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Psychotic experiences are associated with health anxiety and functional somatic symptoms in pre-adolescence.

Abbreviated Title: Psychotic experiences and health anxiety in preadolescence

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Background: Health anxiety (HA) is an increasing public health problem related to increased health service costs, and associated with functional somatic symptoms (FSS) and considerable personal suffering. Abnormal bodily experiences which may resemble HA and FSS are common in psychotic disorders, but a potential link between HA and psychosis vulnerability in childhood is largely unexplored. The current study estimates the association between subclinical psychotic experiences (PE) and HA and FSS in a general population cohort of preadolescents.

Methods: The study population consisted of 1572 11-12-year-old children from the Copenhagen Child Cohort 2000. PE were comprehensibly assessed as either present/not present using the Kiddie Schedule of Affective Disorders and Schizophrenia psychosis section. HA and FSS were assessed by self-report on validated questionnaires. Additional variables on general psychopathology, puberty and chronic somatic illness were also obtained.

Results: PE were associated with the top 10% high scores of HA (Odds Ratio (OR) 3.2 95%Cl 2.1-4.8) and FSS (OR 4.6 95%Cl 3.1-6.9) in univariate analyses. After mutual adjustment, the association was reduced (HA: OR 2.3 95%Cl 1.5-3.5; FSS: OR 3.7 95%Cl 2.4-4.7), suggesting interdependence. Further adjustment for potential confounders and general psychopathology only reduced the associations slightly: HA OR 2.2 (95%Cl 1.4-3.4); FSS OR 3.3 (95%Cl 2.1-5.2). Secondary analyses of subdimensions of HA showed that PE were associated with fears (OR 3.0 95%Cl 2.0-4.6) and daily impact of HA symptoms (OR 5.0 95%Cl 3.4-7.5), but not help seeking (OR 1.2 95%Cl 0.7-2.1)

Conclusion: This is the first study to investigate the associations between PE and HA and FSS, respectively. PE were significantly associated with HA and FSS over and above general psychopathology in preadolescence. Individuals with PE expressed high levels of health-related fears and daily impact, but no corresponding help-seeking behavior.

Abbreviations: PE=Psychotic experiences, HA=Health anxiety, FSS=Functional somatic symptoms

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Key-words: Psychosis; Anxiety; Somatisation; Epidemiology;

Introduction

Health anxiety (HA) is characterized by obsessive rumination and excessive fear of harboring a serious disease which interfere with daily function. Natural and transient bodily sensations (such as a temporary back-ache), and physiological changes (such as natural pubertal development or aging) are misinterpreted as signs of disease processes (Asmundson, Abramowitz, Richter, & Whedon, 2010; Fink et al., 2004). HA is often poorly identified in primary health settings, and many patients undergo excessive and futile medical investigations that do not provide relief from the underlying anxiety (Tyrer, Eilenberg, Fink, Hedman, & Tyrer, 2016). As a result, HA is associated with significantly increased health care expenditure and personal distress (Fink, Ørnbøl, & Christensen, 2010; Rask et al., 2016). Furthermore, increasing levels of HA in the population have been reported (Tyrer et al., 2011), perhaps as a result of increased attention to healthrelated issues in society, along with easily accessible information on the internet (Tyrer et al., 2016). In child and adolescent psychiatric research, HA is a rather new concept. HA has long been assumed to be rare in childhood and adolescence, with very low prevalence of actual disorders of hypochondriasis and somatization according to previous DSM-IV and DSM-III criteria (Schulte & Petermann, 2011). However, retrospective reports indicate that symptoms of HA in adults with hypochondriasis were often already present in childhood (Noyes et al., 2002), and developmentally appropriate assessment of HA have been lacking (Fritz, Fritsch, & Hagino, 1997; Mohapatra, Deo, Satapathy, & Rath, 2014; Wright & Asmundson, 2003). Self-reported HA symptoms are common in childhood in the general population, and high levels are associated with general emotional distress, increased health care costs and unspecific somatic complaints (Rask et al., 2016). Unspecific somatic complaints are commonly referred to as functional somatic symptoms (FSS), and may consist of symptoms from a variety of organ systems, such as unspecific musculoskeletal pain, gastro-intestinal complaints and neurological symptoms (Campo, 2012).

FSS and HA are associated with depression and anxiety (Campo, 2012; Janssens et al., 2010; Rask et al., 2016; G. Simon, VonKorff, Piccilnelli, Fullerton, & Ormel, 1999), however, other domains may play a role in the manifestation of this type of psychopathology. Abnormal bodily sensations and experiences are part of the basic symptom concept in the clinical evaluation of psychosis (Gross, Huber, Klosterkötter, & Linz, 1987), often referred to as 'cenesthopathies'. HA and FSS bear resemblance to those cenesthopathies which constitute central disturbances in body perceptions and information processing described in early stages of psychotic disorders. These include for example organ-specific or non-specific pains and sensations, numbness, hypersensitivities and 'hypochondrisms' with abnormal attributions of salience (Gross et al., 1987). An extreme clinical end-point of such cenesthopathies can be referred to as somatic delusions with bizarre causal explanations, such as "beetles are crawling underneath my skin and eating me up". Abnormal bodily experiences have arguably been largely overlooked in modern psychiatry (Jenkins & Röhricht, 2007), but recent studies have shown that as much as 75% of patients with first episode psychosis experience abnormal bodily experiences (Stanghellini, Ballerini, Fusar Poli, & Cutting, 2012), which in turn have been shown to predict poor long-term outcome in psychosis (Kobayashi & Kato, 2004). A recent review suggests that extensive physical changes in adolescence increase bodily awareness which may lead to health concerns and abnormal bodily experiences (A. Simon, Borgwardt, Lang, & Roth, 2014). The authors of this review highlight an overlap between HA symptoms and psychosis, and argue that disentangling the etiology of these symptoms can indeed be challenging. Such an overlap is in line with a growing body of research suggesting that psychosis is best viewed as a transdiagnostic phenomenon with a distribution in the general population (van Os & Reininghaus, 2016).

Psychosis can be viewed as a spectrum ranging from subclinical psychotic experiences (PE) to functionally impairing psychotic syndromes which usually debut in late adolescence and early adulthood (van Os, Linscott, Myin-Germeys, Delespaul, & Krabbendam, 2009). PE include hallucinations, delusions and thought-disturbances in the absence of psychotic disorders. PE can co-occur with non-psychotic mental health disorders, and mark an increased risk of later psychotic disorder (Kaymaz et al., 2012; Linscott & Van Os, 2013). A meta-analysis found that interview-based PE ranged from 9%-22.6% (median 17%) in 9-12-year-old children (Kelleher et al., 2012). PE are often functionally impairing in this age group, both in the context of mental health disorders and in children without diagnoses (Jeppesen et al., 2015; Kelleher et al., 2015). An affective pathway to psychosis has been studied extensively, supported by studies that report a strong effect of affective disturbances on the formation of PE (Klippel et al., 2017; Myin-Germeys & van Os, 2007). PE often co-occur with anxiety and depression in clinical populations (Achim et al., 2011; Upthegrove, Marwaha, & Birchwood, 2017; Wigman et al., 2012) and in non-clinical populations of children (Jeppesen et al., 2015, Kelleher et al., 2015). Furthermore, affective disturbances may have a causal impact on the formation of PE (Klippel et al., 2015, Kelleher et al., 2017; van Rossum, Dominguez, Lieb, Wittchen, & Van Os, 2011).

A shared association between affective psychopathology and HA and FSS on the one hand, and PE on the other, is intriguing. Such an association may represent either a specific pattern of PE correlates, or merely the expression of the multidimensional nature of psychopathology (Caspi et al., 2014; Stochl et al., 2015) - the notion that different domains of psychopathology are highly overlapping and do not respect diagnostic and categorical 'boundaries'. To our knowledge, the associations between PE and HA and FSS, respectively, have not previously been specifically studied. Therefore, we aimed to estimate the association between PE

and both HA and FSS in preadolescence, and test the following two main hypotheses: 1) PE are associated with both HA and FSS. 2) These associations are reducible in part to general psychopathology, but the associations remain after adjustment for general psychopathology – implying an independent association between PE and HA and FSS, respectively. To disentangle the dimensions of HA in children with PE compared to children without PE, secondary exploratory analyses will examine associations between sub-domains of HA and PE.

Methods

Study population

The current study is part of a longitudinal, prospective general population birth cohort study, the Copenhagen Child Cohort 2000 (CCC2000), comprising 6090 children born in the County of Copenhagen in the year 2000 (Skovgaard et al., 2005). The cohort is representative for all Danish children born that year regarding key perinatal characteristics, except for a relatively higher representation of ethnic minorities compared to the entire Danish population (Olsen, Skovgaard, Weile, & Jørgensen, 2007). Cross-sectional data from the 11-12-year follow-up, collected between May 2011 and October 2012, were utilized in this study. The children and their parents were invited by letter to participate in both web-based questionnaires and face-to-face assessments. Participants in the web-based questionnaires were included in lotteries for cinema-tickets. Children who participated in the face-to-face examination additionally received a schoolbag as a gift and were part of monthly lotteries for a gift card of about €700.

Measures

Psychotic experiences

To determine PE, the Kiddie Schedule for Affective Disorders and Schizophrenia – Present and Lifetime Version (K-SADS-PL) section on psychotic symptoms, was utilized (Kaufman et al., 1997). Hallucinations and delusions were assessed by a semi-structured interview with clinical probing and cross-examination of 22 types of PE, covering nine types of hallucinations and 13 types of delusions. For the analyses, symptoms were scored dichotomously as 'not present' vs. 'likely/definitely present' during the last month and/or lifetime before. We chose to combine the two measures of PE in 'lifetime before' and 'last month' because they showed a large overlap, and under the assumption that the manifestation of PE marks an increased psychosis vulnerability regardless of the timing and actuality of the experience (Jeppesen et al., 2015). PE were rated 'not present' if the child only heard someone calling their name, if the experience was described as hypothetical, or if the belief was culturally accepted (for example, as part of a shared religious belief). Interviews were performed by two medical doctors, two psychologists, one medical student and one psychology student who were all trained in the usage of the K-SADS. Approximately bi-monthly supervision sessions were conducted, supervised by a senior consultant child and adolescent psychiatrist (last author). The four raters who examined the majority of the children independently assessed 75 videotaped interviews, in order to determine inter-rater reliability. The agreement was very good for any PE ($\kappa = 0.94$) and for any hallucination ($\kappa = 0.91$) and moderate for any delusion ($\kappa = 0.64$), as reported previously (Jeppesen et al., 2015).

Health anxiety

The Childhood Illness Attitude Scale (CIAS) was used to assess HA. The CIAS has no time-focus and is based on the Illness Attitudes Scale which is the gold-standard instrument for measuring HA in adults. It consists of 35-items evaluating fears, beliefs, and attitudes associated with HA and abnormal illness behaviors in school-age children (Wright & Asmundson, 2003). All items are scored on a 3-point Likert scale, 1=none of the time, 2=sometimes, 3=a lot of the time. The current study used 21 items of the CIAS as recommended in a recent factor analysis (Thorisdottir et al., 2017), based on two samples from Canada and Denmark respectively (a sub-sample of the CCC2000). The 21 items inquire about 3 sub-dimensions of HA: i) fears e.g. "If you have pain, do you worry that it may be caused by a bad sickness?", ii) help-seeking e.g. "If pain lasts for a week or more, do you tell your mom or dad?", and iii) symptom effects (impact of symptoms) e.g. "Do strange feelings in your body stop you from going to school?". The total score range was 21-63 (11 items on fears scored 11-33, 6 items on help-seeking scored 6-18 and 4 items on symptom impact scored 4-12). The internal consistencies of the three factors were good (fears α =0.87, help-seeking α =0.83 and symptom impact α =0.74) (Thorisdottir et al., 2017). No clinically relevant cut-off points have been established for the CIAS, and we chose to arbitrarily dichotomize the scores into estimated high top 10% and low 90%, in line with our previous study (Rask et al., 2016).

Functional somatic symptoms

The Children's Somatization Inventory, Child Report Form, revised (CSI-24) assesses self-reported severity of unspecific somatic symptoms during the past 2 weeks. The CSI-24 measures a one-factor construct of somatization with good internal consistency reliability (α =0.88) (Walker, Beck, Garber, & Lambert, 2009). All items are scored on a 5-point scale ranging from 0 (not at all) to 4 (a whole lot), resulting in total FSS scores ranging from 0–96. The total score was dichotomized into estimated high top 10% and low 90% scores in the current study, as with HA.

General psychopathology

The Strengths and Difficulties Questionnaire (SDQ) is a highly structured, multi-informant questionnaire and screening instrument for child and adolescent psychopathology, and can be completed by the parent, teacher and the child itself from age 11. Validation studies of SDQ have shown good internal consistency (α =0.73) and predictive validity of high scores regarding the probability of being diagnosed with mental disorders (Goodman, 2001). The SDQ consists of 25 questions scored 0–1–2 on a Likert scale ('not true'– 'somewhat true'–'certainly true'). The 'total score' encompasses 20 questions within the following 4 domains: hyperactivity/inattention, conduct problems, emotional symptoms and peer relationship problems. For the current study we removed one item regarding somatic complaints, 'Often complains of headaches, stomach-aches or sickness', from the total score to ameliorate the risk of over-adjustment. Hence 19 items from the SDQ made up the measure of general psychopathology in this study, generating scores between 0-38. Furthermore, the parent version, and not the self-report, was chosen in this study to avoid same-rater bias.

DSM-IV diagnoses

For secondary analyses, DSM-IV emotional disorders (any DSM-IV diagnosis of anxiety and/or depressive disorders) were included instead of general psychopathology. The diagnoses were made using the Development and Well-Being Assessment (DAWBA) (Goodman, Ford, Richards, Gatward, & Meltzer, 2000). The DAWBA includes comprehensive information from the child and its parent, encompassing psychopathology broadly. Highly structured questions, together with open-ended descriptions, were synthesized by clinicians who decided on the final diagnoses. Information on all children were assessed by pairs of two consultant child and adolescent psychiatrists. The inter-rater validity for any diagnosis was good (Kappa = 0.81), as previously reported (Jeppesen et al., 2015). In cases of disagreement, consensus ratings were performed by the whole group of seven raters.

Chronic psychical conditions and puberty

Due to the potential confounding effect of actual somatic illness and bodily changes related to preadolescence, measures on puberty and chronic physical conditions were included in the current study. Chronic physical conditions were assessed using a list, asking parents to report if their child suffered from any chronic physical disease diagnosed by a doctor (e.g., asthma, diabetes, cardiac disease, epilepsy). Pubertal stage was assessed by self-report of Tanner staging presented as drawings, which is the most frequently used method of self-reported puberty (Coleman & Coleman, 2002). Onset of puberty was defined as Tanner stage 2≥ vs. no onset of puberty.

Register Data

Data from the Medical Birth Register and the Integrated Database for Labor Market Research were used to describe the perinatal and sociodemographic characteristics of the CCC2000 children.

Ethics

The study was approved by The Danish Data Protection Agency (J.nr. 2010-41-4438) and by the Capital Region of Denmark (J.nr. 2007-58-0015). The National Committee on Health Research Ethics was consulted (J.nr. H-C-FSP-2010). Participation was voluntary, and consent was given through participation. Data was analyzed anonymously and data kept confidentially.

Statistics

Differences in sociodemographic and perinatal characteristics between participants and non-participants alive at the time of examination were examined using χ^2 analyses. Univariate binomial regression analyses tested whether children who experienced PE had increased levels of HA and FSS. We performed multivariate binomial logistic regression analyses (method=enter), first mutually adjusting for HA and FSS, to examine to what degree any association with one would be reducible to an association with the other. Subsequently we did stepwise further adjustment for sex, stage of puberty, chronic somatic disorders and general psychopathology.

PE in relation to sub-dimensions of HA were explored using univariate logistic regression analyses.

In additional sensitivity analyses we excluded children with somatic delusions and tactile hallucinations, to assess if the associations were merely due to a common expression of psychopathology in these specific types of PE on one hand, and HA and FSS on the other.

All analyses were performed using SPSS version 24.

Results

Full data were available for 1572 children on the three variables of main interest (PE, HA and FSS) - see figure 1 for details on participation. Lacking puberty assessments on 35 children and missing data on the parental measure of general psychopathology for another 34, left 1503 children for the final model with all variables included.

The 1572 participants and the 4498 nonparticipants alive at the time of follow-up were compared regarding perinatal and socioeconomic factors. Participants had fewer psychosocial and perinatal adversities compared to non-participants (see online Appendix S1).

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PE were experienced by 9.9 % (n=156) of the sample. PE were significantly associated with both HA and FSS in univariate analyses (table 1). In the multivariate models, the associations of HA and FSS with PE were mutually adjusted (table 2, model 1) and further adjusted for sex, puberty, chronic somatic illness and general psychopathology. PE was still statistically significantly associated with both HA and FSS after adjustment for all the above variables (table 2, model 5a). Secondary analyses including emotional disorders, instead of general psychopathology, did not substantially change the results (table 2, model 5b).

Sensitivity analyses showed that the association between PE and HA and FSS did not change after excluding children with somatic delusions (n=10). Further exclusion of children with tactile hallucinations showed a trend towards attenuation of the association (n=47 excluded in total): OR HA 1.85 (95%CI 1.05-3.25) and OR FSS 2.48 (CI95% 1.41-4.37) in the final model (5a).

Table 3 depicts the secondary analyses investigating the specific associations between PE and the three dimensions of HA (fears, help-seeking and symptom impact). Fears and especially symptom impact were statistically significantly associated with PE, whereas parental help-seeking was not.

Discussion

Main results

In a large general population study of preadolescents, we found robust associations between PE and HA and FSS, respectively. The hypothesis that PE were associated with HA and FSS over and above adjustment for general psychopathology was confirmed. The associations were reduced after controlling for general psychopathology. However, most of the reduction in the multivariate analyses were due to the interdependence of HA and FSS. Sex, onset of puberty and chronic somatic illness did not markedly affect the associations.

Methodological considerations

The interpretation of our findings should consider the limitations and strengths of the study design. First, the cross-sectional design precludes interpretations concerning temporality and causality of the associations reported here. Second, the low participation rate resulted in a selection characterized by fewer social and perinatal adversities in the participants compared to non-participants. Consequently, less variation in PE, HA and other psychopathology might be found in the participants, most likely biasing the findings towards the null, resulting in too conservative estimates. However, a scenario of differential attrition resulting in a selection bias is unlikely, given that the underestimation of PE (primary outcome)

was in fact small: a previous CCC2000 study reported a weighted prevalence of 10.9% (95% CI 9.1–12.7) for PE at the 11-12-year follow-up (Jeppesen et al., 2015), compared to a prevalence of 9.9% among the participants in the current study. Third, same-reporter bias is an innate risk in epidemiological studies relying on self-report measures. In the current study, same-reporter bias was attenuated because i) PE were based on interviewer assessments, blinded to self-reported HA and FSS and ii) the adjusted multivariate analyses included general psychopathology assessed by the parent instead of the child itself. Fourth, to reduce the strain on the children during the face-to-face examinations, interview evaluation of HA and FSS were not available, and were assessed using only self-report measures. However, the self-report measures that were utilized in the current study are the most commonly used and validated self-report measures for children (Thorisdottir et al., 2017; Walker et al., 2009). Furthermore, we cannot preclude that the measure of FSS enquires about somatic symptoms which are in fact part of actual somatic illness in some participants. Nonetheless, actual somatic conditions in 11-12-year old children are relatively rare, and after adjusting for the confounding effect of chronic somatic conditions informed by the parents, the reported associated with offspring HA (Thorgaard, 2017).

Strengths of the current study include the large study sample, enabling studies of relatively low-power conditions such as PE in the general population. The population is well defined and representative for the Danish population regarding social and perinatal characteristics. PE was assessed thoroughly using an indepth face-to-face interview by trained professionals. The children were broadly evaluated, which allowed for adjustment for general psychopathology and emotional disorders.

Interpretation

The current study, to our knowledge, is the first to specifically study PE in relation to HA and FSS. It is notable that the association between PE and both FSS and HA held statistical significance after mutual adjustment and additional adjustment for general psychopathology. This shows that HA and FSS were independently associated with PE, and these associations were not explained by the level of concurrent general psychopathology. The secondary analysis, which included adjustment for emotional disorders instead of general psychopathology, did not change the estimated statistical effects markedly. This implies that the association between PE and high levels of HA and FSS exist across a continuum in the general population, and is not solely driven by children with emotional disorders. Also, the associations remained in sensitivity analyses after strict exclusion of all children with PE who had somatic delusions and/or tactile hallucinations (30% of all PE cases), suggesting a robust association.

Previous studies on child populations have shown that help-seeking is an important dimension of HA in this age group loading on a single factor of HA (Thorisdottir et al., 2017; Wright & Asmundson, 2005). However, when examining children with PE specifically, we found that they had high scores on fears and impact of symptoms, yet did not report increased help-seeking behavior. This finding could be of clinical importance, as it suggests that children with PE might be 'silent sufferers' of HA with high impact of symptoms. Probing for HA in children with PE may consequently be of added value in clinical assessment. HA and FSS have arguably been overlooked and neglected in childhood (Fritz et al., 1997; Mohapatra et al., 2014; Noyes et al., 2002; Wright & Asmundson, 2003). Our finding of a specific association with psychosis vulnerability supports the idea, that although HA and FSS symptoms in childhood might seldom add up to fulfilling diagnostic criteria for hypochondriasis or other somatoform and related disorders (Schulte & Petermann, 2011), they are still associated with considerable suffering (Rask et al., 2016). Whether a child initially presents with PE or HA, knowledge of the overlap between these symptom-domains is important, and assessment of both domains of psychopathology is of key importance to sufficient and appropriate intervention. Psychological treatment, with cognitive behavioral therapy, is well-established and effective for HA in adults (Eilenberg, Fink, Jensen, Rief, & Frostholm, 2016; Fallon et al., 2017; Thomson & Page, 2007; Tyrer et al., 2014), although studies evaluating therapies specifically directed towards children are lacking. Considering the overlap found in the current study between HA and FSS with PE, such treatment might decrease the overall load of psychopathology in vulnerable children, and hence reduce the risk of more disabling psychosis and other psychopathology later in life (Hall, 2017; van Os & Reininghaus, 2016). The overlap found in the current study might be an early manifestation of abnormal bodily experiences in first-episode psychosis, which are associated with poor prognosis (Kobayashi & Kato, 2004), giving further support to the importance of early intervention.

The present results are in line with several psychometric studies that have provided evidence for a transdiagnostic and dimensional approach to psychopathology in adults (Caspi et al., 2014; Krueger, 1999), as well as in children (Patalay et al., 2015). Specifically, the importance of anxiety has been emphasized in relation to both clinical psychosis (Achim et al., 2011; Hall, 2017) and PE (van Os & Reininghaus, 2016; Varghese et al., 2011). A recent study by Stochl and colleagues found that PE and anxiety and depressive symptoms were associated with an underlying latent continuum of mental distress in which PE indicated higher severity of symptoms. However, the proposed model did not explain for the full variation of PE (Stochl et al., 2015). The question whether HA and FSS are a part of the well-established transdiagnostic continuum between psychosis and anxiety, or if they constitute a more specific entity, cannot be answered with the current cross-sectional study. The specific finding of a lack of increased help-seeking behavior for HA reported by children with PE, despite overall high levels of fears and impact of symptoms, could suggest

that children presenting both HA and PE may constitute a subgroup with more fundamental disturbances in body perception and information processing, which characterize abnormal bodily experiences in psychotic disorders (Jenkins & Röhricht, 2007; A. Simon et al., 2014). However, due to the cross-sectional nature of data, the results, in terms of causality, should be interpreted with caution.

Future longitudinal studies are needed to disentangle temporal and causal mechanisms between PE on the one hand, and HA and FSS on the other. Such studies will provide further insights into developmental trajectories of both psychosis vulnerability and HA, and will potentially guide interventions that relieve children and adolescents of symptoms. Reduction in overall psychopathology might decrease the risk of development of severe mental health disorder in adulthood.

Supporting Information

Additional Supporting Information may be found in the online version of this article:

Appendix S1. Attrition analysis reporting differences in perinatal and socioeconomic adversities between participants and non-participants.

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Key Points:

- Abnormal bodily symptoms are common in emerging psychosis, but the association between the symptom domains of psychotic experiences, health anxiety and functional somatic symptoms are previously unexplored.
- Our study shows that psychotic experiences were strongly associated with health anxiety and functional somatic symptoms in a general population cohort of 1572 11-12-year-old preadolescents.
- The associations remained after adjustment for general psychopathology, indicating an independent association.
- Children with psychotic experiences reported high levels of health-related fears with impact on daily functioning, but no increased help-seeking behavior, suggesting unmet needs and a window of opportunity for early intervention in children presenting with health anxiety and psychotic experiences.

<u>References</u>

- Achim, A. M., Maziade, M., Raymond, É., Olivier, D., Mérette, C., & Roy, M. A. (2011). How prevalent are anxiety disorders in schizophrenia? a meta-analysis and critical review on a significant association. *Schizophrenia Bulletin*, 37(4), 811–821. https://doi.org/10.1093/schbul/sbp148
- Asmundson, G. J. G., Abramowitz, J. S., Richter, A. A., & Whedon, M. (2010). Health anxiety: Current perspectives and future directions. *Curr Psychiatry Rep*, *12*(4), 306–312. https://doi.org/10.1007/s11920-010-0123-9
- Campo, J. V. (2012). Annual research review: Functional somatic symptoms and associated anxiety and depression - Developmental psychopathology in pediatric practice. *Journal of Child Psychology and Psychiatry*, 53(5), 575–592. https://doi.org/10.1111/j.1469-7610.2012.02535.x
- Caspi, A., Houts, R. M., Belsky, D. W., Goldman-Mellor, S. J., Harrington, H., Israel, S., ... Moffitt, T. E. (2014).
 The p factor: One general psychopathology factor in the structure of psychiatric disorders? *Clinical Psychological Science*, 2(2), 119–137. https://doi.org/10.1177/2167702613497473

Coleman, L., & Coleman, L. (2002). The measurement of puberty: a review. Journal of Adolescence, 25(5),

535-550. https://doi.org/10.1006/jado.2002.0494

- Eilenberg, T., Fink, P., Jensen, J. S., Rief, W., & Frostholm, L. (2016). Acceptance and commitment group therapy (ACT-G) for health anxiety: A randomized controlled trial. *Psychological Medicine*, 46(1), 103– 115. https://doi.org/10.1017/S0033291715001579
- Fallon, B. A., Ahern, D. K., Pavlicova, M., Slavov, I., Skritskya, N., & Barsky, A. J. (2017). A randomized controlled trial of medication and cognitive-behavioral therapy for hypochondriasis. In *American Journal of Psychiatry* (Vol. 174, pp. 756–764). https://doi.org/10.1176/appi.ajp.2017.16020189
- Fink, P., Ørnbøl, E., & Christensen, K. S. (2010). The outcome of Health anxiety in primary care. a two-year follow-up study on health care costs and self-rated health. *PLoS ONE*, 5(3). https://doi.org/10.1371/journal.pone.0009873
- Fink, P., Ørnbøl, E., Toft, T., Sparle, K. C., Frostholm, L., & Olesen, F. (2004). A new, empirically established hypochondriasis diagnosis. *American Journal of Psychiatry*, 161(9), 1680–1691. https://doi.org/10.1176/appi.ajp.161.9.1680
- Fritz, G. K., Fritsch, S., & Hagino, O. (1997). Somatoform disorders in children and adolescents: A review of the past 10 years. *Journal of the American Academy of Child and Adolescent Psychiatry*. https://doi.org/10.1097/00004583-199710000-00014
- Goodman, R. (2001). Psychometric Properties of the Strengths and Difficulties Questionnaire. *Journal of the American Academy of Child & Adolescent Psychiatry*, *40*(11), 1337–1345. https://doi.org/10.1097/00004583-200111000-00015
- Goodman, R., Ford, T., Richards, H., Gatward, R., & Meltzer, H. (2000). The Development and Well-Being Assessment: Description and Initial Validation of an Integrated Assessment of Child and Adolescent Psychopathology. *Journal of Child Psychology and Psychiatry*, *41*(5), 645–655. https://doi.org/10.1177/017084068800900203
- Gross, G., Huber, G., Klosterkötter, J., & Linz, M. (1987). Bonner Skala für die Beurteilung von Basissymptomen/Bonn Scale for the Assessment of Basic Symptoms Manual. Berlin: Springer.
- Hall, J. (2017). Schizophrenia An anxiety disorder? *British Journal of Psychiatry*, 211(5), 262–263. https://doi.org/10.1192/bjp.bp.116.195370
- Janssens, K. a M., Rosmalen, J. G. M., Ormel, J., van Oort, F. V. a, Oldehinkel, A. J., Van, F. V. A., & Oldehinkel, A. J. (2010). Anxiety and depression are risk factors rather than consequences of

functional somatic symptoms in a general population of adolescents: the TRAILS study. *Journal of Child Psychology and Psychiatry*, *51*(3), 304–12. https://doi.org/10.1111/j.1469-7610.2009.02174.x

- Jenkins, G., & Röhricht, F. (2007). From cenesthesias to cenesthopathic schizophrenia: A historical and phenomenological review. *Psychopathology*, *40*(5), 361–368. https://doi.org/10.1159/000106314
- Jeppesen, P., Clemmensen, L., Munkholm, A., Rimvall, M. K., Rask, C. U., Jørgensen, T., ... Skovgaard, A. M. (2015). Psychotic experiences co-occur with sleep problems, negative affect and mental disorders in preadolescence. *Journal of Child Psychology and Psychiatry*, 56(5), 558–565. https://doi.org/10.1111/jcpp.12319
- Kaufman, J., Birmaher, B., Brent, D., Rao, U., Flynn, C., Moreci, P., ... Ryan, N. (1997). Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime Version (K-SADS-PL): Initial Reliability and Validity Data. *Journal of the American Academy of Child & Adolescent Psychiatry*, *36*(7), 980–988. https://doi.org/10.1007/s13398-014-0173-7.2
- Kaymaz, N., Drukker, M., Lieb, R., Wittchen, H., Werbeloff, M., Lataster, T., & van Os, J. (2012). Do subthreshold psychotic experiences predict clinical outcomes in unselected non-help-seeking population-based samples? A systematic review and meta-analysis, enriched with new results. *Psychological Medicine*, 42, 2239–2253. https://doi.org/10.1017/S0033291711002911
- Kelleher, I., Connor, D., Clarke, M. C., Devlin, N., Harley, M., & Cannon, M. (2012). Prevalence of psychotic symptoms in childhood and adolescence: a systematic review and meta-analysis of population-based studies. *Psychological Medicine*, 42(9), 1857–63. https://doi.org/10.1017/S0033291711002960
- Kelleher, I., Wigman, J. T. W., Harley, M., O'Hanlon, E., Coughlan, H., Rawdon, C., ... Cannon, M. (2015).
 Psychotic experiences in the population: Association with functioning and mental distress.
 Schizophrenia Research, 165(1), 9–14. https://doi.org/10.1016/j.schres.2015.03.020
- Klippel, A., Viechtbauer, W., Reininghaus, U., Wigman, J., van Borkulo, C., Myin-Germeys, I., & Wichers, M. (2017). The Cascade of Stress: A Network Approach to Explore Differential Dynamics in Populations Varying in Risk for Psychosis. *Schizophrenia Bulletin*, (December), 1–10. https://doi.org/10.1093/schbul/sbx037
- Kobayashi, T., & Kato, S. (2004). Psychopathology and outcome of first-admission schizophrenic patients: Hypochondriac-cenestopathic symptoms as predictors of an unfavorable outcome. *Psychiatry and Clinical Neurosciences*, *58*(5), 567–572. https://doi.org/10.1111/j.1440-1819.2004.01301.x

Krueger, R. (1999). The structure of common mental disorders. Archives of General Psychiatry, 56(10), 921-

926. Retrieved from http://dx.doi.org/10.1001/archpsyc.56.10.921

- Linscott, R. J., & Van Os, J. (2013). An updated and conservative systematic review and meta-analysis of epidemiological evidence on psychotic experiences in children and adults: On the pathway from proneness to persistence to dimensional expression across mental disorders. *Psychological Medicine*, 43(6), 1133–1149. https://doi.org/10.1017/S0033291712001626
- Mohapatra, S., Deo, S. J. K., Satapathy, A., & Rath, N. (2014). Somatoform disorders in children and adolescents. *German Journal of Psychiatry*, *17*(1), 19–24.
- Myin-Germeys, I., & van Os, J. (2007). Stress-reactivity in psychosis: Evidence for an affective pathway to psychosis. *Clinical Psychology Review*, 27(4), 409–424. https://doi.org/10.1016/j.cpr.2006.09.005
- Noyes, R., Stuart, S., Langbehn, D. R., Happel, R. L., Longley, S. L., & Yagla, S. J. (2002). Childhood Antecedents Of Hypochondriasis. *Psychosomatics*, *43*(4), 282–289. https://doi.org/10.1176/appi.psy.43.4.282
- Olsen, E. M., Skovgaard, A. M., Weile, B., & Jørgensen, T. (2007). Risk factors for failure to thrive in infancy depend on the anthropometric definitions used: The Copenhagen county child cohort. *Paediatric and Perinatal Epidemiology*, *21*(5), 418–431. https://doi.org/10.1111/j.1365-3016.2007.00851.x
- Patalay, P., Fonagy, P., Deighton, J., Belsky, J., Vostanis, P., & Wolpert, M. (2015). A general psychopathology factor in early adolescence. *British Journal of Psychiatry*, 207(1), 15–22. https://doi.org/10.1192/bjp.bp.114.149591
- Rask, C. U., Munkholm, A., Clemmensen, L., Rimvall, M. K., Ørnbøl, E., Jeppesen, P., & Skovgaard, A. M. (2016). Health Anxiety in Preadolescence Associated Health Problems, Healthcare Expenditure, and Continuity in Childhood. *Journal of Abnormal Child Psychology*, 44, 823–832. https://doi.org/10.1007/s10802-015-0071-2
- Schulte, I. E., & Petermann, F. (2011). Somatoform disorders: 30 years of debate about criteria!. What about children and adolescents? *Journal of Psychosomatic Research*, 70(3), 218–228. https://doi.org/10.1016/j.jpsychores.2010.08.005
- Simon, A., Borgwardt, S., Lang, U., & Roth, B. (2014). Cenesthopathy in adolescence: an appraisal of diagnostic overlaps along the anxiety-hypochondriasis-psychosis spectrum. *Comprehensive Psychiatry*, 55(5), 1122–9. https://doi.org/10.1016/j.comppsych.2014.02.007

Simon, G., VonKorff, M., Piccilnelli, M., Fullerton, C., & Ormel, J. (1999). An international study of the

relation between somatic symptoms and depression. *The New England Journal of Medicine*, *341*(October 28), 1329–1335. https://doi.org/10.1177/0268580910380980

- Skovgaard, A. M., Olsen, E. M., Houmann, T., Christiansen, E., Samberg, V., Lichtenberg, A., & Jørgensen, T. (2005). The Copenhagen County child cohort: design of a longitudinal study of child mental health.
 Scandinavian Journal of Public Health, 33(3), 197–202. https://doi.org/10.1080/14034940510005662
- Stanghellini, G., Ballerini, M., Fusar Poli, P., & Cutting, J. (2012). Abnormal bodily experiences may be a marker of early schizophrenia? *Current Pharmaceutical Design*, 18(4), 392–8. https://doi.org/10.2174/138161212799316181
- Stochl, J., Khandaker, G. M., Lewis, G., Perez, J., Goodyer, I. M., Zammit, S., ... Jones, P. B. (2015). Mood, anxiety and psychotic phenomena measure a common psychopathological factor. *Psychological Medicine*, 45(7), 1483–1493. https://doi.org/10.1017/S003329171400261X
- Thomson, A. B., & Page, L. A. (2007). Psychotherapies for hypochondriasis. *Cochrane Database of Systematic Reviews*, (4). https://doi.org/10.1002/14651858.CD006520.pub2
- Thorisdottir, A. S., Villadsen, A., LeBouthillier, D. M., Rask, C. U., Wright, K. D., Walker, J. R., ... Asmundson, G. J. G. (2017). Measurement invariance across Genders on the Childhood Illness Attitude Scales (CIAS). *Journal of Psychosomatic Research*, *98*(March), 34–39. https://doi.org/10.1016/j.jpsychores.2017.05.006
- Tyrer, P., Cooper, S., Crawford, M., Dupont, S., Green, J., Murphy, D., ... Tyrer, H. (2011). Prevalence of health anxiety problems in medical clinics. *Journal of Psychosomatic Research*, 71(6), 392–394. https://doi.org/10.1016/j.jpsychores.2011.07.004
- Tyrer, P., Cooper, S., Salkovskis, P., Tyrer, H., Crawford, M., Byford, S., ... Barrett, B. (2014). Clinical and costeff ectiveness of cognitive behaviour therapy for health anxiety in medical patients: A multicentre randomised controlled trial. *The Lancet*, *383*(9913), 219–225. https://doi.org/10.1016/S0140-6736(13)61905-4
- Tyrer, P., Eilenberg, T., Fink, P., Hedman, E., & Tyrer, H. (2016). Health anxiety: The silent, disabling epidemic. *BMJ (Online)*, *353*(April), 10–11. https://doi.org/10.1136/bmj.i2250
- Upthegrove, R., Marwaha, S., & Birchwood, M. (2017). Depression and Schizophrenia: Cause, Consequence, or Trans-diagnostic Issue? *Schizophrenia Bulletin*, *43*(2), 240–244. https://doi.org/10.1093/schbul/sbw097

- van Os, J., Linscott, R. J., Myin-Germeys, I., Delespaul, P., & Krabbendam, L. (2009). A systematic review and meta-analysis of the psychosis continuum: Evidence for a psychosis proneness-persistenceimpairment model of psychotic disorder. *Psychological Medicine*, *39*(2), 179–195. https://doi.org/10.1017/S0033291708003814
- van Os, J., & Reininghaus, U. (2016). Psychosis as a transdiagnostic and extended phenotype in the general population. *World Psychiatry*, *15*(June), 118–124. https://doi.org/10.1002/wps.20310
- van Rossum, I., Dominguez, M. D. G., Lieb, R., Wittchen, H. U., & Van Os, J. (2011). Affective dysregulation and reality distortion: A 10-year prospective study of their association and clinical relevance. *Schizophrenia Bulletin*, *37*(3), 561–571. https://doi.org/10.1093/schbul/sbp101
- Varghese, D., Scott, J., Welham, J., Bor, W., Najman, J., O'Callaghan, M., ... McGrath, J. (2011). Psychotic-like experiences in major depression and anxiety disorders: A population-based survey in young adults. *Schizophrenia Bulletin*, 37(2), 389–393. https://doi.org/10.1093/schbul/sbp083
- Walker, L. S., Beck, J. E., Garber, J., & Lambert, W. (2009). Children's somatization inventory: Psychometric properties of the revised form (CSI-24). *Journal of Pediatric Psychology*, *34*(4), 430–440. https://doi.org/10.1093/jpepsy/jsn093
- Wigman, J. T. W., Van Nierop, M., Vollebergh, W. A. M., Lieb, R., Beesdo-Baum, K., Wittchen, H. U., & Van Os, J. (2012). Evidence that psychotic symptoms are prevalent in disorders of anxiety and depression, impacting on illness onset, risk, and severity Implications for diagnosis and ultra-high risk research. *Schizophrenia Bulletin*, 38(2), 247–257. https://doi.org/10.1093/schbul/sbr196
- Wright, K. D., & Asmundson, G. J. G. (2003). Health anxiety in children: development and psychometric properties of the Childhood Illness Attitude Scales. *Cognitive Behaviour Therapy*, 32(April 2013), 194– 202. https://doi.org/10.1080/16506070310014691
- Wright, K. D., & Asmundson, G. J. G. (2005). Brief report: Factor structure of the Childhood Illness Attitude Scales (CIAS). *Journal of Pediatric Psychology*, *30*(2), 213–218. https://doi.org/10.1093/jpepsy/jsi009

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Table 1: Univariate associations between psychotic experiences (PE) and health anxiety and functionalsomatic symptoms for top 10% symptom score

	0	R of PE	9	5% CI		
Health Anxiety symptoms (10 % high)		3.19	2.12-4.79			
Functional Somatic symptoms (10 % high)		4.61	3.08-6.89			
5						
S	OR of PE	95%	CI	p- value		
<u>Model 1 (n=1572)</u>				value		
Health anxiety	2.26	1.46-3	50	<0.001		
Functional somatic symptoms	3.72	2.43-5		< 0.001		
Model 2 (<i>n</i> =1572)						
Health anxiety	2.26	1.46-3	.50	<0.001		
Functional somatic symptoms	3.73	2.43-5	.70	<0.001		
Sex	1.01	0.72-1	.43	0.938		
<u>Model 3 (n=1537)</u>						
Health anxiety	2.21	1.41-3	.45	0.001		
Functional somatic symptoms	3.70	2.41-5	.70	<0.001		
Sex	1.05	0.74-1	.49	0.402		
Puberty onset	0.68	0.43-1	.10	0.167		
<u>Model 4</u> (n=1503)						
Health anxiety	2.31	1.46-3	.65	<0.001		
Functional somatic symptoms	3.68	2.36-5	.73	<0.001		
Sex	1.07	0.75-1	.54	0.715		
Puberty onset	0.61	0.371	.01	0.055		
Chronic somatic illness	0.86	0.52-1	.41	0.547		
<u>Model 5a (n=1503)</u>						
Health anxiety	2.15	1.36-3	.41	0.001		
Functional somatic symptoms	3.31	2.11-5	.18	<0.001		
Sex	1.00	0.69-1	.44	0.992		
Puberty onset	0.62	0.37-1	.02	0.060		
Chronic somatic illness 0.89 0.54-1.46 0.649 This article is protected by copyright. All rights reserved						

General psychopathology	1.07	1.04-1-11	<0.001	Table 2: Multivariate logistic
				regression analysis of the
				independent associations of
				health anxiety (top 10% score)
<u>Model 5b (n=1502)</u>				and functional somatic symptoms
Health anxiety	2.00	1.25-3.22	0.004	(top 10% score), respectively, with
Functional somatic symptoms	3.13	1.97-4.96	<0.001	psychotic experiences (PE), and
Sex	1.09	0.76-1.57	0.992	successively adjusted for sex,
Puberty onset	0.64	0.39-1.07	0.060	puberty onset, chronic somatic
Chronic somatic illness	0.87	0.53-1.44	0.649	illness and general
Diagnosis of anxiety or	3.24	2.02-5.22	<0.001	psychopathology,
depression				
ð				

Author M



Table 3: Secondary analyses investigating which specific dimensions of health anxiety (fears, help-seeking and symptom effects) are associated with psychotic experiences (PE).

\mathbf{O}	OR of PE	95% CI
Fears (10% high score)	3.01	1.98-4.59
Help-seeking (10 % high score)	1.17	0.67-2.06
Symptom effects (10% high score)	5.01	3.38-7.51

Author Mai

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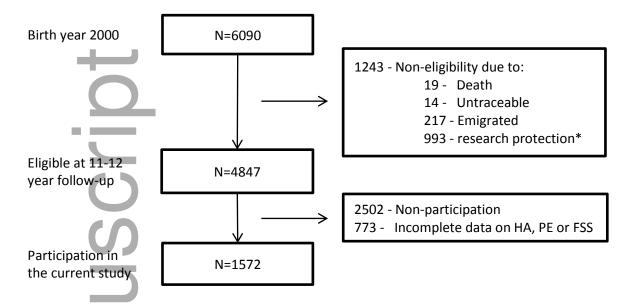


Figure 1: Flowchart of participants from the Copenhagen Child Cohort 2000 for this study

*Research protection was an option for individual families to avoid inquiries from all research and consumer surveys.

HA=Health anxiety, PE=Psychotic experiences, FSS=Functional somatic symptoms



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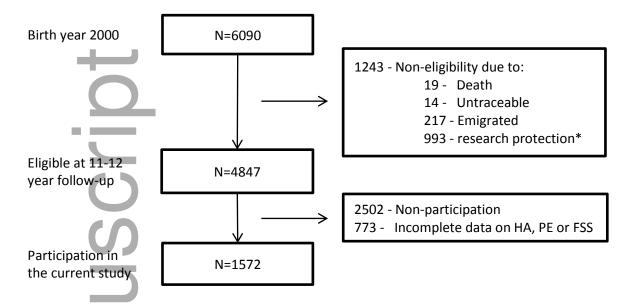


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