specific to psychotic illness.

Severe mood and psychotic disorders (SMPD) are mental disorders that cause functional impairment and substantially interfere with one or more major life activities. These disorders often follow a chronic or recurrent course and available treatments have limited efficacy.[1–4] Improving upon our ability to predict SMPD may be useful to inform targeted early interventions to prevent its onset.[5] Recent research has shown that there is substantial overlap in the genetic and environmental contributors to various forms of SMPD.[6–10] Consequently, it may be useful to identify overlapping, transdiagnostic predictors of mood and psychotic disorders that can be detected early enough to allow for preventive interventions. Self-experienced disruptions in thought, perception and other essential mental processes, referred to as basic symptoms, are potential early indicators of SMPD risk.[11]

Basic symptoms and risk of mental illness

Basic symptoms may represent an early manifestation of mood and psychotic disorders, particularly psychotic illness.[5,11,12] Positive symptoms of psychosis include hallucinations and/or delusions, which are perceived by the affected individual as real experiences. In contrast to positive psychotic symptoms, basic symptoms are immediately recognised by the individual as abnormal disturbances to their typical thoughts, senses and feelings.[13] These symptoms are often present years before the onset of illness and can be assessed in children as young as 8 years old.[14] Basic symptoms have been examined in detail as a potential precursor to psychotic illness. Basic symptoms strongly predict the onset of psychotic illness.[5] Basic symptoms have also been linked to other forms of mental illness, including affective disorders[15,16] and are associated with lower global functioning among individuals with a range psychiatric disorders.[17] However, the utility of basic symptoms as an indicator of risk for a broader range mental disorders remains to be examined.

Family high-risk approach

The best-known predictor of mood and psychotic disorders is a family history of illness.[18] Risk of illness is proportional to the degree of biological relatedness to the affected individual.[18] However, familial risk of mental illness is not disorder-specific. Individuals with a family history of schizophrenia are also at risk of mood disorders, and vice versa.[19] This finding is supported by molecular data that show that a substantial proportion of genetic variants and gene expression abnormalities associated with mental illness are shared across psychiatric disorders.[8,9,20,21] Taken together, these findings suggest that it may be useful to identify measurable experiences and behaviours that predict SMPD and are shared across disorders. By examining early manifestations of risk among offspring of parents with SMPD, we are able to distinguish possible causes or predictors of illness from the effects of SMPD and its treatment. Individuals who have a first-degree biological relative living with schizophrenia experience more basic

symptoms than controls.[22,23] However, basic symptoms have not yet been examined among youth at high familial risk for other forms of mental illness.

Aims

Here we examine the relationship between basic symptoms and family history of a spectrum of non-severe mood disorders (NSMD) and SMPD. We assessed basic symptoms in a sample of youth enriched for offspring of parents with major depressive disorder, bipolar disorder and schizophrenia, including both NSMD and SMPD. We aimed to test whether offspring basic symptoms are associated with parent mental illness, its severity, psychotic features or specific psychiatric diagnosis.

Method

Participants

The present study includes information from 909 assessments of 332 participants aged 8–26 years from 201 families, enrolled in the Families Overcoming Risks and Building Opportunities for Well-being (FORBOW) study.[24] Assessors masked to information on parents, assessed basic symptoms annually with the baseline assessment occurring at an average age of 11.84 years (range 8–24 years). Each participant completed a median of three assessments (range 1–6) at 12-month intervals. Repeated basic symptom measures from all assessments were included in analyses. We included offspring of parents with major depressive disorder, bipolar disorder, psychosis spectrum disorders and offspring of control parents. Offspring of parents with SMPD were recruited through their parents' contact with mental health services in Nova Scotia, Canada. Offspring were included regardless of whether or not they had psychopathology. Age matched offspring of control parents were recruited through local school boards. To ensure that control offspring were approximately matched with offspring of affected parents on socioeconomic status, we selectively recruited control offspring from the same schools and neighbourhoods of the offspring of affected parents. We excluded offspring with a lifetime diagnosis of schizophrenia ($n = 2$ observations), schizoaffective disorder ($n = 2$ observations) or bipolar disorder ($n = 8$ observations).

We assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008. The study protocol was approved by the Research Ethics Board of the Nova Scotia Health Authority (file number 100 266). We obtained written informed consent from participants who had the capacity to provide it. For participants who did not have the capacity to make an informed decision, a parent or guardian provided written informed consent and the participant provided assent.

Parent assessment

Diagnoses of mental disorders and psychotic symptoms according to the DSM-IV and DSM-5 were established using the Schedule for Affective Disorders and Schizophrenia (SADS-IV)[25] or the Structured Clinical Interview for DSM-5 Disorders (SCID-5).[26] Diagnoses were confirmed in consensus meetings with a psychiatrist masked to offspring psychopathology.

We defined SMPD as a diagnosis of major depressive disorder, bipolar disorder or a psychosis spectrum disorder accompanied by two or more of the following five severity criteria: (a) recurrent, (b) chronic, (c) presence of psychotic symptoms, (d) life-threatening suicide attempt(s) or (d) required hospital admission.[24] We defined NSMD as a diagnosis of any Axis I mood disorder that did not

meet two or more severity criteria. In situations where one biological parent had NSMD and one biological parent had SMPD, the offspring were placed in the SMPD group.

Offspring assessment

General psychopathology

Offspring were assessed for all Axis I disorders at 12-month intervals using the Kiddie Schedule for Affective Disorders and Schizophrenia – Present and Lifetime Version (K-SADS-PL; in offspring younger than 18 years)[27] or the SCID-5 (in offspring ≥18 years old).[26] A single assessor completed both the diagnostic interview and the basic symptoms interview. Offspring assessors were masked to parent psychopathology. Diagnoses were confirmed in consensus meetings with a psychiatrist masked to parent diagnoses.

Basic symptoms

We assessed basic symptoms using the Schizophrenia Proneness Instrument – Child and Youth Version (SPI-CY).[14] The SPI-CY was designed to be administered to children and youth and it has been used among children aged 8 years and older with good inter-rater reliability.[14,28] The SPI-CY contains two psychosis-risk basic symptom profiles: Cognitive-Perceptive (COPER) and Cognitive Disturbances (COGDIS). COGDIS items have been shown to strongly predict psychotic illness and are part of the clinical high-risk criteria that have been recommended for the early detection of psychosis.[5] Descriptions of the items in both high-risk profiles are provided in the Appendix. We calculated the SPI-CY risk score as the total number of COPER or COGDIS items scored 3 (several times in a month or weekly) to 6 (daily), divided by the total number of items with a valid frequency rating. We calculated a COGDIS score, which incorporates the nine items included in the COGDIS criteria, using the same process. For analyses, we standardised the SPI-CY risk score and COGDIS score by the means and standard deviations of the control offspring scores.

Antecedent basic symptoms

It may be desirable to use a dichotomous indicator of basic symptoms in applications that require yes or no decisions. Therefore, we defined antecedent basic symptoms as the presence of COPER and/or COGDIS criteria.[24] We report the rates of offspring who met our predefined antecedent basic symptoms threshold at their first assessment and at any assessment.

Statistical analysis

We tested the effect of parent mental illness on offspring basic symptoms in mixed-effects linear regression models using the lme4 package,[29] implemented in R Studio (R version 3.4.3).[30] We accounted for the non-independence of observations from related individuals and from repeated measures within the same individual by including family and individual identifiers as random effects in the models. We included fixed effects of age, biological gender and time in the study as covariates. To test the effect of parent's primary illness severity (control, NSMD, SMPD) on offspring basic symptoms, we fitted a linear mixed regression model with standardised offspring SPI-CY risk score as the dependent variable and parent illness severity as the independent variable. We tested the effect of parent psychosis (control, non-psychotic illness, psychotic illness) on offspring basic symptoms by fitting a linear mixed regression model with standardised offspring SPI-CY risk score as the dependent variable and parent psychosis as the independent variable. We tested the effect of parent's primary diagnosis (control, major depressive disorder, bipolar disorder, psychosis spectrum disorder) on offspring basic symptoms by fitting a

linear mixed regression model with standardised offspring SPI-CY risk score as the dependent variable and parent diagnosis as the independent variable (see supplementary Tables 9 and 10 and supplementary Fig. 2 available at https://doi.org/10.1192/bjo.2019.40). We also tested the effects of parent illness severity, parent psychotic symptoms and parent diagnosis on offspring COGDIS scores separately, using the same methodology as described above. Effect sizes are summarised with standardised beta coefficients and their 95% confidence intervals.

Sensitivity analyses

We opted not to exclude offspring with major depressive disorder from the primary analyses because depression was common and excluding it would reduce the representativeness of the sample. However, to ensure that our results were not unduly influenced by offspring depressive disorders, we performed sensitivity analysis by excluding observations in which offspring had experienced a major depressive episode within the 12 months prior to the assessment. Additionally, the prevalence and clinical significance of basic symptoms has been shown to vary with age.[31] As we included participants across a broad range of ages, we stratified analyses by age and tested the effect of parent illness severity (control, NSMD, SMPD) on offspring basic symptoms among participants aged 11 years and under and 12 years and older separately (see supplementary materials).

Fig. 1 Mean Schizophrenia Proneness Instrument – Child and Youth Version (SPI-CY) risk score and Cognitive Disturbances (COGDIS) score, stratified by parent illness severity group.

NSMD, non-severe mood disorder, SMPD, severe mood and psychotic disorders. Error bars represent standard error of the mean.

Results

Participant characteristics and basic symptom scores

The sample included 93 offspring of control parents, 92 offspring of a parent with NSMD and 147 offspring of a parent with SMPD. The characteristics of the participants and the rates of antecedent basic symptoms across parent groups are shown in Table 1.

Differences in SPI-CY risk scores by parent illness severity

Across the 909 assessments of 332 children and youth with valid SPI-CY risk scores, basic symptoms were significantly elevated among the offspring of parents with SMPD compared with controls ($B = 0.69$, 95% CI 0.22–1.16, $P = 0.004$; see Figures 1 and 2). Basic symptom scores were numerically elevated among offspring of parents with NSMD, but this difference was not statistically significant ($B = 0.22$, 95% CI −0.30 to 0.73, $P = 0.415$). When we excluded observations at which offspring experienced a major depressive
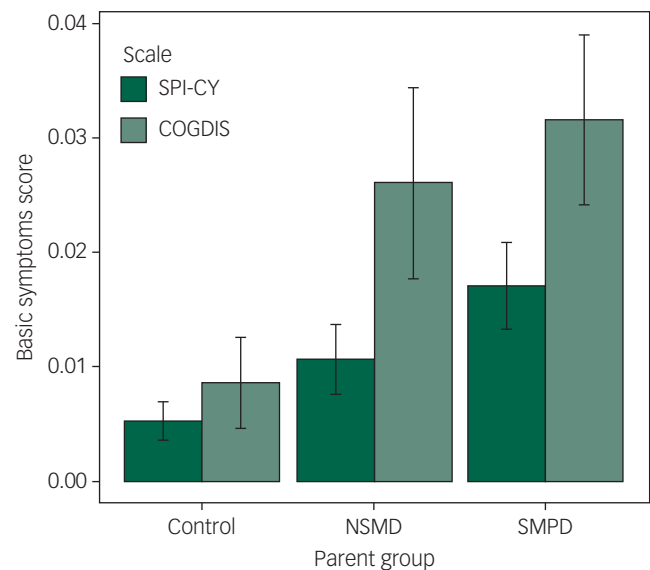
episode within 12 months prior to the assessment, basic symptoms remained significantly elevated among the offspring of parents with SMPD ($B = 0.49$, 95% CI 0.10–0.87, $P = 0.014$). Full regression results are shown in supplementary Tables 1 and 2. In age-stratified analyses, these findings remained consistent in both the younger (8–11 year olds) and older (12 years and older) subsets (see supplementary Tables 11 and 13 and supplementary Figs. 3 and 4).

Differences in COGDIS score by parent illness severity

Across the 905 assessments of 331 children and youth with valid COGDIS scores, basic symptoms were significantly elevated among the offspring of parents with SMPD compared with controls ($B = 0.53$, 95% CI 0.13–0.93, $P = 0.009$; see Figs. 1 and 2). When we excluded observations at which offspring experienced a major depressive episode within 12 months prior to the assessment, basic symptoms remained significantly elevated among the offspring of parents with SMPD ($B = 0.39$, 95% CI 0.04–0.73,

Table 1 Demographic and clinical characteristics of the participants[a]

	Parent group		
	Control (*n* = 93)	Non-severe mood disorder (*n* = 92)	Severe mood and psychotic disorders (*n* = 147)
Families, *n*	60	59	88
Parent diagnosis			
Major depressive disorder, *n*	0	85	62
Bipolar disorder, *n*	0	7	68
Schizophrenia, *n*	0	0	17
Parent illness psychotic features, *n*	0	1	58
Offspring			
Age, mean (s.d.)[b]	12.11 (3.1)	13.65 (4.2)	13.78 (4.0)
Number of follow-ups, mean (s.d.)[b]	2.43 (1.3)	2.66 (1.4)	3.02 (1.6)
Females, *n* (%)[b]	42 (45.2)	44 (47.8)	83 (56.5)
Antecedent BS at baseline, *n* (%)	12 (12.90)	16 (17.39)	35 (23.81)
Antecedent BS ever, *n* (%)[b]	18 (19.35)	26 (28.26)	54 (36.73)

BS, basic symptoms.
a. Differences between groups were tested using univariate ANOVA for continuous variables or χ² tests for categorical variables.
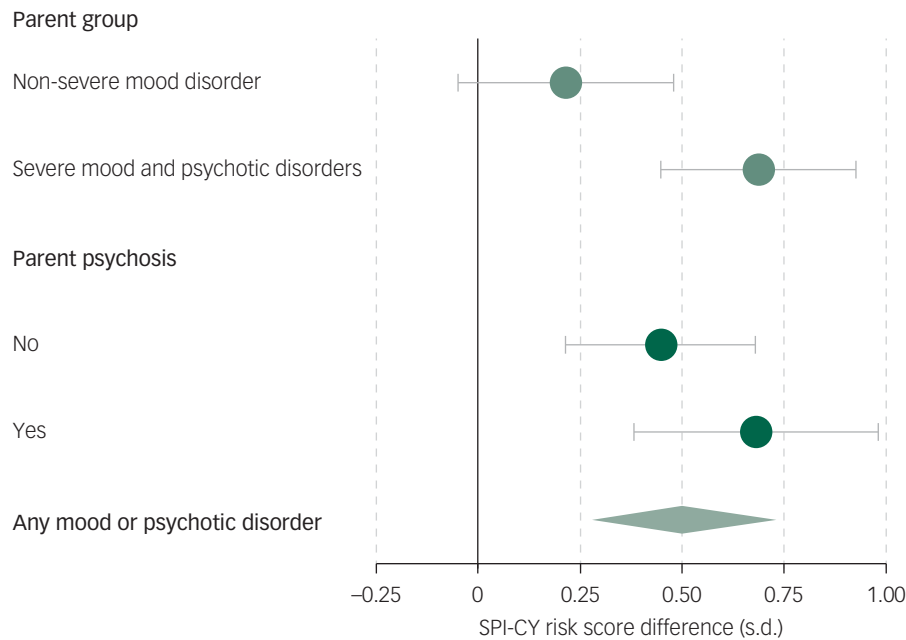b. Denotes statistically significant group differences between the three groups.

Fig. 2 Effect of parent illness on offspring basic symptoms.

Circles represent the effect size of the standard deviation (s.d.) increase in Schizophrenia Proneness Instrument – Child and Youth Version (SPI-CY) risk score compared with controls for each parent group. Whiskers represent the standard error.

$P = 0.028$). Full regression results are shown in supplementary Tables 3 and 4. In age-stratified analyses, COGDIS scores were numerically increased among offspring of parents with SMPD, however these differences were only statistically significant in the younger (8–11 year olds) subset (see supplementary Tables 12 and 14 and supplementary Figs. 3 and 4).

Differences in basic symptom scores by parent psychosis

Across the 909 assessments of 332 children and youth with valid SPI-CY risk scores, basic symptoms were significantly elevated among offspring of a parent with psychotic mental illness compared with controls ($B = 0.68$, 95% CI 0.09–1.27, $P = 0.023$; see supplementary Fig. 1). Offspring of a parent with non-psychotic mental illness had numerically higher SPI-CY risk scores than controls, but this difference was not statistically significant ($B = 0.45$, 95% CI −0.01 to 0.90, $P = 0.055$, see supplementary Fig. 1). When we excluded observations in which offspring experienced a major depressive episode within 12 months prior to the assessment, both the offspring of parents with psychotic mental illness ($B = 0.44$, 95% CI −0.05 to 0.92, $P = 0.078$) and with non-psychotic mental illness ($B = 0.35$, 95% CI −0.02 to 0.72, $P = 0.067$) had numerically higher SPI-CY risk scores than controls, but the difference was not statistically significant. Similarly, COGDIS scores were significantly elevated among the offspring of parents with psychotic mental illness ($B = 0.55$, 95% CI 0.05 to 1.04, $P = 0.030$) and with non-psychotic mental illness ($B = 0.41$, 95% CI −0.02 to 0.80, $P = 0.037$). Full regression results are shown in supplementary Tables 5–8.

Antecedent basic symptoms

We defined antecedent basic symptoms as the presence of COPER and/or COGDIS high-risk criteria. The rate of youth meeting these high-risk criteria increased with increasing parent severity: 12.9% control offspring, 17.4% of offspring of parents with NSMD and 23.8% of offspring of parents with SMPD had antecedent basic symptoms at baseline (Table 1).

Discussion

Main findings

We sought to test whether basic symptoms during childhood and adolescence are elevated among offspring of parents with a spectrum of NSMD and SMPD. We found that basic symptoms were most elevated among offspring of parents with SMPD, intermediate in offspring of parents with NSMD, and lowest in offspring of control parents.

Comparison with findings from other studies

Our study was motivated by a need to identify early transdiagnostic indicators of risk for SMPD among youth. Previous studies have established that basic symptoms predict psychosis, and can be present years before its onset.[5,32] However, basic symptoms have not been previously examined among offspring of parents with a broad range of major mood and psychotic disorders. Consistent with prior studies which show offspring of parents with mental illness are at risk of developing psychopathology themselves,[19] we found that basic symptoms are elevated among the offspring of parents with SMPD compared with controls. We also confirmed that basic symptom scores are elevated among first-degree relatives of individuals with psychosis.[23] Our results are consistent with prior findings showing that offspring of parents with SMPD are at increased risk for multiple forms of psychopathology, in addition to the disorder present in the parent.[19] Additionally, it has been suggested that psychosis may represent a transdiagnostic indicator of illness severity.[33,34] This is supported by studies showing that the presence of psychotic symptoms in non-psychotic disorders has been associated with more severe illness and worse treatment outcomes.[35–38] Our results suggest that basic symptoms represent a

transdiagnostic marker of risk for SMPD that is not specific to psychotic illness.

Strengths and limitations

The present study benefits from the inclusion of offspring of parents with mental illness, resulting in a concentration of familial risk of psychopathology. As a result, our sample has a higher rate of basic symptoms than in the general population. We also benefit from a longitudinal design, with repeated assessments allowing the capture of basic symptoms over the period of several years. However, our results should be interpreted in the context of our study limitations. The main limitation is the smaller number of offspring of parents with a schizophrenia spectrum disorder. The majority of parents in our sample who experience psychosis have bipolar disorder or major depressive disorder with psychotic features. The smaller enrolment of offspring of parents with schizophrenia may be in part be because individuals with schizophrenia tend to have fewer children.[39] However, enrolment in our cohort is ongoing and will include more offspring of parents with schizophrenia spectrum disorders in the future. Additionally, since basic symptoms are more prevalent and may be more clinically relevant among older adolescents,[28,31] our study was limited by the inclusion of younger adolescents and children. However, in our age-stratified sensitivity analyses, we found that basic symptom scores were independently associated with parent mental illness among 8- to 11-year-old and 12- to 27-year-old offspring.

Implications

The results of our study have potential implications for future research. The finding that basic symptoms are elevated among young offspring of parents with SMPD can help target interventions to youth at high risk of mood and psychotic disorders, long before the onset of illness. Interventions aimed at preventing psychosis among individuals experiencing prodromal symptoms have been criticised, in part because 'good' outcomes may be synonymous with onsets of other, non-psychotic illnesses among intervention recipients.[34] It has been shown that earlier interventions produce better outcomes.[40,41] Our results suggest that basic symptoms may represent a useful transdiagnostic risk indicator. Basic symptoms could be used, in combination with other factors, to identify high-risk youth who may benefit from targeted interventions before the onset of major mental illnesses. Our results warrant further investigation in other familial high-risk cohorts. Additionally, the basic symptom assessment tool[14] could be adopted by cohorts currently using interview measures of psychopathology.

In conclusion, we found that basic symptoms are elevated among offspring of parents with SMPD, in addition to offspring of parents with psychosis. Our results suggest that basic symptoms during childhood are a marker of familial risk for psychopathology that is related to severity and is not specific to psychotic illness. Future studies could explore the value of basic symptoms as a transdiagnostic predictor of mental illness.

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Supplementary material

Supplementary material is available online at https://doi.org/10.1192/bjo.2019.40.

Appendix

Appendix Items included in the basic symptoms high-risk profiles.

Item name (item number)	Description	Example prompt
Decreased ability to discriminate between ideas and perception, fantasy and true memories (B1)	Difficulty locating the source of a memory resulting in an inability to distinguish between fantasy and true memories.	Do you become confused about whether you actually did something in the past or whether you just imagined it?
Unstable ideas of reference (B2)	Experiences of self-reference that are almost immediately rectified upon further consideration.	Do you ever think that the actions or comments of others are about you – but yet you are certain they are not?
Visual perception disturbances (B3, O1, O3)	Aspects of vision are misperceived but the individual is aware of their true appearance.	Do the outlines of objects sometimes appear broken, curved or wavy?
Acoustic perception disturbances (B4.2, B5)	Non-verbal auditory pseudo-hallucinations, changes in the quality of sounds, or abnormally long-lasting residual sounds.	Do you sometimes have sudden short-lived difficulty with your hearing – like sounds being muffled or less loud?

(Continued)

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Appendix *(Continued)*

Item name (item number)	Description	Example prompt
Derealisation (B7)	A change in how one relates emotionally to the environment: (1) the environment appears unreal or altered, or (2) an increased emotional affinity for the environment.	Do you sometimes experience your surroundings as changed or strange? As if the world around you is not real?
Thought interference (D9)	Irrelevant thoughts are intruding on and disturbing the train of thought.	If you want to concentrate on something, is your concentration suddenly interrupted by unimportant, irrelevant thoughts?
Thought pressure (D10)	Thoughts or images randomly enter the mind and disappear again in quick succession, without the individual being able to suppress or guide them.	Do you sometimes have the feeling that you are not able to control your thoughts anymore?
Disturbance of receptive speech (D11)	Disturbance in the understanding of words that are either read or heard.	Do you sometimes have difficulty understanding conversations that you know you should be able to follow?
Thought perseveration (D14)	The annoying rehearsal of unimportant, emotionally neutral thoughts related to trivial events of the recent past.	Do you sometimes find yourself thinking about past events that have no special meaning, even though you want to think about something else or go to sleep?
Thought blockages (D15)	A sudden interruption in the flow of thoughts, of the mind suddenly going blank, or the fading of thoughts.	Do your thoughts sometimes disappear suddenly, as if they were cut short?
Disturbances of abstract thinking (D7)	Deficits in the ability to understand abstract, figurative or symbolic phrases beyond their literal meaning.	Do you have difficulty understanding the meaning of metaphors or abstract things like a saying or an idiom?
Inability to divide attention (D8)	Difficulty in dealing with demands that involve more than one sensory modality at a time.	Can you do two things at once as easily as you could before?
Disturbances of expressive speech (D12)	Subjective difficulty in finding the right words when trying to express oneself.	When you want to say something, do you struggle to find the right words?
Captivation of attention by details of the visual field (O2)	An ordinary visual stimulus stands out in a striking manner so that it appears almost isolated from the rest of the environment.	Is your attention sometimes caught by a detail in your surroundings, so that you need to look at it without wanting to?

The first five items are only in the Cognitive-Perceptive (COPER) high-risk profile, the next five items are included in both the COPER and COGDIS and the final four items are included only in the Cognitive Disturbances (COGDIS) high-risk profile. To fulfil COPER criteria, an individual must experience one of the first ten items at least several times in a month within the 3 months prior to assessment and the first occurrence must have been at least 12 months prior to the assessment. To fulfil COGDIS criteria, an individual must experience two of the last nine items, each at least several times in a month within the 3 months prior to assessment. Items B7, D7 and D15 can be consistently assessed in individuals aged 13 years and older.

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