



PhD thesis

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Hyper-Theory-of-Mind in Children with Psychotic Experiences



**Mental Health
Services**

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1. Preface

This PhD thesis investigates the relation between Psychotic Experiences and Hyper-Theory-of-Mind.

The PhD study is based on the 11-12 year follow-up of the Copenhagen Child Cohort 2000 (CCC2000) as well as data from the previous waves of data collection at child age 0-1 year and 5-7 years. The main body of my data was collected in close collaboration with the PhD students, MD Anja Munkholm and MD Xiao Qiang Li with assistance from research year student Martin Rimvall, Psychologist Maja Gregersen and Psychologist Anne Dorothee Müller. The thesis also includes data from a Dutch population-based sample generously supplied by Agna Bartels-Velthuis and Els Blijd-Hoogewys, and data from a clinical sample of children with high-functioning autism spectrum disorders recruited and assessed by colleagues in the child and adolescent mental health centres in the Capital Region of Denmark and Region of Zealand Denmark. Psychology student Rókur av Flötum Jespersen assisted me in the assessment of the clinical sample as well as the sample of typical developing children, recruited to match the clinical sample.

As member of the CCC2000 study group, I had the opportunity to cooperate closely with other studies of the developmental pathways to psychosis, and this work is referred to in the current thesis. During my PhD study I had the pleasure and great learning experience to visit Prof. Jim van Os at the Department of Psychiatry and Psychology at the Maastricht University Medical Centre for two months in the spring of 2013 and again in the spring of 2014.

Other than the ones already mentioned I would like to thank my main supervisor Pia Jeppesen (for a lot of things, but not least for allowing me to stick with my idea, even when I could not really explain it. Some say stubborn, I prefer persistent), and my three co-supervisors Jim van Os, Anne Mette Skovgaard and Mette Væver. Also thank you to my de facto fifth supervisor on the study on validation of the Theory-of-Mind task (article I) Jens Richardt Møllegaard Jepsen

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2. Summary in English

Research into psychotic symptoms has usually been guided by the assumption that these symptoms mark distinct diseases such as schizophrenia and bipolar disorder. Nevertheless, psychotic symptoms are common not only across a range of psychotic and non-psychotic disorders, but also among the general population. There appears to be a continuum between psychotic and ordinary experiences, and hallucinations, delusions and thought disturbances in the absence of diagnosable psychotic illness are referred to as Psychotic Experiences (PE).

Longitudinal studies have found associations between PE in childhood or adolescence and later psychotic spectrum disorder. However, only a small proportion of individuals with PE develop psychotic disorder and some develop other psychiatric outcomes, while the majority of individuals with PE stay below the clinical threshold. Thus, it is unclear if the presence of PE constitutes a specific risk marker of psychosis liability or a common risk marker of psychopathology and increased severity of psychopathology. This raises the question of whether it is possible to identify other markers of psychosis liability among individuals with PE, which may enable clinicians and researchers to identify those individuals with substantially higher risk of transition from PE to clinical psychotic disorder.

Patients prone to psychosis and schizophrenia in particular, show certain cognitive deficits that may trigger the onset and maintenance of PE. Deficits in Theory-of-Mind (ToM) abilities are among the most well-established deficits, but these are also prominent in patients across different diagnostic categories. This suggests that ToM alterations are not specific to schizophrenia. Rather, while general alterations in ToM may be a vulnerability marker for psychosis and other psychopathology, more specific types of alterations may have a mediating role in the development of different types of specific symptoms.

The purpose of this thesis was to investigate the relationships between PE and HyperToM (being the tendency to exaggerate attributions of affective and motivational states of other people) in preadolescent children. To that end the thesis had three main aims. Firstly, it aimed at validating the

ToM-Frederik task as a psychometric instrument for the measurement of ToM by use of a sample of typically developing children (TD) and a sample of children with high-functioning autism spectrum disorders (HFASD). Secondly, it aimed at exploring the associations between HyperToM and PE in a general population-based sample of Danish children aged 11–12 and a general population-based sample of Dutch children aged 12–13. The third aim of the thesis was to explore the specificity of HyperToM in terms of impacting the risk for having PE in preadolescence as opposed to any mental disorder in the Danish sample.

The results support the validity of the Danish version of the Theory-of-Mind Storybook Frederik. This task represents a gain for both research and clinical practice, as it is relatively fast to administer and has very nuanced outcome results, although norms are not yet established.

The results of the PhD study point to an association between HyperToM and PE that is not fully explained by an association between poor ToM and PE. The results suggest that particularly the HyperToM type of impaired ToM is associated with PE, and that this association is strongest for delusional ideas with paranoid content such as delusions of persecution, mind-reading and/or receiving messages from TV/radio.

The present study confirmed that many predictors of schizophrenia, including familial psychiatric liability; low family income; regulatory problems in infancy and concurrent mental disorder, are also associated with PE. However, the findings suggest that whereas a wide range of family and child variables are associated with PE and psychopathology in general, HyperToM is independently and specifically associated with PE and thus might mark a risk for PE specifically.

Looking at PE without psychiatric diagnosis specifically, only HyperToM and bullying were significantly associated to this group when we adjusted for all other potential risk variables included in the study. On this basis it might be suggested that HyperToM points to a pathway to PE that is preceded to a lesser extent by early developmental alterations. However HyperToM was not predicted by any other included variable other than a marker of general IQ, so whereas HyperToM appears to possess an inborn increased risk of PE, there is not necessarily any specificity for any diagnosis yet.

The present study is the first to point at the possibility of a specific pathway to PE associated with HyperToM. These results suggest that it may be productive to apply more differentiated measures of the various qualities of ToM functioning instead of relying on an overall score based on the number of correct answers. This could be helpful not only when conducting research on the development of PE and psychosis, but also when applying ToM tasks as part of a clinical assessment in child mental health services settings. The construct of HyperToM may be useful in delineating differential pathways to psychopathological outcomes.

3. Resumé på dansk

Forskning i psykotiske symptomer har ofte været styret af den antagelse, at disse symptomer er udtryk for distinkte lidelser såsom skizofreni og bipolære lidelser. Psykotiske symptomer ses dog også hyppigt ved flere ikke-psykotiske sygdomme, samt i den generelle befolkning. Der synes at være et kontinuum fra psykotiske til ordinære oplevelser. Såfremt der ikke er tale om en egentlig psykotisk sygdom, benævner man hallucinationer, vrangforestillinger og tankeforstyrrelser for Psykotiske Oplevelser (Den engelske betegnelse er Psychotic Experiences - PE).

Longitudinelle studier har fundet sammenhæng mellem PE i barndom og pubertet og senere psykotisk sygdom. Imidlertid udvikler kun en mindre del af de personer, der har PE en egentlig psykotisk sygdom. Nogle udvikler andre psykiatriske lidelser, men størstedelen forbliver under den kliniske tærskel. Det er således ikke klart, hvorvidt PE er en specifik risikomarkør for psykose eller en generel risikomarkør for psykopatologi og eventuelt bidrager til øget sværhedsgrad heraf. Det er således relevant at undersøge, hvorvidt det er muligt at identificere andre markører for tilbøjeligheden til psykose blandt individer med PE. Dette vil måske kunne hjælpe klinikere og forskere til at identificere de individer med PE, der har en væsentligt øget risiko for udvikle klinisk psykotisk sygdom.

Patienter med sårbarhed for psykose udviser visse kognitive vanskeligheder, som måske forårsager og opretholder PE. Vanskeligheder ved Theory-of-Mind (ToM) menes at være blandt de mest veletablerede vanskeligheder i denne gruppe, men sådanne vanskeligheder er også fremtrædende hos patienter i andre diagnostiske kategorier. Dette peger på, at ToM-afvigelser ikke er specifikke for skizofreni. Det er nok snarere sådan, at mens generelle ToM-vanskeligheder kan være en

sårbarhedsmarkør for psykose og anden psykopatologi, så kan mere specifikke former for ToM-vanskeligheder have en medierende rolle i udviklingen af forskellige former for specifikke symptomer.

Det overordnede formål med den foreliggende afhandling var at undersøge forholdet mellem PE og HyperToM (overdreven attribuering af affektive og intentionelle tilstande til/hos andre) hos børn i præ-puberteten. Med henblik herpå blev tre hovedformål opstillede. Først var målet at validere ToM-Frederik, som et psykometrisk instrument til måling af ToM i en gruppe af normalt udviklede børn og børn med højt-fungerende autisme-spektrum forstyrrelser. Dernæst var målet at undersøge sammenhængen mellem HyperToM og PE i en populationsbaseret gruppe af danske børn på 11-12 år, samt i en populationsbaseret gruppe af Hollandske børn på 12-13 år. Det tredje mål for denne afhandling var at undersøge specificiteten af HyperToM, som udtryk for at have PE i modsætning til at have en hvilken som helst anden mental lidelse i præ-puberteten i den danske gruppe af børn.

Resultaterne var til fandt støtte for validiteten af den danske version af Theory-of-Mind Storybook Frederik. Denne test er en gevinst for både forskning og klinisk praksis, da den er relativ hurtig at administrere og har nuancerede resultater. Normer er dog endnu ikke fastlagt.

Resultaterne fra dette Ph.d.-studie tyder på en sammenhæng mellem HyperToM og PO, som ikke kan forklares af en sammenhæng mellem generelle ToM vanskeligheder og PO. Resultaterne peger på, at især den form for ToM vanskeligheder, der forstås som HyperToM, er associeret med PE. Det tyder på at dette særligt gælder for den undergruppe af PE, der udgøres af vrangagtige ideer med et paranoidt indhold, såsom forfølgelsesforestillinger, tankelæsning og/eller budskaber fra TV/radio.

Det foreliggende studie bekræftede at mange prædiktorer for skizofreni (inklusiv familiær psykiatrisk disposition; lav familieindkomst; reguleringsproblemer i spædbarnealderen samt anden mental lidelse), også er associerede med PE. Imidlertid tyder resultaterne på, at en række faktorer omhandlende familien og barnet selv er associerede med psykopatologi generelt, mens HyperToM uafhængigt og specifikt er associeret med PE, hvorfor det muligvis kan forstås som en specifik markør for PE.

HyperToM og mobning var signifikant associeret med PE uden samtidig psykiatrisk sygdom efter justering for alle andre potentielle risikofaktorer inkluderet i studiet. Dette kunne tyde på at HyperToM peger på stier til PE som i ringe grad er forudgået af udviklingsmæssige vanskeligheder. HyperToM var ikke prædikeret af andre af de inkluderede variable end den anvendte markør for intelligens, så mens HyperToM synes at rumme en iboende risiko for PE, så er HyperToM ikke nødvendigvis markør for nogen specifik diagnose.

Indeværende studie er det første, der peger på muligheden for en specifik sti til PE associeret med HyperToM. Resultaterne peger på, at det kan være hensigtsmæssigt at anvende mere differentierede mål for ToM, end blot en overordnet score baseret på antal korrekte svar. Dette kunne være en væsentligt styrke for både forskning vedrørende udviklingen af PE og psykose, samt ved anvendelse af ToM-test, som en del af den kliniske undersøgelse i børne- og ungdomspsykiatrisk sammenhæng. HyperToM kan vise sig nyttig i identifikationen af stier til forskellig psykopatologi.

4. List of papers

Paper I

Clemmensen, L., Bartels-Velthuis, AA., Jespersen, R., van Os, J., Blijd-Hoogewys, EMA., Ankerstrøm, L., Væver, M., Daniel, PF., Drukker, M., Jeppesen, P., & Jepsen, JRM. (submitted): Exploring a new Theory of Mind task for 8-14 year-old children.

Paper II

Clemmensen L, van Os J, Skovgaard AM, Væver M, Blijd-Hoogewys EMA, Bartels-Velthuis AA & Jeppesen, P. (2014): Hyper-Theory-of-Mind in Children with Psychotic Experiences. PLoS ONE 9(11): e113082. doi:10.1371/journal.pone.0113082

Paper III

Clemmensen, L., van Os, J., Drukker, M., Munkholm, A., Rimvall, MK., Væver, M., Rask, CU., Bartels-Velthuis, AA., Skovgaard, AM., Jeppesen, P. (in press): A Longitudinal General Population Birth Cohort Study of Psychotic Experiences, Hyper-Theory-of-Mind, and Putative Antecedents and Correlates in Preadolescence. Psychological Medicine. © Cambridge University Press 2015 doi:10.1017/S0033291715001567

5. Definitions and delimitations

ADHD: Attention Deficit Hyperactivity Disorder

ASD: Autistic Spectrum Disorders.

AT: Animated Triangles

AVH: Auditory (Verbal) Hallucinations

BPD: Borderline Personality Disorder

CCC2000: Copenhagen Child Cohort 2000

CD: Conduct Disorder

DAWBA: The Development and Well-Being Assessment

FB: False Belief

HFASD: High Functioning Autism Spectrum Disorder

HyperToM: Hyper-Theory-of-Mind

HypoToM: Hypo-Theory-of-Mind

MASC: The Movie for Assessment of Social Cognition

ND: Neurodevelopmental Disorders

ODD: Oppositional defiant disorder

Pa: Paranoid Delusions

PE: Psychotic Experiences

PE-NonPa: Psychotic Experiences without Paranoid delusions

PSD: Psychosis Spectrum Disorders

SRS: The Social Responsiveness Scale

SEE: Social Emotional Evaluation

SEQ: SEE Social Emotional Questionnaire

TD: Typically Developing

ToM: Theory-of-Mind

ToM-Frederik: Theory-of-Mind Storybook Frederik

6. Introduction

This thesis concerns psychotic experiences in preadolescence and how they are related to the exaggerated type of deficits in Theory-of-Mind (HyperToM).

6.1. Rationale of the Thesis

Research consistently demonstrates that the symptoms of schizophrenia load onto a number of relatively independent clusters including psychotic, negative, affective and disorganization symptoms and also cognitive and/or motor dysfunctions (Garety and Freeman, 2013). Thus, as recommended by Owen et al., (Owen et al., 2011) it might be preferable to focus on specific symptoms as well as cognitive endophenotypes thereby removing the confounding effects of diagnostic practices (Garety and Freeman, 2013).

Research into psychotic symptoms including hallucinations, delusions and disturbances of thoughts has usually been guided by the assumption that these symptoms mark distinct diseases such as schizophrenia and bipolar disorder (Bentall and Fernyhough, 2008). Rather psychotic symptoms are common not only across a range of psychotic and non-psychotic disorders, but also among children, adolescents and adults when examined in epidemiological studies of the general population (Bentall and Fernyhough, 2008). There appears to be a continuum between psychotic and ordinary experiences (van Os, 2003). However, only a small proportion of individuals with Psychotic Experiences (PE) develop psychotic disorder (Kounali *et al.*, 2014), and some develop other psychiatric outcomes (Kaymaz et al., 2012, Kounali et al., 2014, van Os et al., 2009), while the majority of individuals with PE stay below the clinical threshold. This raises the question of whether it is possible to identify other markers of psychosis liability among individuals with PE, which may enable clinicians and researchers to identify those individuals with substantially higher risk of transition from PE to clinical psychotic disorder (Kounali et al., 2014).

Alterations in Theory-of-Mind (ToM) are present in a wide range of psychiatric disorders, such as developmental disorders, personality disorders, other non-psychotic disorders as well as schizophrenia and affective disorders (Brune and Brune-Cohrs, 2006). However, despite all that is known about the presentation of psychopathology in these disorders, we lack an understanding of

the relationship between major symptom dimensions and ToM (Ventura et al., 2013). While general alterations in ToM may be a vulnerability marker for psychosis and other psychopathology, more specific types of alterations may have a mediating role in the development of different types of specific symptoms (Shamay-Tsoory et al., 2007, Montag et al., 2011).

6.2. Psychotic Experiences

Hallucinations, delusions and thought disturbances in the absence of diagnosable psychotic illness, referred to as psychotic experiences (PE), are frequent in the general population with a median prevalence estimated at around 7% (Linscott and van Os, 2013). A recent meta-analysis found a median prevalence of 17% among children aged 9–12 and 7.5% among adolescents aged 13–18 (Kelleher et al., 2012). However, frequent use of self-report questionnaires and differences in response-style in the younger age group may confound the relationship between lower age and higher prevalence of PE (Jeppesen et al., 2014a), as a much lower prevalence has been found for interview-and-observer-rated PE (3.8%) compared with self-reported PE (11.9%) in the general population as a whole (Linscott and van Os, 2013).

Longitudinal studies have found associations between PE in childhood or adolescence and later psychotic spectrum disorder (PSD). Poulton and colleagues found that children from the Dunedin birth cohort study who reported psychotic symptoms at age 11 were at a 5- to 16-fold increased risk of schizophrenia-spectrum disorder in adulthood (Poulton et al., 2000), while studies in the Mater-University of Queensland Study of Pregnancy (MUSP) cohort found that hallucinations at age 14 were associated with a 2-5 times increased risk of non-affective psychotic disorder at age 21 (Welham et al., 2008). A recent review concluded that individuals with the non-clinical phenotype represent a valuable population in which to study the etiology of psychosis (Kelleher and Cannon, 2011), and it has been suggested (van Os et al., 2009) that PE might represent a broadly distributed phenotype that is the developmental expression of an underlying, possibly partly genetic, vulnerability to psychotic disorder (Poulton et al., 2000, Welham et al., 2009).

6.2.1 The dimensional approach to Psychotic Experiences

As opposed to the traditional view of PE as categorically distinct from normal experiences and behaviours, the dimensional approach understands PE as being different in quantitative ways (van Os, 2003), and patients as having more or less psychopathology rated on several symptom

dimensions (Kaymaz et al., 2012). In this view there is a continuum ranging from PE to full-blown psychosis resulting in a diagnosable primary psychotic disorder (Esterberg and Compton, 2009). The continuum in psychopathology can best be illustrated by looking at the formation of persecutory delusions, which often develop through ideas of reference and suspicion to gradually more and more uncorrectable and systematic ideas of persecution and plots (see Figure 1 for an example).

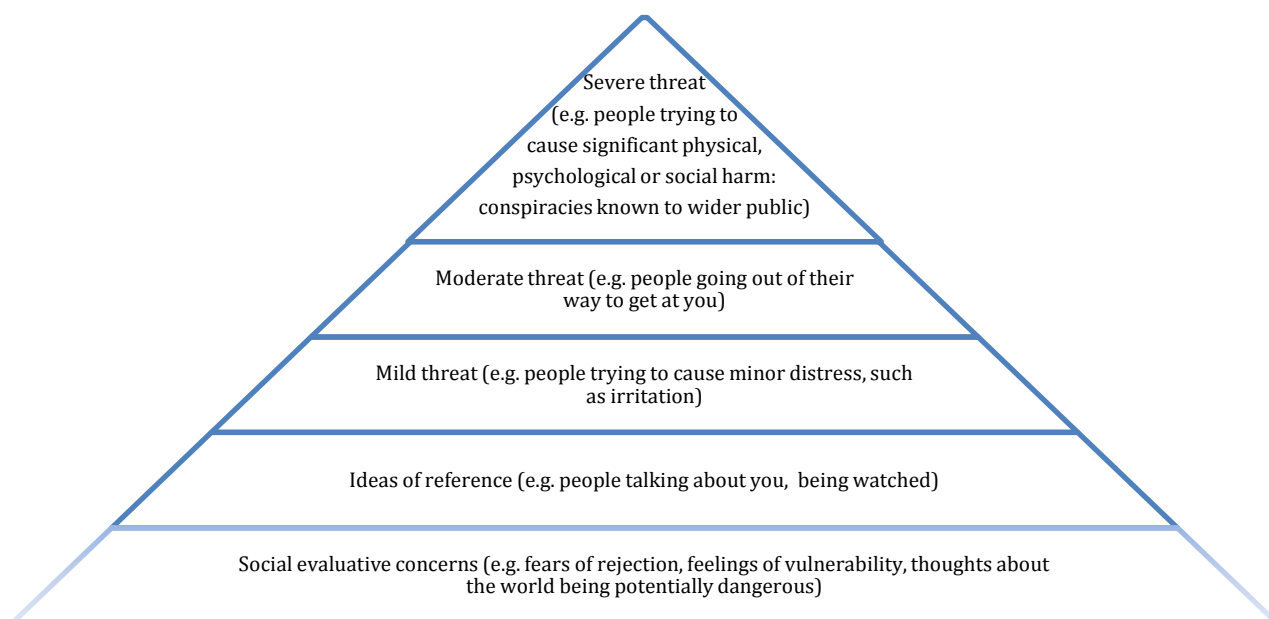


Figure 1: The paranoia hierarchy (Freeman et al., 2002)

This notion of a continuum has been used in many contexts in research on PE.

- **Familial continuity:** The non-ill relatives to patients with clinical psychotic disorder have higher levels of PE than non-related (van Os, 2014).
- **Etiological continuity:** Environmental risk factors associated with psychotic disorder, such as psychosocial adversities, ethnic minority group, urbanicity and cannabis use are also associated, independently, with PE (Lataster et al., 2009), and the same genetic and environmental factors may influence both extreme, frequent PE and milder, less frequent manifestations in adolescents (Zavos et al., 2014).

- **Temporal continuity:** Although usually transitory, PE are associated with an increased risk of developing psychotic disorder later in life (Kaymaz et al., 2012, Poulton et al., 2000, Kelleher et al., 2012, Linscott and van Os, 2013).
- **Psychometric continuity:** An extended psychosis phenotype blending gradually into clinical syndromes, and with milder forms distributed across the whole population (van Os et al., 2009).

6.2.2 Common versus psychopathology-specific risk factors.

PE persist in only a small proportion of the people who report them (Lin et al., 2011), and only an even smaller proportion go on to develop a psychotic disorder. The overlap in the epidemiology of PE and schizophrenia is not entirely consistent (Kounali et al., 2014), and most factors associated with increased risk of schizophrenia and PE are also associated with increased risk of other psychiatric outcomes (Kaymaz et al., 2012, van Os et al., 2009, Kounali et al., 2014). Thus, if made simply on the basis of shared risk factors, the argument that PE mark pathogenic mechanisms underlying schizophrenia is not well supported (Kounali et al., 2014).

PE predict not only psychosis, but also an increased risk for non-psychotic disorders (van Os and Murray, 2013, Kaymaz et al., 2012). as well as increased severity and poor prognosis of non-psychotic disorders (Kelleher et al., 2012, Wigman et al., 2012). Thus, it is unclear if PE are a specific risk marker of psychosis liability or a common risk marker of psychopathology and increased severity of psychopathology (Kounali et al., 2014). Recent findings on the development of psychosis suggest that the first stage may in fact be a diagnostically non-specific stage of potentially more severe psychopathology, which only later may acquire a degree of diagnostic specificity (Fusar-Poli et al., 2014).

In a recent study (Kounali et al., 2014), a range of variables, chosen for their consistent associations with schizophrenia in the literature, most were found to be associated equally strongly with depression as with PE. One interpretation is that PE is an expression of depression rather than an indication of abnormal pathology underlying schizophrenia-related disorders (Kounali et al., 2014). Co-morbidity with depression is in fact one of the most consistent findings regarding PE in general population samples, and it has been suggested that PE and depressive and anxiety symptoms indicate a single, underlying dimension of what is referred to as common mental distress, with PE

indicating the more severe end of this factor (Stochl et al., 2014). However, markers of neurodevelopmental impairment are more strongly associated with PE than with depression, which lends some support to the belief that these phenotypes are not just alternative expressions of mental distress, and that PE may share some etiological mechanisms with schizophrenia (Kounali et al., 2014).

6.2.3 Development and persistence of Psychotic Experiences

The fact that higher risk of PE in early adolescence has been reported in individuals with childhood neurodevelopmental non-psychotic disorders (ND) is consistent with the neurodevelopmental hypothesis of schizophrenia (Khandaker et al., 2014). This hypothesis (Murray and Lewis, 1987, Weinberger, 1996) posits disruption of brain development in early life as underlying the later emergence of psychosis during adulthood. The disruption may be caused by interactions between genetic and environmental factors during critical early periods of brain development (McGrath 2003). This view is supported by findings indicating relations between delays in early developmental milestone attainment (such as lifting the head, sitting without support, crawling longer distance, and walking without support) and later development of schizophrenia (Sorensen et al., 2010). Such developmental impairments have also been found to predict PE at age 11 (Cannon et al., 2002). According to the Stress-Vulnerability Hypothesis in Psychotic Disorders, genetic factors may operate by making individuals selectively vulnerable for environmental risks (Gispens de Wied and Jansen, 2002). Evidence of substantial variation in the incidence across places and minority groups suggests that environmental factors do have an important role (van Os et al., 2010). Distress is an important predictor of onset and relapse in psychosis and a common indicator of mental health problems (Brett et al., 2014). PE are understood as attenuated versions of psychotic symptoms (Chapman and Chapman, 1980) and are not necessarily distressing in themselves. However, the individual's evaluations and responses to such abnormal experiences predict distress (van Os et al., 2009).

Studies have demonstrated that the generally good outcome of PE can be modified to poorer outcomes of persistence and clinical need for care if subjects are exposed to additional environmental risk factors (van Os et al., 2009). In fact, a significant proportion of a psychotic disorder may be conceptualized as the rare poor outcome of a common developmental phenotype characterized by persistence of psychometrically detectable PE (van Os et al., 2009). Following the

prone-to-persistence-impairment model of psychotic disorder (van Os et al., 2009), environmental risks for psychosis act additively in causing abnormal persistence, which in turn increases the risk of subsequent transition to need for care (Cougnard et al., 2007). A dose-response relationship has been reported, so that the longer the period over which subclinical psychosis remained abnormally non-transitory, the greater the risk of developing associated impairment. Such environmental risk factors could be cannabis use, childhood trauma, and urban environment (Cougnard et al., 2007)

6.2.4 Psychological models of delusions and hallucinations

Psychological models of psychosis explain delusions as the result of the individual trying to make sense of unusual experiences (Kapur, 2003). Misinterpretation of such experiences and judgments based on such internal states may be crucial in the development of most delusions (Garety and Freeman, 2013). Kapur (Kapur, 2003) proposed that the symptoms of schizophrenia may arise out of the aberrant assignment of salience to external objects and internal representations. In this framework delusions are a “top-down” cognitive explanation that the individual imposes on these experiences of aberrant salience in an effort to make sense of them (Kapur, 2003). Hallucinations, then, arise from a conceptually similar and more direct process: the abnormal salience of the internal representations of percepts and memories (Kapur, 2003). Other theories on auditory hallucinations (AVH) specifically suggest that these experiences occur as a consequence of a failure to recognize thoughts and mental events such as inner speech as self-generated, and instead misattribute them to an external or alien source (Waters et al., 2012). More specifically, the cognitive processes involved in discriminating between internal and external perceptions, processes known as source monitoring or self-monitoring (Bentall et al., 2014, Frith, 1992), may play a role. Recent meta-analyses have provided robust evidence that AVHs are associated with impaired performance on a variety of source monitoring and self-monitoring measures (Bentall et al., 2014).

Generally the formation of PE (both delusions and hallucinations) may be induced by abnormalities in cognitive, interpersonal, and psychosocial functioning even before the development of frank psychosis (Kapur, 2003). Studies of the psychological mechanisms involved in the formation of different types of PE suggest that they are relatively uninfluenced by broad, more global cognitive deficits thought to be indicative of neuropsychological impairment. Each type of experience appears to be the product of specific biases in reasoning and cognition (Bentall and Fernyhough, 2008).

Patients prone to psychosis, and schizophrenia in particular, show specific biases in probabilistic reasoning and a tendency to “jump to conclusions”, alterations in attributional styles, abnormal levels of perceptual aberrations and “magical ideation”, and deficits in their Theory-of-Mind abilities (Kapur, 2003), and these cognitive deficits may trigger the onset and maintenance of delusions and hallucinations (Kapur, 2003).

6.3. Theory-of-Mind

Theory-of-Mind (ToM) refers to the ability to infer the dispositions, beliefs, emotions and intentions of other people (Fretland et al., 2015), and this allows humans to represent and attribute different types of mental states to others, i.e. inferring beliefs and reading intentions (Ciaramidaro et al., 2015). ToM is often thought of as equivalent to the mastering of False Belief, which is normally acquired by children around 4 years of age. However, ToM does in fact continue to develop until around at least 11 years of age (Baron-Cohen et al., 1999, Abu-Akel, 2003a), with studies indicating that ToM might further improve between late adolescence and adulthood (Dumontheil et al., 2010). ToM appears to be an innate potential ability with known neural correlates (Hamilton et al., 2004), but an ability requiring social and other experiences over many years to bring it successfully to an adult level (Jha and Singh, 2009, Brune and Brune-Cohrs, 2006). Knowledge on what accounts for individual differences in ToM abilities is sparse, but recent studies propose that both shared and non-shared environmental factors may play a greater role than previously assumed (Hughes et al., 2005, Korver-Nieberg et al., 2013). A positive development of ToM abilities might be facilitated by a high quality of the parent-child relationship, secure attachment, cooperative interactions with parents and siblings and verbal ability, whereas poorer ToM performance is predicted by child maltreatment (Hughes et al., 2005, Korver-Nieberg et al., 2013, Carpendale and Lewis, 2004). It has been suggested that whereas basic ToM skills may be more or less innate, later and more complex skills are to a high degree environmentally determined (Hughes et al., 2005, Korver-Nieberg et al., 2013).

Deficits in ToM are widely recognized in schizophrenia (Versmissen et al., 2008, Polanczyk et al., 2010) and are included as “Associated Features Supporting Diagnosis” for schizophrenia in DSM-V (American Psychiatric Association, 2013). However, the nature and extent of the ToM impairments

and their role in the ontogenesis of psychosis remain unclear (Bosco et al., 2009). Furthermore, alterations in ToM are also prominent in patients across different diagnostic categories, including neurodevelopmental disorders, particularly autism spectrum disorder (ASD) (Brune, 2005) and bipolar disorder (Russell et al., 2006). This suggests that ToM alterations are not specific to schizophrenia (Marothi and Keri, 2014) .

Studies of both clinical and non-clinical adult and childhood populations have found ToM alterations to be associated with specific symptoms such as persecutory delusions (Harington et al 2005) rather than with diagnostic categories (Barragan et al., 2011, Russell et al., 2006). ToM alterations are associated with PE in non-clinical adult (Versmissen et al., 2008, Langdon et al., 2010) and adolescent samples (Polanczyk et al., 2010, Barragan et al., 2011, Bartels-Velthuis et al., 2011). Studies have found ToM alterations to be associated with psychotic as well as with negative symptoms of schizophrenia in both clinical and non-clinical samples (Versmissen et al., 2008). A meta-analysis from 2007 did not find an association of psychotic symptoms and ToM performance (Freeman, 2007), whereas a recent meta-analysis (Ventura et al., 2013) did find associations between ToM-deficits and positive symptoms. However, these associations were weak, whereas the associations between ToM deficits and disorganization symptoms as well as between ToM deficits and negative symptoms were moderate (Ventura et al., 2013). This is in line with another meta-analysis (Sprong et al., 2007) finding participants with symptoms of disorganization to have had significantly lower ToM scores than those in subgroups with other types of symptoms.

These divergent findings might partly be due to methodological dissimilarities across studies, e.g regarding the measurement of ToM and the classification of symptom clusters (Brüne, 2005, Bentall et al., 2001, Bora et al., 2009), and partly due to the multifaceted nature of ToM.

6.3.1 Beyond the “right/wrong”-dichotomy: Theory-of-Mind as a heterogeneous and multidimensional construct

ToM is a heterogeneous and multidimensional construct (Fonagy and Luyten, 2009) and describes a complex function activity involving related but different abilities (Bosco et al., 2009). Researchers have started reformulating the concept within a continuum of variation as opposed to viewing it categorically (Sharp, 2012).

Among the most widespread differentiations suggested are cognitive vs affective ToM. That is, the ability to make inference regarding other people's belief vs the ability to make inference regarding others' emotions (Shamay-Tsoory et al., 2007, Tager-Flusberg and Caronna, 2007). Another suggested differentiation is between explicit cognitive-linguistic aspects tapped by the classic false belief tasks, and more fundamental attention and perceptual aspects involving implicit judgment of mental states, based on information available in faces, voices, and body gesture. Implicit aspects of ToM are largely independent of language ability and provide more direct links to social interaction deficits (Tager-Flusberg and Caronna, 2007, Sprung and Harris, 2010).

It has been suggested that ToM deficits might occur in representational abilities (i.e. a conceptual deficit) whereby an individual is unaware that others can hold a false belief about a state of affairs (Baron-Cohen et al., 1994, Frith and Corcoran, 1996), as well as in application abilities (i.e. deficit in performance) whereby an individual has awareness of other's mental life but fails to demonstrate this knowledge due to processing constraints (Ozonoff et al., 1991). However results have been mixed as to whether persons with schizophrenia have a fundamental ToM deficit with poor representational abilities, or if they possess the capacity for ToM but fail to apply it accurately (Fretland et al., 2015, Pickup and Frith, 2001).

Frith (Frith, 1992 Frith, 2004) suggested that schizophrenia patients with predominantly negative symptoms, disorganized behaviours, and early developmental problems lack representational abilities, whereas patients with paranoid symptoms would have the basic representational abilities but tend to excessively attribute intentions or self-referential meaning to others and therefore predict behaviour on the basis of these wrong beliefs (Frith, 2004). Abu-Akel and Bailey (2000) have argued that both disorganized and delusional patients with schizophrenia are able to apply ToM, albeit atypically (Abu-Akel and Bailey, 2000). For instance, patients with delusions of alien control, who misattribute their own intentions to others (Daprati et al., 1997), clearly represent the idea of others' minds and thus are capable of applying ToM representations, but the overall ToM functioning is characterized by over-attribution of particular mental states, rather than inability to mentalize or to apply their mentation. This distinction can also be understood as HyperToM versus HypoToM as introduced by Abu-Akel and Bailey (2000).

6.3.2 Hyper-Theory-of-Mind

This distinction between HyperToM and HypoToM is of potential importance (Fretland et al., 2015). HyperToM, also referred to as overmentalizing, can be defined as a social-cognitive process that involves making assumptions about other people's mental states that go far beyond observable data, and the average observer will struggle to see how these assumptions are justified (Frith, 2004, Montag et al., 2011). As such, it involves over-attribution of mental states to others and their likely misinterpretation (Sharp et al., 2013). HypoToM, also referred to as undermentalizing, refers to the prediction of behaviour on the basis of the actual state of the world rather than on beliefs of intentions and mental states of other people (Frith, 2004, Montag et al., 2011). Individuals with HypoToM will predict behaviour on the basis of the actual state of the world rather than on beliefs of intentions and mental states of other people, whereas individuals with HyperToM will tend to exaggerate attributions of affective and motivational states of other people (Frith, 2004, Montag et al., 2011). Both Hyper- and Hypo-ToM may limit the normal human capacity to attribute mental state, but these different strategies would lead to different kinds of error (Frith, 2004). The construct of "No ToM" can be added to this categorization, referring to the complete lack of a mental state concept (Montag et al., 2010) (see figure 2).

HyperToM may be related to the inability to take perspectives (Sharp, 2012) or to a tendency to an overgeneralization of hypotheses (Frith, 2004, Abu-Akel, 2003a, Abu-Akel and Bailey, 2000, Montag et al., 2011). HyperToM may also be underpinned by a hyper-associative social cognitive style, which does not necessarily imply a pathological process, but rather is linked to an exaggeration of the normal human tendency to attribute mental states. Perceiving meaning in randomness and, more particularly, attributing mental states where none are indicated, may be important factors in the formation of paranormal and delusional beliefs (Fyfe et al., 2008). Equivalent of such bias are found in young children, who over-attribute purpose and function to non-living natural kind. Furthermore, such biases are seen in healthy adults, who over-attribute intentionality under time pressure or under alcohol intoxication (Peyroux et al., 2014).

The appearance of HyperToM may also be stress-related. Increased stress responsiveness affects ToM abilities (Sharp et al., 2013), and women showing high cortisol stress response have been found to make more errors in particular due to a tendency to HyperToM after stress induction in an

experimental design, thereby demonstrating that stress responsiveness modulates ToM (Smeets et al., 2009)

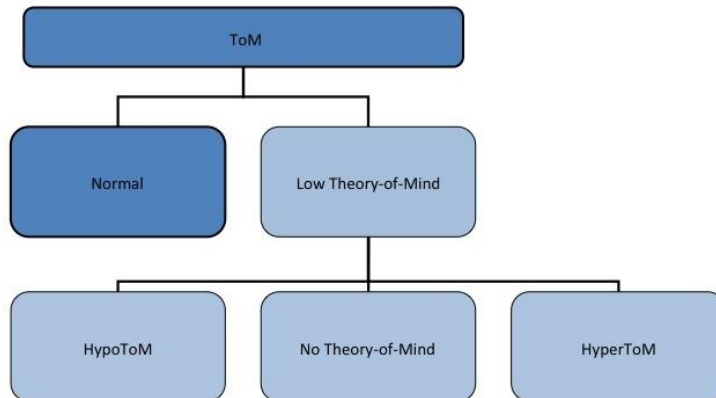


Figure 2: Theory-of-Mind impairments

6.3.3 Diametric Model of the Mind and Mental Illness

According to the Diametric Model of the Mind and Mental Illness, all mental disorders can be located along this dimension of ToM ranging from Hypo- to HyperToM (Badcock, 2011). It has been hypothesized that individuals with Autism Spectrum Disorder (ASD) and individuals with Psychotic Disorders (PD) may be located at the extreme ends of this dimension of ToM impairments (Ciaramidaro et al., 2015).

Individuals with ASD have low ToM skills such as inferring intention or understanding false belief. They therefore can be positioned at the HypoToM side of the continuum. Individuals with PD can be typified as having HyperToM. For example, patients with paranoid schizophrenia symptomatically over-interpret intentions either positively in erotomania (delusions that others are in love with the person) or negatively in delusions of persecution. They may also display bizarre beliefs about replacement of their will by an external force. They lack the normal sense of ownership of thoughts in their mind and may experience some thoughts as alien, i.e. originating from the minds of others. These so-called first-rank symptoms can be understood as extreme examples of excessive mentalism (Badcock, 2011).

6.3.4 Assessment of Hyper-Theory-of-Mind

ToM tests, usually use dichotomous ('right/wrong') response formats (Montag et al., 2011) and merely test the presence or absence of the ability to master facets of ToM such as false beliefs. Only a limited number of ToM tests take on more qualitative ratings, and of those only a few have been applied to measure HyperToM:

The Movie for Assessment of Social Cognition (MASC) (Montag et al., 2011) adopts the traditional social cognition concepts such as first- and second-order false belief, faux pas, metaphor or sarcasm, and operationalizes these concepts through a short movie approximating real-life social interactions. For each query correct answers are presented together with three distractors, corresponding to three types of errors in mental state reasoning tasks. Questions mostly refer to complex mental states and allow a detection of subtle mindreading difficulties. The MASC provides a sum score for all mental state decoding questions, and the following additional error categories: 1) 'undermentalizing' with two forms, either 1a) HypoToM, or 1b) No ToM and 2) HyperToM (Sharp et al., 2011).

The Animated Triangles Task (Abell et al., 2000; Castelli et al., 2000) comprises short, computer-presented animations. There are three conditions: 'random', 'goal-directed' and 'ToM'. After viewing each test item, participants describe what they perceive to be happening in the animation, and these responses are scored for accuracy according to standard criteria (Abell et al., 2000). A HyperToM score is calculated by summing the number of random condition items in which reference is made to the thoughts, feelings, beliefs, intentions or goal-directed behaviours of either triangle, or to any purposeful interaction between the triangles (Fyfe et al., 2008). For further description of the Animated Triangles Task, see the methods section.

The Strange Stories Task (Happé, 1994) originally comprises ToM stories and Natural physical state stories, each followed by a question. However Fyfe (Fyfe et al., 2008) added an additional set of random stories to be able to measure HyperToM. HyperToM is calculated by adding the number of random condition items in which reference is made to the thoughts, beliefs, feelings or intentions of story characters. For further description of the Strange Stories Task, see the methods section.

Despite the strengths of these tests, unfortunately they base the measure of HyperToM solely on the

presence of references to mental states. In contrast, the Dutch Theory-of-Mind Storybook Freek (Blijd-Hoogewys and Bartels-Velthuis, 2007) comprises both yes/no questions and justifications, which allows for a more detailed analysis of the answers and errors of the participants. Therefore, although not having previously been applied to measure HyperToM, this test could provide a stronger foundation for a measure of HyperToM.

6.3.5 Hypo- and Hyper-Theory-of-Mind and associated psychopathology

Studies of both clinical (Montag et al., 2011) and general population (Fyfe et al., 2008) adult samples support an association between HypoToM and autism, negative symptoms (Crespi and Badcock, 2008) and bipolar disorder (Montag et al., 2010) on the one hand and between HyperToM and psychotic disorders (Crespi and Badcock, 2008), PE (Montag et al., 2011, Frith, 2004, Abu-Akel and Bailey, 2000, Fretland et al., 2015), borderline traits (Sharp et al., 2011), Tourette syndrome (Eddy and Cavanna, 2015) and delusions and paranoid delusions in particular (Fyfe et al., 2008, Montag et al., 2011, Frith, 2004, Peyroux et al., 2014, Blakemore et al., 2003) on the other (see Figure 3).

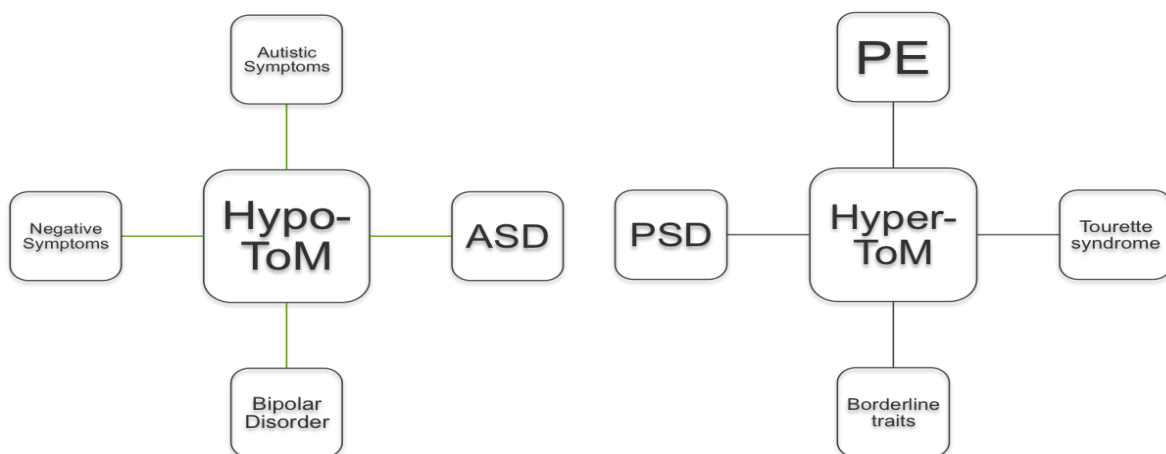


Figure 3: Associations between Theory-of-Mind impairments and psychopathology

ASD: Autism Spectrum Disorder, PE: Psychotic Experiences, PSD: Psychosis Spectrum Disorder.

The suggestion of a relationship between borderline traits and HyperToM (Sharp et al., 2011) is not surprising given that psychotic symptoms are not uncommon in patients with Borderline Personality Disorder (BPD), and it has been suggested that the diagnostic category of BPD requires revision to incorporate psychotic symptoms, especially hallucinations (Schroeder et al., 2012).

7. Aims of the Thesis

Studies are needed to establish if specific rather than global ToM impairments are associated with PE. However, differentiating such ToM impairments from those occurring in other major mental illnesses is complicated by several factors including the limitations of current assessment methods and the high rates of psychiatric comorbidity (Brent et al., 2014).

HyperToM may be a useful conceptual construct to improve the current insufficient differentiation between the various qualitative aspects of ToM (Fyfe et al., 2008, Montag et al., 2012) that may show different patterns of association with different developmental disorders (Abu-Akel and Bailey, 2000). However, very few studies have been carried out investigating this, and none have looked at the specificity of this association to see if HyperToM is correlated to PE specifically as opposed to being correlated to any mental disorder.

We regarded the population of preadolescent children with PE as a valuable population in which to study risk factors underlying psychosis liability. This new research paradigm also allowed us to address the complications of the diagnostic heterogeneity of people with psychosis by exploring the associations of interest at a symptom level. We also addressed the high rates of psychiatric comorbidity by including measures of co-occurring psychiatric diagnoses in order to investigate the specificity of HyperToM as marker of psychosis liability.

7.1. Overall aims and hypotheses

The main aim of this thesis was to investigate the relationships between PE and HyperToM in preadolescent children. We were interested to examine if HyperToM was stronger associated to PE than an overall measure of ToM impairments. Furthermore we were interested in the specificity of the association of HyperToM to PE as opposed to other psychopathology in preadolescence.

7.2 Specific aims and hypotheses

7.2.1 Paper I

The aim of paper I was to examine aspects of validity and reliability of the Danish version of the Theory-of-Mind Storybook Frederik in a sample of Danish children aged 7-14 including typically developing (TD) participants and participants with High Functioning Autism Spectrum Disorder (HFASD) with expected ToM impairments. The rationale for including a group with ASD was that the presence of ToM-deficits in this group is well-established in both children and adults (Colle et al., 2007, Baron-Cohen, 2001, Yirmiya et al., 1998). First, we wanted to explore if ToM-Frederik could detect the expected ToM deficits in the HFASD group as reflected in significant differences in mean scores between the HFASD and the TD groups. Second, we wanted to explore the converging validity as reflected in potential significant associations between scores derived from ToM-Frederik and the Strange Stories, which we consider to be the gold standard ToM Task, and also Animated Triangles. Third, we wanted to compare ToM-Frederik to measures of broader measures of social function looking at potential associations between ToM-Frederik and 1) the *Social Emotional Evaluation* (SEE) (Wigg, 2013) and 2) the *Social Responsiveness Scale* (SRS) (Constantino et al., 2003).

7.2.2 Paper II

The overall aim of paper II was to examine the specificity of the associations between ToM, HyperToM and PE in preadolescent children. We examined associations between HyperToM and PE in a general population sample of Danish children and replicated findings in a high prevalence sample of Dutch children.

We hypothesized that:

1. A lifetime history of PE would be more frequent in the group of children with overall ToM score at or below the median (Low ToM) compared to the group of children with ToM score above the median (High ToM) of the general population of children.
2. A lifetime history of PE would be particularly frequent in the group of children with the exaggerated type of ToM alteration (HyperToM) compared to children without this type of alteration.

3. The exaggerated type of ToM alteration (HyperToM) would be associated more strongly with a lifetime history of paranoid delusions (Pa) compared to a lifetime history of psychotic experiences without paranoid delusions (PE-NonPa).

7.2.3 Paper III

The aim of paper III was to further examine the association between HyperToM and PE by exploring developmental markers of PE in preadolescence with a particular focus on the role of HyperToM as a factor specifically impacting the risk of having PE. To this end the specificity of HyperToM as a correlate of PE as opposed to a correlate of any mental disorder was studied.

The following hypotheses were tested:

1. HyperToM is independently associated with PE. That is, after adjusting for well-known risk factors: familial liability to psychiatric illness, concurrent mental disorders and symptoms, and early developmental problems, HyperToM is still significantly associated with PE.
2. HyperToM is specifically associated with PE rather than with any DSM-IV non-psychotic mental health disorder
3. HyperToM is not associated with either neurodevelopmental disorders (ASD, ADHD, Tics, ODD/CD) or anxiety or depression

8. Method

8.1 Participants

8.1.1 Paper I

For Paper I we included a sample of the following two groups:

Children with Autism Spectrum Disorders (ASD group)

Participants were a clinical sample of 33 children aged 7-14 (M=11.3, SD=1.9) diagnosed at a child and adolescent psychiatry department with an Autism Spectrum Disorder (ASD) (ICD-10

codes F84.0-84.9). Children with $IQ < 70$ were excluded. Three children were aged 7-8, 11 children aged 9-10, 12 children aged 11-12, and 7 children aged 13-14.

Typically Developing children (TD group)

This group consisted of 41 children aged 7-14 ($M=10.9$, $SD=1.7$) from the general population without developmental delay. We included 8 children aged 7-8, 13 children aged 9-10, 14 children aged 11-12, and 6 children aged 13-14.

8.1.2 Paper II & III

For Paper II and III we included two independent samples:

1. 1630 Danish children aged 11-12 ($M=11.6$, $SD=0.4$) from the Copenhagen Child Cohort 2000 (CCC2000). CCC2000 is a general population birth cohort consisting of 6090 children born in 16 municipalities in the Copenhagen County in the year 2000, and followed prospectively since birth (Skovgaard et al., 2005) (For details on attrition, see figure 4)
2. 259 Dutch children aged 12-13 ($M=13.1$, $SD 0.5$). The children were recruited from a case-control sample of 694 children, half of whom had AVH when assessed at age 7 or 8 as part of a population-based study of 3870 children (Bartels-Velthuis et al., 2011b).

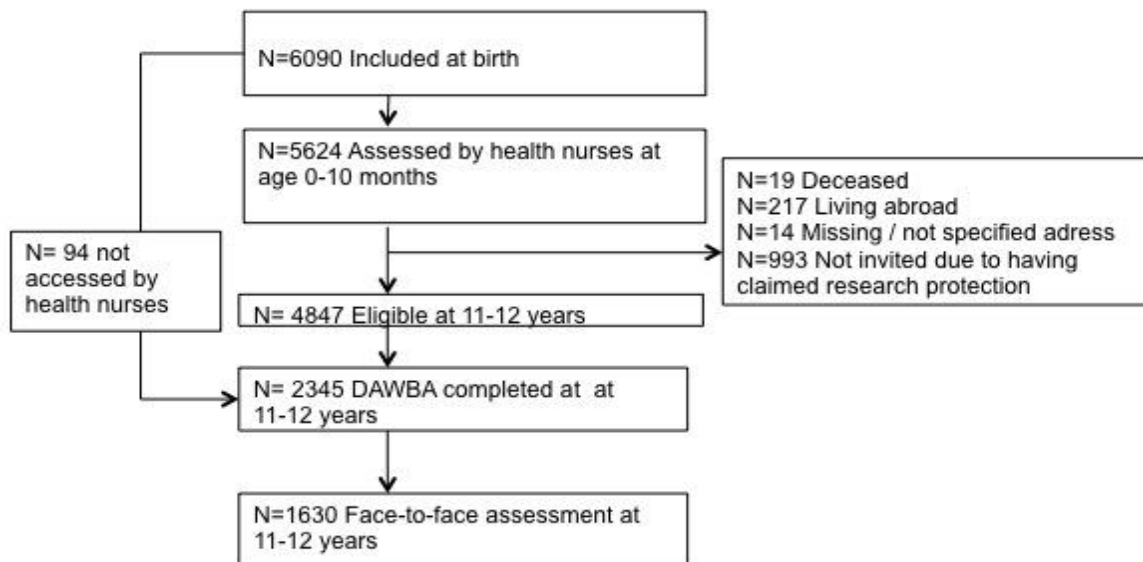


Figure 4: Flow chart with attrition - Sample I (CCC2000)

8.2 Psychometric assessments and register-based data

8.2.1 All three papers

Theory-of-Mind

The ToM Storybook Frederik (ToM-Frederik) was used to assess ToM in all samples. ToM-Frederik is the Danish version of the Dutch ToM Storybook Freek (Blijd-Hoogewys and Bartels-Velthuis, 2007) and is aimed mainly at 10–14-year-old children. The test stories, questions and scoring categories were translated and back-translated by professional translators. A pilot study prior to the PhD-study examined the acceptability of the first Danish version of the task in 50 randomly selected 5th grade children from the general population. This led to some minor changes of the wording, but otherwise the task showed good face validity.

The children are asked a total of 24 questions while being presented with 16 pictures and listening to the storybook read aloud. These questions consist of 16 ‘test’ and 8 ‘justification’ questions. The test answers are scored as right or wrong, and the 8 justification answers are classified according to 23 predefined categories of mentalization. Based on these categories, the answers were scored on an ordinal scale predefined for each situation, resulting in a justification sum score that was summed with the test score to form the total ToM scale score of ToM abilities. The total ToM scale served as the primary measure of overall ToM abilities.

HyperToM: In paper II and III we applied the total score from ToM-Frederik, but also included a measure of HyperToM. To this end, the 8 justifications answers were further scored on a dichotomous scale as a non-mentalizing (‘0’) or mentalizing (‘1’) type of answer, regardless of the classification of the answer as formally right or wrong in the context, resulting in a mentalizing scale-score. Conform previous work, mentalizing answers were defined as those referring to beliefs, desires and similar inner states (Fyfe et al., 2008, Montag et al., 2012). A high number of mentalizing answers (High-Mentalizing) were defined as scores above the median for population sample I. We defined low ToM skills (Low ToM) as scores at or below the median on the total ToM scale. HyperToM was defined on the basis of (i) Low ToM total score combined with (ii) high number of mentalizing answers (see figure 5). By combining low ToM total score and high number of mentalizing answers, individuals who have a low level of overall ToM abilities while making

mental attributions frequently are captured. These children showed a tendency to exaggerate and aberrant mentalizing explanations i.e HyperToM.

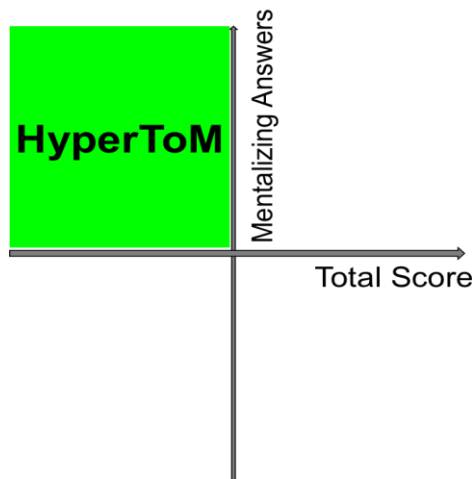


Figure 5: Measure of Hyper-Theory-of-Mind

8.2.2 Paper I

For paper I we included two advanced ToM tests besides ToM-Frederik, as well as tests of the broader aspects of social function to be able to compare them to ToM scores within the HFASD group.

The Strange Stories Task assesses the child's ToM ability (Happé, 1994) and provides means for testing advanced ToM-ability (Brent et al., 2004, Sanders, 2009). Short vignettes are read aloud by the interviewer, whereupon subjects are asked to explain why a character says something that is not literally true (White et al., 2009).

The Animated Triangles Task (AT) (Abell et al., 2000) consists of a series of computer-presented animations. These animations show one large red and one small blue triangle moving around on the screen (White et al., 2011). The participants are instructed that, while watching the animations, they have to give a concurrent verbal description of what they think is happening. These animations span scenarios from 'Random' to 'Goal-Directed' and 'ToM'-type situations, and performances in terms

of verbal descriptions are rated on scales for Appropriateness and Intentionality. The AT Appropriateness score measures the understanding of the event depicted in the animations, as intended by the designers (see (Castelli et al., 2000) for further details). The Intentionality score reflects the use of mental state terms. Separate scores were calculated for the three types of animations. We also applied an objective method using multiple-choice questions (MCQ) (White et al., 2011). At the end of each animation participants were asked to categorize it as one of three types: ‘no interaction’ (Random), ‘physical interaction’ (Goal Directed), and ‘mental interaction’ (ToM) (referred to hereafter as AT MCQ-categorization score). In cases of ToM-type animations they were asked additional questions to test their understanding of the mental states depicted in the animation. The participants could choose between one of five listed adjectives to best match the feelings of each of the triangles at the end of the animation; a separate list was provided for each triangle in each animation (hereafter referred to as MCQ-feelings score).

Performances on the Block Design and the Vocabulary subtests of WISC-III or WISC-IV were used as indices of intelligence level. These subtest scores are known to be highly correlated with IQ on the full Wechsler test of intelligence (Wechsler, 2003).

Social Emotional Evaluation (SEE) evaluates the social skills and higher level language skills that children need for successful interaction in everyday situations at home, at school and in the community. The SEE assesses both the receptive and expressive social skills of children aged 6-12 years (Wigg, 2013).

The SEE Social Emotional Questionnaire (SEQ) is applied to the parents and contains questions on the social skills of the child (Wigg, 2013).

The Social Responsiveness Scale (SRS) is a 65-item questionnaire (score 0-195) administered to the parent covering various aspects of the child’s interpersonal communication, reciprocal and repetitive/stereotypic behaviour. The SRS identifies the presence and extent of autistic social impairments on a quantitative scale across different ranges of severity, with higher scores indicating greater severity of social impairment (Constantino et al., 2003).

8.2.3 Paper II & III

For paper II and III a range of variables, chosen for their consistent associations with schizophrenia in the literature and previously found to also be associated with PE, were included in addition to the main measures of PE, HyperToM and psychiatric diagnoses.

Psychotic Experiences: In Sample I PE were assessed in a semi-structured interview with K-SADS-PL (Kaufman et al., 1997), applying the screening section and the supplement on psychotic symptoms. Possible PE ratings were: absent, likely present, and definitively present. PE were rated present if at least one psychotic symptom was scored as ‘likely’ or ‘definitely’ present. This rating was done for two time periods: the past month, and the ‘lifetime before’. For the present study, a binary variable was created, coding ‘yes’ or ‘no’ PE for the lifetime period, ‘yes’ indicating that the child had experienced at least one psychotic symptom ‘likely’ or ‘definitely’ present in last month and/or in the lifetime before. The subgroup of children with delusional thoughts with paranoid content (Pa) were a priori defined as those with scores of likely or definitely present delusions of persecution, mind-reading and/or receiving messages from TV/radio, as these delusions have a clear paranoid content and can be reliably assessed in the general adolescent population (Kelleher et al., 2009). Based on 75 videotaped interviews, the inter-rater reliability was computed as Fleiss’ Kappa for assignment of children to each group based on life-time presence of PE symptoms. The inter-rater reliability was very good for both the grouping into children with or without PE (Fleiss Kappa = 0.95) and the further grouping into 1) healthy children (NonPE) 2) children with Psychotic Experiences but no delusional thoughts with paranoid content (PE-NonPa) and 3) children with Psychotic Experiences that include delusional thoughts with paranoid content (Pa) (Fleiss Kappa = 0.85) (Landis and Koch, 1977, Altman and Gardner, 1991).

In Sample II PE were assessed using the screening question on AVH from the Auditory Vocal Hallucination Rating Scale (AVHRS; (Bartels-Velthuis et al., 2012) and three items on delusional experiences from the Adolescent Psychotic Symptom Screener (APSS); (Kelleher et al., 2009). The AVHRS is a structured 16-item interview evaluating experiences on AVH during a predetermined period (e.g. past month, past year) (Bartels-Velthuis et al., 2012). The APSS items consist of questions on delusions (mind reading, persecutory delusions and receiving media messages). AVH were rated as: 0 (no) or 1 (yes) and were assessed at baseline over the past year and at follow-up

over the five intervening years. Delusions were rated as: 0 (no), 1 (yes, likely) or 2 (yes, definitely) and were assessed over the lifetime (Kelleher et al., 2009). A variable was constructed indicating presence of at least one (definite) delusion (hereafter: delusions). As in sample I, Pa was defined as any delusion of persecution, mind-reading and/or receiving messages from TV/radio. Based on the 337 children inter-rater reliability for AVH was good ($\kappa = 0.88$).

Psychiatric diagnosis: Psychiatric diagnoses were assessed by the Development and Well-being Assessment (DAWBA). DAWBA is a highly structured interview designed to generate psychiatric diagnoses in children and adolescents according to DSM-IV and ICD-10 and covers child development, psychiatric symptoms, distress and social impairment. A computer algorithm generated the preliminary diagnoses, and subsequent clinical review by senior child psychiatrists determined the final DSM-IV diagnoses (Goodman et al., 2000). The inter-rater reliability was examined in a random sample of 100 children by three senior consultants. DSM-IV-mental disorders were grouped into anxiety disorders, depressive disorders, OCD, tics, behavioural disorders (oppositional defiant/conduct disorder - ODD/CD), attention-deficit/hyperactivity disorder (ADHD) and autism spectrum disorders (ASD). The inter-rater reliability was high for any DSM-IV-diagnosis ($\kappa = 0.81$). Pairwise comparisons of raters revealed Kappas for the main groups of diagnoses in the range 0.63–0.88 (Jeppesen et al., 2014a).

Puberty: Puberty was assessed by Tanner staging based on self-reports (Coleman and Coleman, 2002).

Cognition: Performance on the Block Design (BD) subtest of Wechsler Intelligence Scale for Children (WISC-III) was used as a proxy measure of children's general cognitive abilities. The BD subtest is highly correlated with full-scale IQ in the Wechsler Intelligence Scale for Children (Wechsler, 2003).

Bullying: Bullying was assessed with the Olweus Bully/Victim Questionnaire (Gothwal et al., 2013) for self-report of being involved in bullying as victim and/or as a bully. The Questionnaire covers physical, verbal and relational forms of bullying to which we added questions on cyber bullying following Kowalski & Limber (Kowalski and Limber, 2007).

Infancy problems: In Denmark, a community health nurse with specific training in infant health visits the same families regularly during the first year of life. For the CCC2000 study, a standardized record and manual was developed to record information on the health nurses' assessments prospectively from birth at four scheduled home visits conducted when the children were at the ages 1-5 weeks (visit 1), 2-3 months (visit 2), 4-6 months (visit 3), and 8-10 months (visit 4) (Skovgaard et al., 2005). For the present study we included: **Infancy regulatory problems** defined as the child having either feeding, sleeping, or tactile (whether the child shows pleasure being touched and/or can easily be comforted in the parent's arms) problems at least at one visit. **Mother-child relation** with abnormal mother-child relationship defined as deviances in the mother's caretaking of the child, including her handling, expectations, reactions and reciprocity during interaction with the child; and **Infancy contact problems** defined as the child having problems within at least one of three domains: Eye contact, Contact smile, and Contact babbling. These measures of infancy development were chosen because they have previously been found to predict psychopathology in the children later at age 1½ and/or age 5-7 in CCC2000, as early problems in communication predicted neuro-developmental disorders at children aged 1 1/2 years (Skovgaard et al., 2008) and 5-7 (Elberling et al., 2010).

Registry Data: CCC2000 children and their first degree relatives were linked via the Central Person Registry numbers to the following Danish National Registries: Psychiatric Central Registry and the Family Database to acquire the following:

- **Familial psychiatric liability and parental mental illness during early child development:** Any diagnosed psychiatric disorder as in- or outpatient at any psychiatric hospital or centre in Denmark in any first-degree relative (including father, mother and siblings) was included from the Danish Psychiatric Central Registry in order to detect a family history of mental disorders. Any mental disorder in first-degree relatives before the birth of the child was applied as a measure of familial psychiatric liability and considered a proxy measure of genetic liability. Parental mental disorder during early child development covered the first three years of the child's life. Details on included ICD-8 and ICD-10 diagnoses are described elsewhere (Jeppesen et al., 2014b).

- **Socioeconomic status:** Data on duration of mother's education and change in family income 2000-2010 were acquired to describe socioeconomic status (SES). Low maternal education is consistently associated with poor mental health of the child (Boyle et al., 2011), and low family income is associated with several different lifetime mental disorders (Sareen et al., 2011). Change in family income (the lowest tertile for increase in time period 2000-2010) was applied to best capture this condition over the full period with a single variable. Furthermore, we included changes in the family composition in the time period 2000-2010 (whether the child lived with both parents, one parent or new partners of the parent).

8.3 Statistical analyses

Analyses were carried out using Stata 12 software (StataCorp LP, College Station, TX) and SPSS 20 (SPSS Inc., Chicago IL). Level of statistical significance was set at $p < 0.05$.

8.3.1 Paper I

Students' t-tests and chi-square tests were applied to compare continuous and categorical background variables (gender, age in months, Wechsler Block Design scale score, and Wechsler Vocabulary scale score). The test-retest reliability of the ToM-Frederik for the 11-12 years-old children in the TD group was established by means of a Pearson product-moment correlation coefficient. Furthermore, a paired samples t-test was applied to measure the test-retest effect.

Between-group comparisons were carried out to assess whether the outcome variable from the ToM-Frederik differed between the TD and the HFASD group. The between-group comparisons were done using ANCOVA, with the background variable(s) as the co-variate(s). In case the raw data deviated significantly from a normal distribution, they were logarithmically or square root transformed to approximate a normal distribution before analyses were performed. The same procedure was followed for the outcome variables from Strange Stories, AT, SEE, and SRS. To determine the convergent validity of ToM-Frederik potential associations with the core variables derived from Strange Stories and AT were analyzed using Pearson correlations in the full sample, as well as in the HFASD and TD groups separately. Finally, the potential associations between ToM-Frederik and the SRS total score were analyzed using Pearson correlations.

8.3.2 Paper II

Descriptive statistics were used to analyse sample characteristics. Group differences on demographic variables, ToM scores as well as the proxy measures of general cognitive ability were tested by chi-squared tests for categorical variables and by independent samples t-tests for continuous variables.

Logistic regression analyses were conducted with HyperToM, ToM total score, low mentalizing, gender and the proxy measures of general cognitive ability (BD respectively “school level”) as independent variables. In each logistic regression analysis the predictive effect of each of the ToM scale scores was estimated while adjusting for the proxy measures of general intelligence. The logistic regression analyses were used to estimate 1) the risk of having a lifetime presence of PE (yes/no) for the group of children with low ToM compared to the group of children with high ToM in the two samples; and 2) the risk of a lifetime presence of PE (yes/no) for the group of children with HyperToM compared to those children without HyperToM in the two samples. The relative risk was calculated as odds ratio (OR) with 95% CI. Finally, multinomial logistic regression analyses were used to estimate the dose-response relationship between HyperToM (yes/no) and having a lifetime history of paranoid delusions (Pa), a lifetime history of psychotic symptoms without paranoid delusions (PE-NonPa), and no lifetime history of PE. The hypothesis being tested was that the risk for Pa versus no PE when exposed to HyperToM would be higher than the risk for PE-NonPa versus no PE when exposed to HyperToM. Thus, the estimated ORs express the risk of experiencing Pa relatively to no PE, and the risk of experiencing PE-NonPa relatively to no PE for children with HyperToM compared to the children without HyperToM. All analyses of risk of HyperToM status were repeated substituting HyperToM as predictor with each of the underlying dimensions of HyperToM, i.e. low ToM score and high mentalizing answers in order to be able to compare the OR of HyperToM to the OR of these variables. All multinomial logistic regression analyses were adjusted for gender. Post-estimation analysis was carried out to examine if the estimated OR of HyperToM for Pa was significantly different from the OR of HyperToM for PE-NonPa.

8.3.3 Paper III

Associations between the family and developmental variables, and PE and HyperToM were tested using chi-square tests for categorical variables and independent t-tests for continuous variables.

Logistic regression analyses were conducted including PE as the dependent variable, and all other variables as independent variables. This was done in order to analyse the independent association with HyperToM when adjusted for all other predictive variables. In order to answer the research question on the specificity of HyperToM as an associated variable to PE, multinomial logistic regression analyses were performed with illness category as the dependent variable, and the remaining variables as independent variables. Finally, associations between HyperToM and neurodevelopmental disorders (ND), anxiety and depression were tested using logistic regression analyses. In all regression analyses, variables were entered simultaneously as no predictions were made about the inter-dependence of variables. Entering the variables simultaneously made it possible to test which variables were significantly associated with PE and illness category, respectively, when adjusting for all other included variables.

Due to missing data (between 7-249 cases) in seven variables (changes in family structure; change in family income 2000-2010; length of mother's completed education 2010; family mental illness liability; infancy regulatory problems; mother-child relationship and child contact problems) imputations were performed using the STATA multiple imputation suite of commands (mi). Data were assumed to be missing at random (MAR), and sex and age were used to impute the missing values. All variables were imputed 30 times. This enabled us to use the full sample (N=1630) and not only the children without missing values (N=1369).

9. Results

9.1 The validity of the ToM-Frederik test (paper I)

Based on all 74 participants the inter-rater reliability for ToM-Frederik was excellent ($r=0.96, p<0.001$) (George and Mallery, 2003), and based on ten out of the 14 participants aged 11-12 years in the TD group the test-retest reliability estimate of the ToM-Frederik total score was good ($r=0.84, p=0.003$)

ToM-Frederik total score was significantly lower in the group of children with HFASD than in the TD group. ($M=20.44$ vs 22.88 , $F(2,70)=4.027$, $p=0.049$). In the full sample the ToM-Frederik score

was significantly and positively correlated with both the Strange Stories Mental State score ($r=0.551$ $p<0.001$, $N=72$) and the AT ToM intentionality score ($r=0.379$ $p<0.001$ $N=68$). In the HFASD group the score on ToM-Frederik was also significantly and positively correlated with both the Strange Stories Mental State score ($r=0.570$ $p<0.001$, $N=31$) and the AT ToM intentionality score ($r=0.484$ $p=0.011$, $N=27$). However while the score on ToM-Frederik was significantly and positively correlated with the Strange Stories Mental State score ($r=0.462$ $p=0.002$, $N=41$) in the TD group, it was not significantly correlated to the AT ToM intentionality score. Analyses showed that ToM-Frederik was significantly and negatively correlated with SRS in the full sample ($r=-0.253$, $p=0.032$, $N=73$). However these correlations were not statistically significant in neither the HFASD nor the TD group.

9.2 The associations between PE and ToM measures (paper II)

A total of 171 (10.5%) of the 1630 children in sample I reported lifetime PE. The further subgrouping of these 171 children based on the presence or absence of Pa yielded a Pa group of 70 (41%) children, and a PE-NonPa group of 101 (59%) children. Based on these numbers, a total of 827 (51%) were classified as having low ToM, and among these 202 (12%) children were classified as having HyperToM. The children with a low ToM score had an increased risk of having PE compared to the children with high ToM score (adjusted OR = 1.6, 95% CI 1.1–2.3, $\chi^2(4) = 12.42$ $p = 0.010$). The children with HyperToM compared to the children with no HyperToM also had an increased risk of PE (adjusted OR= 1.8, 95%CI: 1.2–2.7 $\chi^2(3) = 10.11$) $p = 0.006$). The estimated risks of PE for poor ToM and for HyperToM were within the same range with almost identical 95% CI. The adjusted OR for Pa in the HyperToM group versus the group without HyperToM was 2.0 (95% CI: 1.1–3.7 $\chi^2(4) = 9.93$ $p = 0.021$), whereas the adjusted OR for having PE-NonPa was non-significant albeit directionally similar.

Of the 259 children in sample II, 156 (60.2%) reported lifetime PE. The further subgrouping of these 156 yielded a Pa group of 71 children (46%) and a PE-NonPa group of 85 children (54%). 21 (8%) of the children in sample II were classified as having HyperToM. The children with low ToM did not have a significantly increased risk of having PE compared to the children with high ToM. The children with HyperToM had an increased risk of PE compared to the children without HyperToM (OR =4.6, 95% CI 1.3–16.2, $\chi^2 = (2)7.56$ $p = 0.018$). The OR for Pa in the HyperToM group versus the group without HyperToM was 6.2 (95% CI 1.7–23.6 $p = 0.002$), whereas the OR for having PE-NonPa was non-significant albeit directionally similar (figure 6).

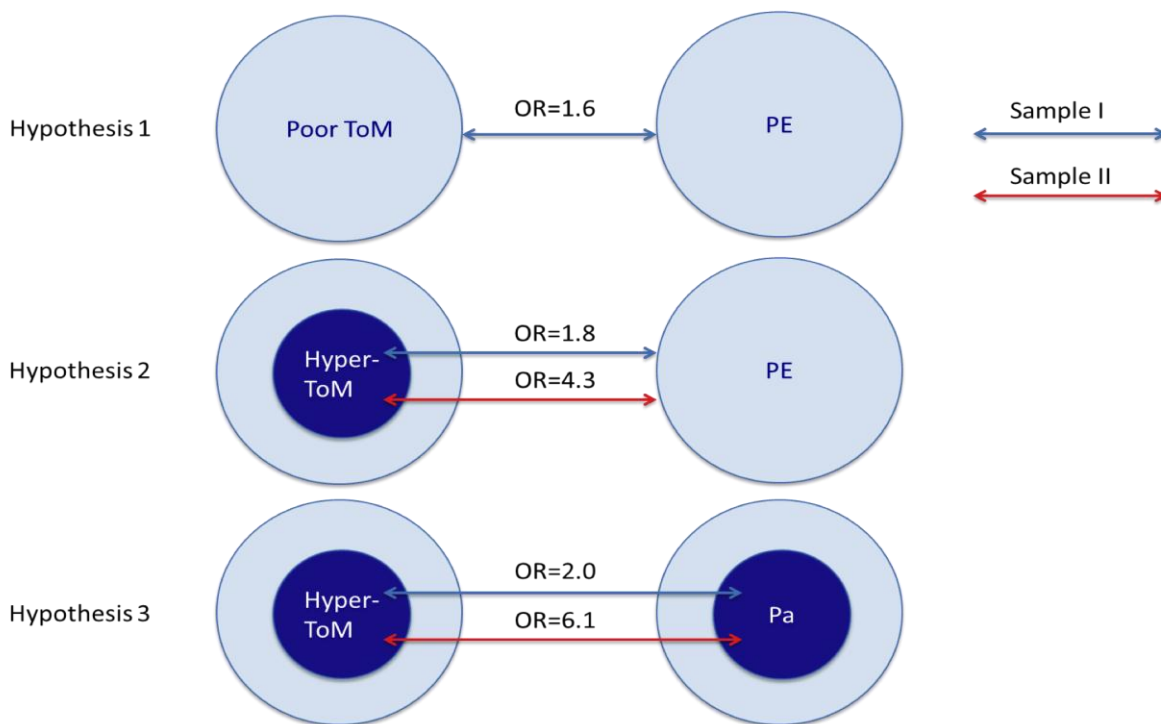


Figure 6: Significant associations between Hyper-Theory-of-Mind and Psychotic Experiences in Sample I & II.

OR: Odds Ratio, PE: Psychotic Experiences Pa: Paranoid Delusions

9.3 The specificity of the association between PE and HyperToM (paper III)

The results from paper III showed that PE were significantly more prevalent in groups of children with: familial psychiatric liability (15.0% vs 9.8 %), parental mental illness during early development (21.3% vs 10.0%), changes in family composition (13.7% vs 9.5%) change in family income (15.1% in the lowest tertile vs 9.8% in the middle and 7.8% in the highest tertile), regulatory problems (12.8% vs 9.2%), onset of puberty (11.4% vs 7.4%), having a psychiatric diagnosis (23.8% vs 8.3%) and being involved in bullying (19.5% vs 8.0%). None of these predictors of PE were associated with HyperToM. Only a low cognitive score on BD was significantly associated with HyperToM.

The regression analyses showed that HyperToM was significantly associated with PE after adjusting for all other included variables (OR=1.81 95% CI 1.2-2.8, $p=0.007$). Apart from

HyperToM, having a concurrent psychiatric diagnosis, being involved in bullying and lowest increase in family income remained significantly associated with PE

Multinomial regression analyses showed that HyperToM was the only variable exclusively associated with PE without concurrent mental illness (OR=1.71 95% CI 1.0-2.8, $p=0.034$). Involvement in bullying remained significantly associated with PE without mental illness (OR=2.37 95% CI 1.6-3.7, $p<0.001$) in a model including HyperToM, but involvement in bullying was also significantly associated with having any psychiatric diagnosis (OR=2.28 95% CI 1.6-3.2 $p<0.001$), and with having both a psychiatric diagnosis and PE (OR=4.11, 95% CI 2.3-7.3, $p<0.001$).

Looking specifically at the most prevalent concurrent diagnoses, HyperToM was not associated with either neurodevelopmental disorders (ND), anxiety or depression.

10. Discussion

10.1 Summary of results

The results from paper I showed ToM-Frederik to be able to identify the expected ToM deficits in the group of children with HFASD. Furthermore, convergent validity was supported by the within-group associates between test scores of ToM abilities. The inter-rater reliability for ToM-Frederik was excellent.

The results from paper II on cross-sectional associations between HyperToM and PE in two population-based samples partly confirmed our first hypothesis on PE being more frequent in children with low ToM in sample I, but not in sample II, where no significant association was apparent. Hypothesis two on PE being particularly frequent in children with HyperToM was confirmed, as the OR for having PE in both samples was higher for the HyperToM group than for the group without HyperToM. Hypothesis three was confirmed as HyperToM was associated more strongly with Pa than PE-NonPa in both samples.

The results from paper III on the further examination of the association between HyperToM and PE confirmed hypothesis one on HyperToM being independently associated with PE, in that

HyperToM remained significantly associated with PE after adjusting for the following risk factors: gender, familial liability, having a concurrent mental disorder, gender, parental mental illness during early child development, changes in family structure, change in family income 2000-2010, length of maternal education, regulatory problems, abnormal mother-infant relation, infancy contact problems, onset of puberty, lower proxy-measures of cognition and bullying. Hypothesis two was confirmed as HyperToM was exclusively associated with PE and not with either any psychiatric diagnosis (without PE) or with having both PE and a psychiatric diagnosis. Hypothesis three was confirmed as HyperToM was not associated to ND, anxiety or depression either. HyperToM was the only variable being independently and specifically associated with PE.

10.2 Strengths and Limitations

The main strength of the study of the validity of the ToM-Frederik test reported in paper I is the relatively comprehensive test battery, which made us able to assess convergent validity of the three ToM tasks. However, the present study also has some limitations. The gender distribution differed between the HFASD and the TD group, with more boys in the HFASD group. Also, due to the different intelligence assessment methods between the groups, analyses of the potential effects of intelligence on the ToM scores were not performed.

A main strength of the study of PE and ToM in paper II and III is the inclusion of two population-based samples, with one being a large general population birth cohort sample with data from infancy to age 11-12. The data set included a broad range of variables from different sources and PE and ToM were assessed using the same items and cut-offs. The age range was fixed around the onset of puberty and was roughly the same in the two samples.

We found a prevalence of PE of 10.5%, which is within the range of what could be expected based on previous studies applying a diagnostic interview in that age group (Kelleher et al., 2012, Linscott and van Os, 2013).

The 1630 children participating in the face-to-face interview showed statistically significant, but minor, differences in sociodemographic and perinatal characteristics, with lower frequencies of biological and psychosocial adversities compared to the nonparticipating children, including a

slightly lower frequency of a family history of psychiatric disorders (Jeppesen et al., 2014b). However, when adjusting for the distribution of gender, season of birth, gestational age, birth weight, parity, maternal age, years of education, ethnicity, family composition, change in family composition and income, the weighted lifetime prevalence of PE was only slightly higher at 10.9% compared to a crude prevalence of 10.5% (Jeppesen et al., 2014a).

Due to its recency the psychometric properties of the Danish version of ToM-Frederik task have not yet been examined extensively. However, the results reported in paper I were supportive. Furthermore, the internal consistency of the task was found to be fair and comparable across the population-based samples, and the scores were close in range. Also, ToM-Frederik is based on the ToM Storybooks Sam for younger children, which have good psychometric qualities (Blijd-Hoogewys et al., 2008, Bulgarelli et al., 2014).

We were not able to control for general cognition with a measure of full IQ. Nevertheless, the Block Design test result, used as proxy measure of IQ, is strongly associated with full scale IQ (Wechsler, 2003). There is general consensus that neurocognition and social cognition (such as ToM) are related but different constructs, and there seems to be only a modest association between neurocognition and social cognition (Couture et al., 2006). Possibly, general cognitive abilities represent a necessary but not sufficient condition for adequate mentalisation (Sprong et al., 2007).

Both HyperToM and PE were assessed cross-sectionally at age 11-12, so the present results do not make it possible to determine the direction of the relationships of these. However the results are in line with theories suggesting that cognitive biases contribute to the development of PE (Kapur, 2003) and each type of experience is the product of specific biases in reasoning and cognition (Bentall and Fernyhough, 2008). Nevertheless, future longitudinal studies need to further explore the developmental trajectories of HyperToM in childhood and adolescence and to assess both the causal and temporal relationships between PE and HyperToM. The fact that both PE and HyperToM are only assessed at one time point also means that the stability of these phenomena cannot be explored, and future longitudinal studies should explore the stability of HyperToM over time and if HyperToM is specifically associated to the persistent type of PE.

As HyperToM and PE are associated, a higher prevalence of HyperToM might be expected in the Dutch sample, since PE are more prevalent in this sample. However, the participants in this sample are slightly older. They are therefore expected to achieve a higher ToM score, and thus fewer would be getting a ToM score low enough to fulfil the first of the two criteria for HyperToM. HyperToM might in part depend on brain maturation and learning (Abu-Akel, 2003b), and therefore be less common in an older age group, and constitute a greater disadvantage and thereby a higher risk for PE.

10.3. Theoretical and clinical implications

The findings of ToM-Frederik reported in paper I confirm previous findings in a study comparing 3-12-year-old children with PDD-NOS and TD children applying the Dutch version of the test (Blijd-Hoogewys et al., 2008), and the results are in line with numerous others tests comparing ToM performance in HFASD and TD children. The task represents a gain for both research and clinical practice, as it is able to identify impairments of ToM in older children and is relatively fast to administer. The development of an advanced and nuanced way of measuring HyperToM is crucial. The number of participants with HyperToM was found to be about 10% in both of the population based samples. However, this should not be considered the prevalence of HyperToM in the general population, as the criteria for HyperToM was not set to define an impairment you either have or do not have. Rather, the participants categorized in the HyperToM group represent those with a certain degree of tendency to HyperToM.

The fact that HyperToM was not predicted by any of the early developmental variables included in the study supports the view that whereas basic ToM skills may be more or less innate, later and more complex skills may be environmentally determined to a large extent (Hughes et al., 2005, Korver-Nieberg et al., 2013). Equivalents of HyperToM are found in young children, who over-attribute purpose and function to non-living natural kind such as rivers (Peyroux et al., 2014), and HyperToM may depend on both brain maturation and learning (Abu-Akel, 2003b). HyperToM does not necessarily imply a pathological process, but rather is linked to an exaggeration of the normal human tendency to attribute mental states (Fyfe et al., 2008) and may be considered not so much as a deficit but rather as a cognitive strategy or style (Sharp et al., 2011).

The present study confirmed that many predictors of schizophrenia are also associated with PE. However, looking at PE without psychiatric diagnosis specifically, only HyperToM and bullying were significantly associated to this group when we adjusted for all other potential risk variables included in the study. On this basis it might be suggested that HyperToM points to a pathway to PE that is preceded to a lesser extent by early developmental alterations. Our finding that HyperToM is more strongly associated with PE specifically than with any diagnosis supports the belief that HyperToM is aetiologically related to mechanisms underlying psychotic illness. However, HyperToM was not predicted by any other included variable other than BD, so whereas HyperToM appears to possess an inborn increased risk of PE, there is not necessarily any specificity for any diagnosis yet. Such an interpretation is in line with the view that the first stage in the development of psychosis may be a diagnostically non-specific stage of potentially more severe psychopathology, which only later may acquire a degree of diagnostic specificity (Fusar-Poli et al., 2014).

A recent review found that bullying does predict the later development of PE (Edmondson, Whitehead & Smith, 2014), and Kelleher et al. (2013) found direct evidence that a reduction in bullying could lead to a reduced incidence of PE (Kelleher et al., 2013). However, the current results do not show a specific association between bullying and PE, but instead suggest that bullying is a non-specific risk factor of general psychopathology. The effect of bullying on PE may be more indirect, considering that the effects of being bullied can be seen later in life in the form of avoidant coping styles and persistent feelings of loneliness/exclusion (Adams et al., 2011).

11. Conclusion and perspectives

11.1 Conclusion

The focus of this thesis was to investigate the relationships between PE and HyperToM in preadolescent children. To that end the thesis had three main aims. Firstly, it was aimed at validating the ToM-Frederik as a measure of ToM; Secondly, it aimed at exploring the associations between low ToM, HyperToM and PE in two independent population-based samples, and thirdly to explore the specificity of HyperToM in terms of impacting the risk for having PE in preadolescence.

We found support for the validity of the Danish version of the Theory-of-Mind Storybook Frederik. This task represents a gain for both research and clinical practice, as it is relatively fast to administer and has very nuanced outcome results, although unfortunately norms are not yet established.

Our results point to an association between HyperToM and PE that is not fully explained by an association between poor ToM and PE. The results suggest that particularly the HyperToM type is associated with PE, and that this association is strongest for delusional ideas with paranoid content, i.e. delusions of persecution, mind-reading, and/or receiving messages from TV/radio.

The present study confirmed that many predictors of schizophrenia are also associated with PE. However, the findings suggest that whereas a wide range of family and child variables are associated with psychopathology in general, HyperToM is independently and specifically associated with PE and thus might mark a risk for PE specifically.

Our findings suggest that it may be productive to apply more differentiated measures of ToM instead of relying on an overall score based on the number of correct answers. This could be helpful not only when conducting research on the development of PE and psychosis, but also when applying ToM tasks as part of a clinical assessment in child mental health services settings.

The construct of HyperToM may be useful in delineating differential pathways to psychopathological outcomes, and may help us to understand more about mechanisms in the aetiology of different symptoms. Our findings also indicate the possibility of a specific pathway to PE associated with HyperToM.

11.2 Perspectives for future studies and clinical implementation

Future longitudinal studies with assessment of PE and HyperToM should look at who will transit to psychosis, who will develop other psychopathology, and who will not experience considerable distress. Studies have indicated that PE alone do not indicate the presence of a clinical disorder (Brett et al., 2015), but persistent PE constitute the greatest risk for conversion to clinical psychosis (Dominguez et al., 2011). Their impact on need-for-care may be mediated by other factors, such as

deficits in cognition and attention, and pervasiveness of the experiences (Brett et al., 2015). HyperToM might constitute a deficit in higher-order cognitive functioning associated with increased risk of transition from PE to a state of persisting and impairing psychotic symptoms and need-for-care.

High cortisol response to stress has been linked to HyperToM (Smeets et al., 2009) and exposure to chronic and episodic life stress may contribute to the development of HyperToM (Sharp, 2012). Considering previous research showing that an individual's sensitivity to everyday stressors (e.g. losing one's car keys) may be particularly important in the etiology of psychosis (Palmier-Claus et al., 2012), a possibly productive future area of study is the relation between HyperToM, stress reactivity and psychosis in adolescence. Therefore, longitudinal follow-up studies may want to include measures of stress sensitivity, negative life events, and perceived daily stress in addition to measures of social cognition and psychopathology at age 16-17. This is especially interesting because stress exposure, including social stress, during adolescence may be longer lasting and qualitatively different from stress exposure during other periods of life (Blakemore and Mills, 2014).

A recent study exploring the association between HyperToM and borderline traits in adolescents demonstrated an association between a reduction in HyperToM between admission and discharge of all inpatients and a reduction of borderline symptoms. No significant improvements were found in a number of other ToM measures (Sharp et al., 2013), which indicates that the reduction in HyperToM was specifically associated to the reduction of borderline symptoms. If this is also the case for PE, then this would constitute a promising focus for clinical intervention.

13. References

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14. Appendix: Papers and co-author declarations

Title of paper:

Exploring a new Theory of Mind task for 8-14 year-old children.

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Abstract

Background. Theory-of-Mind (ToM) keeps on developing in late childhood and early adolescence, and the study of ToM development later in childhood had to await the development of sufficiently sensitive tests that challenge the more mature children. The current study aimed to investigate the psychometric properties of the Danish version of the Theory-of-Mind Storybook Frederik (ToM-Frederik). **Methods** Between-group comparisons were carried out to assess whether ToM-Frederik score differed between a group of 41 typically developing (TD) children and a group of 33 children with High functioning Autism Spectrum Disorder (HFASD) and an expected lower score. To determine the convergent validity of ToM-Frederik potential associations with Strange Stories and Animated Triangles (AT) were analyzed. Furthermore potential associations between ToM-Frederik and the Social Responsiveness Scale (SRS) and between ToM-Frederik and the *Social Emotional Evaluation* (SEE) total score were analyzed.

Results Significant between-group differences were found for ToM-Frederik. Furthermore, the convergent validity of TOM-Frederik as a measure of TOM was supported by significant associations with the Strange Stories and the AT scores in the full sample. This was also the case

in the HFASD group, whereas ToM-Frederik was significantly correlated with Strange Stories, but not with AT, in the TD group. ToM-Frederik was significantly associated with SRS in the full sample, but not in neither the HFASD nor the TD group.

Conclusion The findings are supportive of ToM-Frederik as a valid indicator of deficits at the group level in children aged 7-14 years. Furthermore, the convergent validity is supported.

Introduction

In order to study the interplay between social cognition and psychopathology in the pathogenesis of mental disorders we need more sensitive and specific measures of the various aspects of social cognition including different levels of Theory-of-Mind.

Theory-of-Mind (ToM) is the ability to infer intentions, desires and beliefs (Frith and Frith, 2012). Deficits in this ability are present in a wide range of mental disorders, such as autism spectrum disorders (ASD) and other neurodevelopmental disorders, personality disorders, other non-psychotic disorders, schizophrenia, and affective disorders (Brune and Brune-Cohrs, 2006).

The ‘gold standard test’ of comprehending other persons’ minds is to grasp that others can hold false-beliefs (FB), that are different from one's own (correct) knowledge (Brune and Brune-Cohrs, 2006). The original and still prevailing ‘litmus’ tests for this ability are (first-order) FB tasks (Abell *et al.*, 2000), such as the Sally & Anne test (Wimmer and Perner, 1983). False-belief reasoning has been shown to be detectable as early as infancy (Baillargeon *et al.*, 2010), but the general perception is that typically developing (TD) children will attain this ability at the age of 4 years, through a progression of stages starting at 9 months with early aspects of joint attention (Paparella *et al.*, 2011). A developmental milestone has been observed at around the age of 18 months, when children become aware that their own mental states are distinct from others (Korkmaz, 2011). At the age of 4 years there is still considerable instability in the understanding of FB (Hughes *et al.*, 2005), but from the age of 4 to 6 years, this understanding becomes firmly established (Blakemore, 2008, Brune and Brune-Cohrs, 2006, Jha and Singh, 2009).

Still, ToM comprises far more than FB alone, like for instance the understanding of desires and emotions of others (Blijd-Hoogewys *et al.*, 2008). Testing ToM with only FB-tasks leaves out more sophisticated social-cognitive capacities such as understanding metaphor, irony and ‘faux pas’ (a socially awkward or tactless act) (Brune and Brune-Cohrs, 2006). Also, first-order FB comprehension might be mastered at younger ages, but second-order FB comprehension, will not be mastered before the age of 6 to 7 years in TD children (Dumontheil *et al.*, 2010). Second-order FB, where the child must think about a second individual’s thoughts about a third individual’s thoughts about an event (meta-representation), is often assessed through the ‘Ice-cream man’ task (Sullivan *et al.*, 1994). Lies and jokes (Happé, 1994) and ‘faux pas’ may not be reliably understood by TD children before the age of 8 to 11 years (Brune and Brune-Cohrs, 2006), indicating that ToM further improves in late childhood and early adolescence (Dumontheil *et al.*, 2010). Although ToM seems to continue to develop after the age of 6-7 years, Dumontheil *et al.*, (2010) found little evidence to support this assumption. Since most standard ToM-tasks are passed by the age of 5 years, ceiling effects are presumably obscuring the observation of any further development, as these tests do not

measure more complex abilities (Dumontheil *et al.*, 2010, White *et al.*, 2009). Therefore, more comprehensive and challenging ToM-tests, such as the Strange Stories task have been developed (Brent *et al.*, 2004, Happé, 1994).

Children and adults with ASD and with average or above average intelligence (High-Functioning Autism Spectrum Disorder – HFASD (Jacobs and Richdale, 2013)), typically also pass standard tests of first-order ToM such as FB tasks, although they have been delayed in acquiring this understanding (Brent *et al.*, 2004). The majority of individuals with HFASD also pass second-order FB tests (Kaland *et al.*, 2008), but might not do so before their teens (Korkmaz, 2011). However, difficulties get more pronounced with increasing complexity. As an example, the study by Kaland and colleagues (Kaland *et al.*, 2005) found that children and adolescents with high-functioning autism or Asperger's syndrome pass standard ToM-tasks. Yet, when more 'advanced' ToM-tests with a more complex social context were used, significant impairments of social cognition were still observed in these individuals.

Among the most widely used advanced ToM tasks are the (*revised*) *Strange Stories task* (Happé, 1994, White *et al.*, 2009). The Strange Stories include tasks on pretense, joke, lie, white lie, misunderstanding, persuasion, appearance/reality, figure of speech, irony, double bluff, contrary emotions, and forgetting. The task focuses on participants' understanding of belief but is developmentally appropriate for older children because of the additional demands it places on using this understanding of beliefs in complex, contextualized scenarios (Devine and Hughes, 2013). The Strange Stories task has been widely used in studies of clinical populations and, more recently, in studies of typically developing school-aged children (e.g., Lecce, Zocchi, Pagnin, & Palladino, 2010; Ronald, Viding, Happé, & Plomin, 2006). It has proven successful in numerous studies in older children showing that children, adolescents and even adults with HFASD, perform significantly worse on the Strange Stories task than TD individuals (Happé, 1994; White, Hill, Happé, & Frith, 2009). Group differences between samples of TD and HFASD children and adolescents have also been shown with the Danish version of the original Strange Stories task (Kaland *et al.*, 2008).

A more recent, advanced ToM task is the *Animated Triangles test* (Abell *et al.*, 2000). This task consists of series of computer-presented animations, and measure both the understanding of the events depicted in the animations (Appropriateness) and the degree of intentional attribution (Intentionality) (Salter *et al.*, 2008). This test has successfully been used in a growing number of experiments to investigate ToM and agency attribution in individuals with and without ASD (White *et al.*, 2011). Studies in both children and adolescents (Abell *et al.*, 2000, Salter *et al.*, 2008, Schwenck *et al.*, 2012) and adults (Castelli *et al.*, 2002, White *et al.*, 2011) have found lower Appropriateness score in ASD compared to TD. However whereas differences in Intentionality have been found in adults (White *et al.*, 2011), this is often not the case in samples of children and adolescents (Abell *et al.*, 2000, Salter *et al.*, 2008). Nevertheless this is considered a promising way to investigate the more subtle differences in ToM abilities in HFASD children and adolescents (Salter *et al.*, 2008).

In the present study a new advanced ToM task will be explored. The *Theory-of-Mind Storybook Frederik* (ToM-Frederik - (Blijd-Hoogewys and Bartels-Velthuis, 2007), which was developed for children aged 10 to 14 years, contains ToM tasks of different levels of difficulty, including first-order FB, deception, second-order FB, white lie, irony, double bluff and 'faux-pas' (Bartels-Velthuis *et al.*, 2011). This task has the advantage of comprising both yes/no questions and justifications, to

evaluate whether children spontaneously refer to mental states in order to explain the behaviour of others and allowing for a more detailed analysis of the answers and errors of the participants. This makes the task suited for research based on the assumption that while general alterations in ToM may be a vulnerability marker for psychopathology in general, more specific types of alterations may have a mediating role in the development of different types of specific symptoms (Shamay-Tsoory et al., 2007, Montag et al., 2011)..

The overall aim of the present study was to examine aspects of validity and reliability of ToM-Frederik. To accomplish this we included a group of TD children and a group of children with HFASD aged 7 to 14 years. The rationale for including a group with ASD was that the presence of ToM-deficits in this group is well-established in both children and adults (Baron-Cohen, 2001, Colle *et al.*, 2007, Yirmiya *et al.*, 1998).

First, we wanted to explore if ToM-Frederik could detect the expected ToM deficits in the HFASD group as reflected in significant differences in mean scores between the HFASD and the TD groups. Second, we wanted to explore the converging validity as reflected in potential significant associations between scores derived from ToM-Frederik and the Strange Stories, which we consider to be the gold standard ToM Task, and also Animated Triangles. Third, we wanted to compare ToM-Frederik to measures of broader measures of social function looking potential associations between ToM-Frederik and 1) the *Social Emotional Evaluation* (SEE) test which evaluates the social skills and higher level language skills that children need for successful interaction in everyday situations (Wigg, 2013), and 2) the *Social Responsiveness Scale* (SRS) covering various aspects of interpersonal communication, reciprocal behavior and repetitive/stereotypic behavior. Finally, we wanted to examine the test-retest reliability, and a possible test-retest effect, of the ToM-Frederik.

Methods and materials

Autism Spectrum Disorder group

The sample consisted of children diagnosed with Autism Spectrum Disorder (ASD) at the Child and Adolescent Psychiatric Center in the Zealand Region of Denmark or at the Child and Adolescent Mental Health Centre, the Mental Health Services in the Capital Region of Denmark. The children were recruited during the study period from August 2013 until September 2014. The inclusion criteria were as follows: 1) age 7-14 years, 2) a diagnosis of ASD according to the ICD-10 criteria (DF 84.0-84.9), 3) the diagnosis is based on a formal evaluation by a specialist in child and adolescent psychiatry following the Danish, national clinical guidelines for assessment and diagnosis of ASD, 4) the absence of an intelligence level below the normal range, as reflected in the absence of a mental retardation diagnosis (DF 70.x), and an Intelligence Quotient (IQ) at >70 measured by a full WISC-III or WISC-IV or by a scale score of four or above in both the Vocabulary and Block Design subtests from the WISC-III or WISC-IV (if full test not administered), 5) sufficient Danish language skills to participate in the ToM-tasks, and 6) parental written informed consent. As ToM-Frederik is primarily aimed at children aged 10-12 year, the majority of the children were recruited within in this age-range. Originally, 37 participants with ASD were included but four participants were excluded as they did not fulfill the criteria regarding intelligence level. Thus, a total of 33 children with HFASD were included: three children aged 7-8, 11 children aged 9-10, 12 children aged 11-12, and seven children aged 13-14.

Typically developing group

The names and addresses of a random sample of children aged 7-14 years were extracted from the Civil Registration System (Det Centrale Personregister; CPR). The TD children were invited to participate in the study by mail in a neutral white envelope, addressed to the child's parents. The parents were asked to sign up (through an online booking system) for an assessment of their child at the clinic. Inclusion criteria were as above except no parental report of 1) developmental disorders, or 2) special educational needs. Originally, 43 participants were included but two participants were excluded due to not fulfilling the criteria for intelligence level. We included a total of 41 TD children: eight children aged 7-8, 13 children aged 9-10, 14 children aged 11-12, and 6 children aged 13-14.

Procedure

The HFASD group was tested at the clinic by clinically experienced staff who received training and supervision in administration of the tests. Trained researchers also tested the TD group, either at home or at the clinic as preferred by the parents. The tests were administered in a pseudo-randomized order with the order of the ToM-tasks and the SEE test rotating one step for each administration.

Instruments

The *ToM Storybook Frederik* (ToM-Frederik) is the Danish version of the *ToM Storybook Frank* (Blijd-Hoogewys and Bartels-Velthuis, 2007), which tests the understanding of first-order FB, deception, second-order FB, white lie, irony, double bluff and 'faux pas'.

Children are presented 16 pictures while listening to a tape recording of the storybook read aloud by a professional actor. Children are asked a total of 16 'test' and 8 'justification' questions, covering a range of ToM-abilities. The 16 'test' answers are scored 1 (for a correct understanding of the situation) or 0 (for an incorrect answer). The range of the 'test' sum score is 0-16. The justifications are classified according to 23 predefined categories and scored on an ordinal scale (predefined for each situation). Scores depend on the level and quality of references made to the thoughts, beliefs, feelings or intentions of the story characters or the child itself. The range of the 'justification' sum score is 0-20. The test and justification scores are summed in a total score of ToM-skills (range 0-36, with a higher score indicating better performance) that serves as the primary measure (Clemmensen *et al.*, 2014). Ratings for ToM-Frederik were carried out by LC and RJ. Based on all 74 participants the inter-rater reliability was excellent ($r=0.96, p<0.001$) (George and Mallery, 2003).

The *ToM Storybook Frank* originally included 32 questions, but 8 questions were omitted in the Danish version. This reduction was done to adapt to situation where the task was part of a larger assessment battery and thus needed to be shortened to keep the total time for the clinical assessment at a reasonable level, and minimize the strain on the children. The questions omitted were the ones producing the least differentiation between the children in a previous study (Bartels-Velthuis *et al.*, 2011).

The test stories, questions and scoring categories were translated and back-translated by professional translators. A feasibility study of The Danish adaption of the ToM Storybook was carried out on 50 Danish school children between 10-12 years old. This led to some minor changes of the wording, but otherwise the task showed good face validity and good acceptance of the instrument among the children.

To measure the test-retest reliability, and a possible test-retest effect, of the ToM-Frederik, we administered this test for a second time to the 11-12 years-old children in the TD group 2 to 3 weeks after the first administration.

The *Strange Stories* test assesses the child's understanding of: pretense, joke, lie, white lie, misunderstanding, persuasion, appearance/reality, figure of speech, irony, double bluff, contrary

emotions, and forgetting (Happé, 1994) and provides means for testing advanced ToM-ability, suitable for TP as well as for both children (Brent *et al.*, 2004) and adults with HFASD (Sanders, 2009). Short vignettes are read aloud by the interviewer, whereupon subjects are asked to explain why a character says something that is not literally true (White *et al.*, 2009). We used a Danish translation of the revised version of the Strange Stories (White *et al.*, 2009) and included the eight Mental State Stories (awarded 0,1 or 2 points per story. The range of the sum score is 0-16) and the eight new Natural Physical State Stories (awarded 0,1 or 2 points per story. The range of the sum score 0-16). The mental and physical state sets both requires the integration of information between sentences and inference from implicit information, but only the mental state set requires mentalizing (White *et al.*, 2009). Thus adjusting the Strange Stories Mental State score for the Strange Stories Physical State score results in a more focused measure of the ability to reason about mental states specifically. Ratings for the Strange Stories were carried out by LC and RJ. Based on independent ratings of the responses of 20 randomly selected participants, the inter-rater reliability for the Mental State Stories was good ($r=0.73$, $p<0.001$) and the Natural Psychological State Stories ($r=0.92$ $p<0.001$) was excellent (George and Mallery, 2003). All ratings were compared to the ratings of a senior researcher (JRJ). No interrater-reliability with the senior researcher was calculated, as consensus scores were determined via discussion in all cases of differences in ratings.

The *Animated Triangles* (AT) (Abell *et al.*, 2000) task consists of a series of computer-presented animations. These animations show one large red and one small blue triangle moving around the screen (White *et al.*, 2011). The participants are instructed that, while watching the animations they have to give a concurrent verbal description of what they think is happening. These animations span scenarios from 'Random' to 'Goal-Directed' and 'ToM'-type situations, and performance in terms of verbal descriptions were rated on scales for Appropriateness and Intentionality. The AT Appropriateness score measures the understanding of the event depicted in the animations, as intended by the designers (0-3, with 3 being a clear precise answer). A total score ranging from 0-12 was calculated for each type of animation (see (Castelli *et al.*, 2000) for further details). The Intentionality score reflects the use of mental state terms, with scores ranging from 0 (non-deliberate action) to 5 (deliberate action aimed at affecting another's mental state). Total AT Intentionality score was calculated as the mean for each animation type. If the participant failed to produce a verbal description, AT Appropriateness was rated 0 and AT Intentionality as the mean of the other answers for that type of animations. Failure to produce verbal descriptions for two or more animations within a given category meant exclusion from this particular analysis. Separate scores were calculated for the Random, Goal Directed and ToM sets of animations. Ratings were carried out by LC and RJ. Based on 20 randomly selected participants, the inter-rater reliability for both the AT Appropriateness score ($r=0.824$ $p<0.001$) and the AT Intentionality score ($r=0.894$ $p<0.001$) were excellent (George and Mallery, 2003). These ratings were compared to the ratings of a senior researcher (JRJ). No interrater-reliability with the senior researcher was calculated, as consensus scores were determined via discussion in all cases of difference in ratings.

We also applied an objective method, originally developed for adults, using multiple-choice questions (MCQ) (White *et al.*, 2011). At the end of each animation participants would be asked to categorize it as one of three types: 'no interaction' (Random), 'physical interaction' (Goal Directed), and 'mental interaction' (ToM) (referred to hereafter as AT MCQ-categorization score: 0-12 points). In cases of ToM type animations they were asked additional questions to test their understanding of the mental states depicted in the animation. The participants could choose between one of five listed adjectives to best match the feelings of each of the triangles at the end of the

animation; a separate list was provided for each triangle in each animation (referred to hereafter as MCQ-feelings score: 0-8 points).

Performances on the *Block Design* and the *Vocabulary* subtests of *WISC-III* or *WISC-IV* were used as indices of the intelligence level. These subtest scores are known to be highly correlated with IQ on the full Wechsler test of intelligence (Wechsler, 2003).

The *Social Responsiveness Scale (SRS)* is a 65-item questionnaire (score 0-195), applied to the parents who report on various aspects of child's interpersonal communication, reciprocal behavior and repetitive/stereotypic behavior. The SRS identifies the presence and extent of autistic social impairments on a quantitative scale with higher scores indicating greater severity of social impairment (Constantino *et al.*, 2003).

Social Emotional Evaluation (SEE) is a task administered to the child. The SEE evaluates the social skills and higher level language skills that children need for successful interaction in everyday situations at home, at school and in the community. The SEE assesses both the receptive and expressive social skills of children aged 6-12 years, and includes tasks in which the child must identify common emotions, recognize emotional reactions, understand social gaffes, and understand conflicting messages. The following three scores are calculated: Receptive (0-59 points), Expressive (0-64 points), and Total score (0-123 points). A validation study reported in the SEE manual including children with ASD and TD children revealed large between-group effect sizes (Wigg, 2013).

The *SEE Social Emotional Questionnaire (SEQ)* is applied to the parents and contains 45 questions on the social skills of the child. The SEQ Raw score was divided by the total possible points (max 180 points with no excluded questions) after excluding questions with checkmarks in the 'Don't Know/Not Applicable' column to obtain the Parent SEQ Total Percentage (Wigg, 2013).

We hypothesized that the variables derived from Strange Stories respectively AT reflect theoretically similar aspects of ToM as those measured by ToM-Frederik. Before using these scores as gold standard for our examination of the converging validity, we wanted to make sure that we could replicate findings of lower ToM-functioning in ASD children compared with TD children in our sample when using the Strange Stories and the AT test scores. The same argument holds for SRS and SEE, that performance in our sample was described before using these measures to examine the discriminating validity of ToM Frederik.

Statistical analyses

Analyses were carried out using SPSS 20. Student's t-tests and chi-square tests were applied to compare continuous and categorical background variables (gender, age in months, Wechsler Block Design scale score, and Wechsler Vocabulary scale score).

The test-retest reliability of the ToM-Frederik for the 11-12 years-old children in the TD group was established by means of a Pearson product-moment correlation coefficient. Furthermore, a paired samples t-test was applied to measure the test-retest effect.

Between-group comparisons were carried out to assess whether the outcome variable from the ToM-Frederik differed between the TD and the HFASD group. The between-group comparisons were done using ANCOVA, with the background variable(s) as the co-variate(s). In case the raw data deviated significantly from a normal distribution, they were logarithmically or square root transformed to approximate a normal distribution before analyses were performed. The same procedure was followed for the outcome variables from Strange Stories, AT, SEE, and SRS.

To determine the convergent validity of ToM-Frederik potential associations with the core variables derived from Strange Stories and AT were analyzed using Pearson correlations in the full sample, as well as in the HFASD and TD groups separately.

Finally, the potential associations between ToM-Frederik and the SRS total score were analyzed using Pearson correlations.

RESULTS

Background variables

There was a considerable, and statistically significantly, larger percentage of boys in the HFASD compared to the TD group, consequently all between-group analyses were adjusted for gender (see Table 1).

(insert Table 1 about here)

Test-retest reliability of ToM-Frederik

Ten out of the 14 participants aged 11-12 years in the TD group, participated in the retest assessment of ToM-Frederik. The test-retest reliability estimate of the ToM-Frederik total score was good ($r=0.84$ $p=0.003$). In addition, the test-retest effect of this score appeared relatively low and statistically non-significant (ToM-Frederik Total score: $M_{\text{time 1}} = 22.70$, $SD = 4.06$) and $M_{\text{time 2}} = 24.30$, $SD = 2.58$; $p=0.17$).

Between-group comparisons

Theory-of-Mind tasks

ToM-Frederik total raw score was significantly lower in the group of children with HFASD than in the TD group.

Both the Strange Stories Mental State raw score and the Strange Stories Physical State (logarithmically transformed) raw score were significantly lower in the group of children with HFASD than in the TD group. Still, the Mental State raw score remained significantly lower in the HFASD group than in the group of children when adjusted for Physical State raw score (see Table 2).

With regard to the Animated Triangles the score for AT Appropriateness was significantly lower for the HFASD than for the TD group in the Random, Goal-directed, and ToM type of animations. The AT Intentionality score for the ToM-type animations was significantly lower in the HFASD group than the TD group. Conversely, for Random-type animations, the intentionality score was

significantly higher in the HFASD group than in the TD group. For the Goal-directed-type animations, there was no significant difference between the HFASD group and the TD group (see Table 2). The AT MCQ-categorization (square root transformed) total score was significantly lower in the HFASD group than in the TD group. No significant difference was observed between the groups for the AT MCQ-feelings total score, though a statistical trend was observed. A post hoc analysis revealed the participants in the HFASD group had significantly more AT missing answers than the participants in the TD group (see Table 2)

(insert Table 2 about here)

Social Emotional Evaluation (SEE)

The HFASD and the TD group did not differ with respect to the SEE Receptive (logarithmically transformed) score, the SEE Expressive (square root transformed) score or the SEE Total (logarithmically transformed) score. For the SEE Social Emotional Questionnaire (SEQ), a significantly lower percentage of the maximum possible points was awarded to the HFASD than the TD group. As SEE is only aimed at children aged 6-12 years, these analyses were repeated without the children aged 13-14 years. However, this did not significantly change the results (data not shown). For this reason SEE was not included in the further analyses.

Social Responsiveness Scale (SRS) The HFASD group had significantly higher SRS (square root transformed) total score than the TD group, indicating greater severity of social impairment for the HFASD group.

Convergent validity

In the full sample the ToM-Frederik score was significantly and positively correlated with both the Strange Stories Mental State score and the AT ToM intentionality score. Furthermore the Strange Stories Mental State score and the AT ToM intentionality score were significantly and positively correlated with each other. In the HFASD group the score on ToM-Frederik was also significantly and positively correlated with both the Strange Stories Mental State score and the AT ToM intentionality score. Furthermore the Strange Stories Mental State score and the AT ToM intentionality score were significantly and positively correlated with each other. However while the score on ToM-Frederik was significantly and positively correlated with the Strange Stories Mental State score in the TD group, it was not significantly correlated to the AT ToM intentionality score. Furthermore the Strange Stories Mental State score and the AT ToM intentionality score did not correlate significantly.

Social Responsiveness Scale (SRS)

Analyses showed that ToM-Frederik was significantly and negatively correlated with SRS in the full sample. However these correlations were not statistically significant in neither the HFASD nor the TD group (see Table 4).

(Insert Table 4 about here)

DISCUSSION

The main aim of the present study was to examine aspects of validity and reliability of the Danish versions of the ToM-Frederik as a measure of ToM deficits

Our findings supports the validity of ToM-Frederik as a measure of ToM as it was able to identify, at the group level, the expected ToM deficits in this sample of older children and young adolescents with HFASD. This is in line with previous findings in a study comparing 3-12 year-old children with PDD-NOS and TD children using the Dutch version of ToM-Frederik (Blijd-Hoogewys *et al.*, 2008).

Furthermore, the convergent validity of TOM-Frederik as a measure of TOM was supported by it's significant associations with the Strange Stories and the AT scores in the full sample. This was also the case in the HFASD group, whereas ToM-Frederik was only significantly correlated with Strange Stories, but not with AT, in the TD group.

ToM-Frederik was significantly associated with SRS in the full sample, but not in neither the HFASD nor the TD group. Whereas ToM-impairments in ASD may be more associated with impairments of reciprocal interaction and communication, the repetitive/stereotypic behaviors in ASD may be associated with executive functions deficits (Hughes *et al.*, 1994, Joseph, 1999). Since the SRS summarizes the scores derived from items representing all these three domains of functioning in a single total score, the repetitive/stereotypic behavior items scores may have confounded the potential associations between real life communication and social interaction deficits and ToM.

The findings are also in support of the Danish versions of the Strange Stories and AT as measures of ToM as they were able to identify, at the group level, the expected ToM deficits in this sample of older children and young adolescents with HFASD. The findings on the Strange Stories task are in line with previous findings reporting significant group differences in the Mental State stories in a study comparing 7-12 year-old children with autism and TD children (White *et al.*, 2009). However, in contrast to the latter study we also found significant group differences in the Psychical State stories. Nevertheless, when adjusted for Psychical State stories the group differences for the Mental State stories remained significant. Thus the difference in score seems to reflect a specific impairment of ToM.

In terms of AT, the current findings are in line with previous results in children and adolescents finding significant differences between groups of HFASD and TD (Salter *et al.*, 2008, Schwenck *et al.*, 2012). Only one of these studies did assess AT Intentionality, but in contrast to the current study, Salter and colleagues (2008) did not find significant between-group differences in the AT Intentionality score for any type of animations. In terms of the objective AT scoring, we only found a significant lower MCQ categorization score in the children and adolescents with HFASD, whereas White *et al.* (2011) also observed a significant difference for the MCQ feelings in adults. This objective AT scoring measure has not previously been applied to children and young adolescents. The fact that the TD group only had about 50% correct answers may reflect an inability to keep the proposed feelings on line in working memory, and the non-significant result may be related to a less efficient working memory among the youngest in the TD group (De Luca *et al.*, 2003).

The findings are in support of the Danish version of the SRS, with scores on this test representing the biggest gap between HFASD and TD. In addition, our findings support validity of the Danish version of SEQ parent questionnaire as a sensitive measure of the real life social and

communicative behavior deficits of children and adolescents with HFASD. On the other hand, the SEE task was not supported as a valid measure of impairments of social skills, as the scores did not differ significantly between the groups on any SEE scales.

Strengths and Limitations

The main strength of this study is the relatively comprehensive social cognitive test battery, so that we could assess convergent validity of the TOM-Frederik Task. However, the present study also has some limitations. The gender distribution differed between the HFASD and the TD group, with more boys in the HFASD group. Also due to the different intelligence assessment methods between the groups, analyses of the potential effects of intelligence on the ToM scores were not performed.

Directions for Future Research

Future research on TOM-Frederik should include groups with other psychiatric diagnoses in order to assess trans-diagnostic applicability of the tests. Further research should also include more participants across the age-span in order to be able to identify at what age AT MCQ Feelings becomes able to identify significant group differences.

Finally the separation of the two groups by ToM-Frederik may be due to other differences picked up by the instruments, e.g. differences in language, motivation etc. However previous studies Future studies should further explore to what degree the performance on the ToM-Frederik is influenced by these, as compared to other ToM-tasks.

Conclusion

In conclusion, the current study provides overall support for the validity of the Danish version of the Theory-of-Mind Storybook Frederik as a measure of ToM. The task was able to identify, at the group level, the expected ToM deficits in this sample of older children and young adolescents with HFASD. Furthermore, the convergent validity of ToM-Frederik as a measure of ToM was supported by significant associations with the Strange Stories and the AT scores in the full sample. This was also the case in the HFASD group, whereas ToM-Frederik was significantly correlated with Strange Stories, but not with AT, in the TD group. Finally ToM-Frederik was significantly associated with SRS in the full sample, but not in neither the HFASD nor the TD group. The task represents a gain for both research and clinical practice, as it is relatively fast to administer and provides outcome based on a highly nuanced scoring.

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Tables

Table 1: Background variables

	HFASD		TD		Analysis
	N	M (SD)	N	M (SD)	
Age in months	33	136.15 (23.04)	41	130.85 (20.81)	t(72)=1.038 p=0.303
Vocabulary	27	9.15 (3.13)	40	10.60 (3.15)	t(65)=-1.853 p=0.068
Block Design	27	10.78 (2.72)	41	10.92 (4.14)	t(66)=-0.160 p=0.874
FSIQ	14*	103.43 (16.89)	0	-	-
	N	N (%)	N	N (%)	
Gender (N, % boys)	33	24 (73)	41	17 (41)	R ² (1)=7.233 p=0.007

HFASD: High Functioning Autism Spectrum Disorders, TD: Typically Developing, SD: Standard Deviation, FSIQ: Full Scale IQ.

*eight of the patients with ASD assessed with the two subtests also had a FSIQ score.

Table 2: Between-group comparisons

	HFASD		TD		
	N	M (SD)	N	M (SD)	
ToM-Frederik	32	20.44 (4.9)	41	22.88 (4.4)	F(2,70)=4.027, p=0.049
Strange stories					
Mental state stories	31	8.45 (3.2)	41	10.90 (2.7)	F(2,69)=10.407, p=0.002
Physical state stories	31	8.16 (2.3)	41	9.83 (2.5)	F(2,69)=7.854 p=0.007
Mental state stories (adjusted for physical state stories)	31	8.45 (3.2)	41	10.90 (2.7)	F(2,69)=6.810 p=0.011
Animated Triangles					
Subjective					
Appropriateness					
Random	33	6.33 (3.9)	41	11.12 (1.4)	F(2,71)=49.394, p<.0001
Goal-directed	33	7.00 (3.7)	41	10.37 (1.1)	F(2,71)=26.433, p<0.001
ToM	33	4.21 (2.3)	41	8.66 (1.7)	F(2,71)=76.682, p<0.001
Intentionality					
Random	26	1.03 (0.6)	41	0.47 (0.5)	F(2,64)=14.663 p<0.001
Goal-directed	28	2.27 (1.0)	41	2.42 (0.4)	F(2,66)=1.151, p=0.287
ToM	27	3.12 (0.6)	41	3.70 (0.4)	F(2,65)=21.169, p<0.001
Missing answers	33	2.79 (4.3)	41	0.02 (0.2)	t(72)=4.099 p<0.001
Objective					
MCQ-categorization	33	8.55 (2.7)	41	9.88 (1.5)	F(2,71)=8.249 p=0.005
MCQ-feelings	33	3.30 (2.2)	41	4.24 (2.1)	F(2,71)=3.403, p=0.069
The Social Emotional Evaluation (SEE)					
Receptive score	32	52.19 (4.1)	41	54.09 (2.9)	F(2,70)=3.080 p=0.084
Expressive score	32	37.69 (10.5)	41	40.02 (6.6)	F(2,70)=1.102 p=0.297
Total score	32	89.88 (13.3)	41	94.12 (9.0)	F(2,70)=1.736 p=0.192
The SEE Social Emotional Questionnaire (SEQ)					
Percent of maximum points	33	0.57 (0.2)	41	0.87 (0.2)	F(2,71)=32.679, p<0.001
Social Responsiveness Scale (SRS)	33	85.52 (30.0)	41	19.76 (13.2)	F(2,71)=171.359 p<0.001

Table 3: Correlations between measures of Theory-of-Mind

	Strange Stories			AT		
	r	p	N	r	p	N
FULL SAMPLE						
ToM-Frederik	0.551	<0.001	72	0.379	0.001	68
Strange Stories	-	-	-	0.461	<.001	68
HFASD						
ToM-Frederik	0.570	0.001	31	0.484	0.011	27
Strange Stories	-	-	-	0.521	0.005	27
TD						
ToM-Frederik	0.462	0.002	41	0.125	0.434	41
Strange Stories	-	-	-	0.117	0.468	41

HFASD: High Functioning Autism Spectrum Disorders, TD: Typically Developing, SRS: Social Responsiveness Scale.

Table 4: Correlations between Social Responsiveness Scale (SRS) and measures of Theory-of-Mind

	SRS		
	r	p	N
FULL SAMPLE			
ToM-Frederik Total score	-0.253	0.032	73
Strange Stories Mental State score	-0.353	0.002	72
Animated Triangles			
ToM Intentionality score	-0.403	0.001	68
HFASD			
ToM-Frederik Total score	-0.061	0.738	32
Strange Stories Mental State score	-0.084	0.653	31
Animated Triangles			
ToM Intentionality score	-0.137	0.495	27
TD			
ToM-Frederik Total score	-0.100	0.532	41
Strange Stories Mental State score	-0.200	0.009	41
Animated Triangles			
ToM Intentionality score	-0.121	0.434	41

HFASD: High Functioning Autism Spectrum Disorders, TD: Typically Developing, SRS: Social Responsiveness Scale.



Hyper-Theory-of-Mind in Children with Psychotic Experiences

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Abstract

Background: Alterations in Theory-of-Mind (ToM) are associated with psychotic disorder. In addition, studies in children have documented that alterations in ToM are associated with Psychotic Experiences (PE). Our aim was to examine associations between an exaggerated type of ToM (HyperToM) and PE in children. Children with this type of alteration in ToM infer mental states when none are obviously suggested, and predict behaviour on the basis of these erroneous beliefs. Individuals with HyperToM do not appear to have a conceptual deficit (i.e. lack of representational abilities), but rather they apply their theory of the minds of others in an incorrect or biased way.

Method: Hypotheses were tested in two studies with two independent samples: (i) a general population sample of 1630 Danish children aged 11–12 years, (ii) a population-based sample of 259 Dutch children aged 12–13 years, pertaining to a case-control sampling frame of children with auditory verbal hallucinations. Multinomial regression analyses were carried out to investigate the associations between PE and ToM and HyperToM respectively. Analyses were adjusted for gender and proxy measures of general intelligence.

Results: Low ToM score was significantly associated with PE in sample I (OR = 1.6 95%CI 1.1–2.3 $\chi^2(4) = 12.42$ $p = 0.010$), but not in sample II (OR = 0.9 95%CI 0.5–1.8 $\chi^2(3) = 7.13$ $p = 0.816$). HyperToM was significantly associated with PE both in sample I (OR = 1.8, 95%CI 1.2–2.7 $\chi^2(3) = 10.11$ $p = 0.006$) and II (OR = 4.6, 95%CI 1.3–16.2 $\chi^2(2) = 7.56$ $p = 0.018$). HyperToM was associated particularly with paranoid delusions in both sample I (OR = 2.0, 95%CI: 1.1–3.7% $\chi^2(4) = 9.93$ $p = 0.021$) and II (OR = 6.2 95%CI: 1.7–23.6% $\chi^2(4) = 9.90$ $p = 0.044$).

Conclusion: Specific alterations in ToM may be associated with specific types of psychotic experiences. HyperToM may index risk for developing psychosis and paranoid delusions in particular.

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Introduction

A systematic review [1] documents that alterations in Theory-of-Mind (ToM) are found in people at familial risk of psychotic disorder. In addition, longitudinal studies propose that individuals who later develop schizophrenia, show ToM deficits in childhood [1]. Therefore, altered ToM may constitute an underlying, partly genetically mediated [1,2], indicator of vulnerability for development of psychosis and schizophrenia [1,3]. Recent studies in adult samples of both patients and individuals at familial risk of psychosis [4–9] have found altered ToM abilities to be associated

not only with a diagnosis of schizophrenia but also, and more specifically, with specific psychotic symptoms [10–12]. However, these findings are diverging with regard to which ToM deficits are associated with which symptoms.

Hallucinations, delusions and other psychotic symptoms in the absence of diagnosable psychotic illness occur frequently in the general population. Recent meta-analyses found a median prevalence of such non-clinical Psychotic Experiences (PE) of around 7% in the general population of all ages [13], and around 17% in the subgroup of children aged 9–12 years [14]. PE are

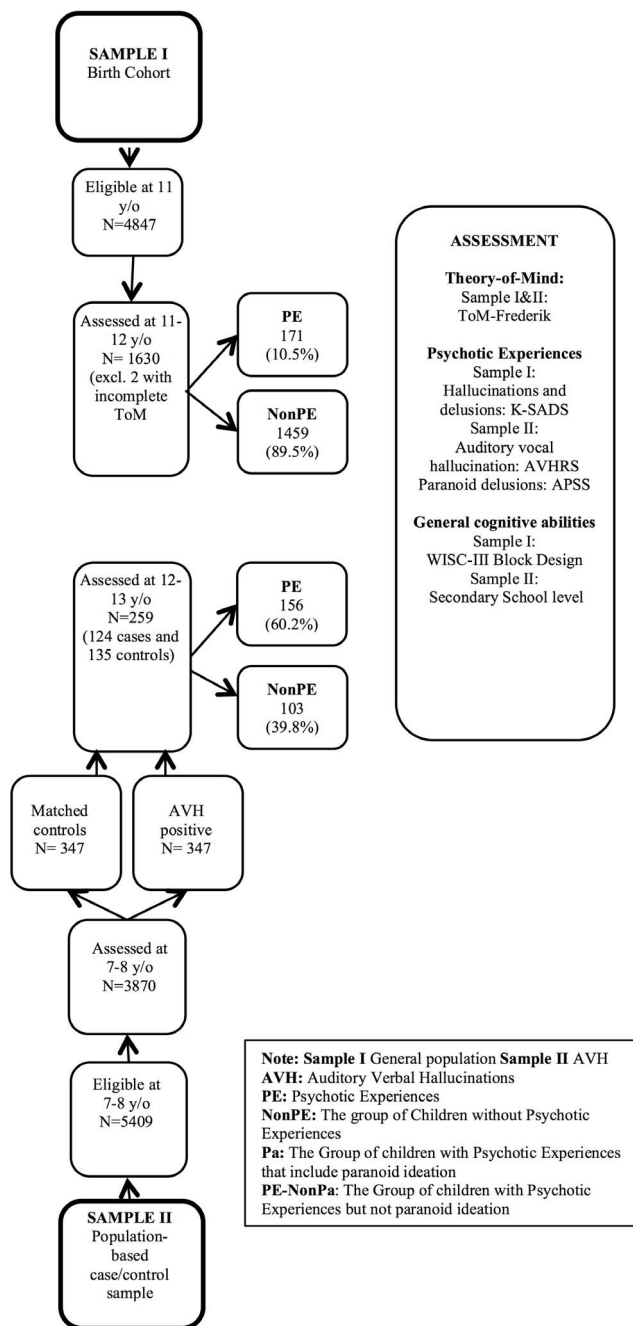


Figure 1. Overview of the study.
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usually transitory, but longitudinal cohort studies have shown an association with later development of psychotic illness, indicating that PE may index psychometric risk for psychotic disorder [13–16].

PE and alterations in ToM are associated with each other [9,17], but studies have for the most part been carried out in adult samples, and only three studies have examined these associations in non-clinical samples of children [18–20]. In two of the studies involving children, associations were found between current PE and poor ToM [18,19]. In the third study, the overall score of ToM did not differentiate between children with and without PE [20]. However, in this study, lower ToM scores mediated the

association between a lifetime history of auditory verbal hallucinations (AVH) and presence of delusions at age 12–13 years, i.e. children with AVH had a higher likelihood of forming secondary delusional ideation given lower ToM skills. This is in line with the other longitudinal study [18] finding that poor ToM at age 5 years predicted PE at age 12 years.

The divergence in findings regarding which symptoms of psychosis are related to ToM may be related to methodological dissimilarities across studies, e.g. regarding the measurement of ToM and the classification of symptom clusters [1,21,22]. A more basic explanation may involve the heterogeneity and multidimensionality of ToM as a construct [23]. It has been suggested that deficits may occur in (i) the representational abilities (i.e. a conceptual deficit), so that an individual is unaware that others can hold a false belief about a state of affairs [24,25], as well as in (ii) application abilities (i.e. deficit in performance), so that an individual has awareness of another person's mental life but fails to demonstrate or apply this knowledge due to processing constraints [26]. Frith (2004) suggested that schizophrenia patients with predominantly negative symptoms, disorganized behaviours, and early developmental problems lack representational abilities, whereas patients with paranoid symptoms would have the basic representational abilities but tend to excessively attribute intentions or self-referential meaning to others and therefore predict behaviour on the basis of these wrong beliefs [27]. This may be conceptualized as HyperToM, which refers to an exaggeration in the application of ToM [28]. Studies of both clinical [29] and general population [30] adult samples suggest that HypoToM is associated with a diagnosis of autism and negative symptoms [1,29,31], whereas HyperToM is associated with psychotic disorder [31] and psychotic symptoms [29,32]. This type of erroneous ToM strategy appears to be specifically associated with delusions and particularly paranoid delusions comprising delusions of persecution, mind-reading and misinterpretation [29,30,32]. Thus, HyperToM may be a useful conceptual construct to improve the current insufficient differentiation between the various qualitative aspects of ToM [33] that may show different patterns of association with different developmental disorders [34].

While a limited number of studies on the presence of HyperToM in patients with psychosis have been carried out, no studies in at-risk individuals have systematically investigated this aspect of social cognition [33].

The aim of the present study was to examine the specific patterns of alterations in ToM (HyperToM) in relation to PE in children, in order to expand current knowledge on the role of ToM in the aetiology of psychosis.

Research Hypotheses

We hypothesized that:

1. A lifetime history of PE would be more frequent in the group of children with overall ToM score at or below the median (Low ToM) compared to the group of children with ToM score above the median (High ToM) of the general population of children.
2. A lifetime history of PE would be particularly frequent in the group of children with the exaggerated type of ToM alteration (HyperToM) compared to children without this type of alteration.
3. The exaggerated type of ToM alteration (HyperToM) would be associated more strongly with a lifetime history of paranoid delusions (Pa) compared to a lifetime history of psychotic experiences without paranoid delusions (PE-NonPa).

Methods

An overview of the study is presented in Figure 1.

The hypotheses were investigated in two studies covering two independent samples: (i) a general population sample of 1630 11–12-year-old Danish children [35] and (ii) a population-based sample of 259 12–13 year-old Dutch children, pertaining to a case-control sample of children aged 7–8 years when assessed for auditory verbal hallucinations (AVH) and 12–13 years when followed up for assessment of PE [20].

Participants

Study I: The Danish general population sample of children aged 11–12 years. The current analysis was conducted as part of the 11–12-year follow-up of The Copenhagen Child Cohort 2000 (CCC2000). CCC2000 is a general population birth cohort, consisting of 6090 children born in 16 municipalities in the Copenhagen County in the year 2000, and followed prospectively since birth [36]. The cohort comprises 9% of all children born in Denmark that year, and is representative for children born in Denmark that year regarding key perinatal characteristics (Olsen, Skovgaard, Weile, & Jorgensen, 2007), except that ethnic minorities were somewhat overrepresented at baseline [36].

The study was conducted from May 1st, 2011 through October 1st, 2012. Cohort members were traced through The Danish Civil Registration System. 1,243 children were lost to follow-up (19 dead, 217 emigrated, 14 not traceable, and 993 whom had claimed ‘research protection’), leaving a total of 4847 children eligible for follow-up at age 11/12 years. The parents of eligible children were contacted by letter inviting them to sign up their child for a face-to-face assessment at the research clinic. Families living far away were offered home visits. Parents were contacted up to four times by letter and/or telephone. Gifts were offered in reward for participation. It was clearly stated that participation was voluntary and that data was kept confidential.

1632 children attended the assessment. Two of those had an incomplete ToM task, resulting in a final sample of 1630 children (34% of the eligible children, 48% boys). The mean age was 11.4 years. In a previous study of PE in the CCC2000 [35], the participating children were found to be slightly positively selected on a range of sociodemographic and perinatal background characteristics compared to the rest of the cohort (those alive at age 11 years).

Study II: Case-control sample of auditory verbal hallucinations. Sample II was recruited from a case-control sample of 694 children, half of whom had AVH when assessed at age 7 or 8 years as part of a population-based study of 3870 children. A total of 337 children from the case-control sample participated in the follow-up at age 12–13 years, in which 259 (49% of the eligible children, 47% boys) completed the ToM assessment (Bartels-Velthuis *et al.*, 2011b). Mean age was 13.1 years (SD 0.5). Socioeconomic status was evenly represented (31% low 38% middle, 31% high). The 78 children, in whom ToM was not assessed, more often were 13 as opposed to 12 years old (73% vs. 54% in the group with ToM assessment; $\chi^2 = 9.3$, $p = 0.002$) and more often reported delusions (40% vs. 27% in the group with ToM assessment; $\chi^2 = 4.3$, $p = 0.04$). No other large or significant differences existed in demographic or outcome variables [20].

Materials

Theory of Mind. The ToM Storybook Frederik (ToM-F) [37] was used to assess ToM in both studies. ToM-F is the Danish version of the ToM Storybook Frank [38] and is aimed at 10–14-

year-old children and tests the understanding of second-order false beliefs, white lie, irony, double bluff and ‘faux pas’ (a socially awkward or tactless act). The children are asked a total of 24 questions while being presented with 16 pictures and listening to the storybook read aloud.

Originally, 32 questions were included but 8 questions were omitted in sample I. This reduction was done to adapt to the present study where the task was part of a larger assessment battery and thus needed to be shortened to keep the total time for the clinical assessment at a reasonable level, and minimize the strain on the children. The questions omitted were the ones producing the least differentiation between the children in a previous study [20]. To make direct comparison between sample I and II possible, analyses were carried out only on the 24 questions applied in both studies. As ToM scores on 8 questions from the original study thus were excluded from the data in sample II, ToM scores will not be identical to those reported in a previous publication [20] concerning sample II.

In both samples, the internal consistency between the 24 questions was moderate (sample I Cronbach’s alpha = .69, sample II Cronbach’s alpha = .64). The 24 questions consist of 16 ‘test’ and 8 ‘justification’ questions. The test answers are scored 0–1; 1 is given for a correct understanding of the situation (range 0–16). The 8 justification answers are classified according to 23 predefined categories (see “Appendix S1 Rating Categories for ToM Storybook” for full set of categories) [39] such as:

Desire: The answer refers to the protagonist’s desire with respect to the situation. It involves wanting or desiring something.

Fact belief: The child refers to the protagonist’s knowledge. It involves thinking, knowing, being sure of, expecting or recognizing.

Situational: Dwelling on the situation without reference to the mental state of the protagonist.

Based on these categories, the answers were scored (‘0’, ‘1’, ‘2’, and for some items ‘3’) on an ordinal scale predefined for each situation, resulting in a justification sum score (range 0–20), that was summed with the test score (‘0’ or ‘1’, range 0–16) to form the total ToM scale score of ToM abilities (range 0–36). Scores on the justification items depend on the level and quality of references made to the thoughts, beliefs, feelings or intentions of the story characters or the child itself.

The total ToM scale served as the primary measure of overall ToM abilities. The 8 justifications answers were also scored on a dichotomous scale as a non-mentalizing (‘0’) or mentalizing (‘1’) type of answer, regardless of the classification of the answer as formally right or wrong in the context, resulting in a mentalizing scale-score (range 0–8). Conform previous work, mentalizing answers were defined as those referring to beliefs, desires and similar inner states [30,33]. Thus the following 11 of the 23 categories were considered mentalizing: Belief; desire; fact belief; value belief; mental state verb rest category; own frame of reference with mental state; emotion with empathy; emotion without empathy; perception with mental state; identification of first order intention; identification of second order intention (see Appendix S1 for a description of all categories). A high number of mentalizing answers (High-Mentalizing) was defined as scores above the median for population sample I.

From these scale scores we defined low ToM skills (Low ToM) as scores at or below the median on the total ToM scale. HyperToM was defined on the basis of (i) total ToM scale score below the median combined with (ii) number of mentalizing answers above the median in general population sample I. Both measures were taken into account, as the aim was to capture

children that had a low level of overall ToM abilities while making frequent mental attributions. Taking both measures into account, a categorical variable was constructed, which captured children who were among the top 50% with regard to number of mentalizing answers, while at the same time among the lowest 50% with regard to overall ToM abilities measured by the total scale score. These children showed a tendency to exaggerated and aberrant mentalizing explanations, labelled HyperToM, in contrast to the children without HyperToM. The phenotype should not be conceptualised as somewhere between high and low levels of overall ToM abilities, rather it is another dimension of ToM skills that was measured as a dichotomised variable. The median cut-offs from sample I ($n=1630$) were also applied to assess HyperToM in sample II, thus providing the opportunity to replicate an association between this level of HyperToM and the presence of PE. The aim was to explore associations between the same quality of HyperToM, captured by this definition, and the presence of PE. Sample I was chosen to provide the level of cut-off, as this was the larger and most representative sample of children in the general population.

Ratings were carried out in close co-operation with the Dutch authors of *The ToM Storybook Frederik (ToM-F)*. An initial training seminar was conducted. Thereafter consensus ratings on a subsample of 200 children were carried out by a Danish rating group headed by the first author, and subsequently the remaining children were rated by the first author under supervision of the Dutch authors. A sample of 50 children was rated separately by one member of the Danish research group in order to measure the inter-rater reliability for assignment of children to each ToM group. The inter-rater reliability (computed as Cohen's Kappa) was very good for the categorizing of children as low ToM ($\kappa=0.86$) and as HyperToM ($\kappa=0.81$) [44,45].

Socioeconomic status. In Sample I socioeconomic status (SES) was derived from length of mothers' education and family disposable income. Low SES was set as low-skilled mother (length of education less than 10 years) and/or low family income (being in the lowest quartile of the entire cohort of 6090 children).

In Sample II SES was derived from parental averaged educational levels and family income, resulting in three levels: low (score = 1), middle (score = 2) and high (score = 3).

General Cognitive ability. As previous studies have pointed to the possibility that the association between schizophrenia and ToM performance may be confounded by general intelligence [1,40], any study investigating cognitive mechanisms in psychosis should take the possible influence of general cognitive abilities into account [9]. Thus, measures of general cognitive ability were treated as a potential confounder of the association between ToM and PE in both studies.

In Sample I performance on the Block Design (BD) subtest of WISC-III was used as a proxy measure of children's general cognitive abilities. The BD subtest is highly correlated with full-scale IQ in the Wechsler intelligence test [41].

In Sample II secondary school level was categorized as follows: 1 (lower vocational) and 2 (higher/pre-academic) and was applied as a proxy measure of children's general cognitive abilities. This was not possible for 12 of the children, as 10 were still at primary school and data were not available for 2.

Psychotic Experiences. In Sample I PE were assessed in a semi-structured interview with K-SADS-PL [42], applying the screening section and the supplement on psychotic symptoms. Possible PE ratings were: absent, likely present, and definitively present. PE were rated present if at least one psychotic symptom was scored as 'likely' or 'definitely' present for two time periods: the past month and 'lifetime before'. For the present study, a

binary variable was created, coding "yes" or "no" PE for the lifetime period, 'yes' indicating that the child had experienced at least one psychotic symptom 'likely' or 'definitely' present in last month and/or in the lifetime before. The subgroup of children with delusional thoughts with paranoid content (Pa) were *a priori* defined as those with scores of likely or definitely present delusions of persecution, mind-reading and/or receiving messages from TV/radio, as these delusions have a clear paranoid content and can be reliably assessed in the general adolescent population [43]. Trained professionals including 2 psychologists, 3 medical doctors, 1 psychology graduate student and 1 medical student performed the interviews. All interviewers were trained by the senior researcher (PJ) and participated in regular training seminars supported by video-taped interviews, and including group discussions, ratings and supervision in order to obtain high inter-rater reliability in the observer-based ratings of the presence of psychotic symptoms, while taking into account attributions of symptoms to sleep, somatic disorders or toxic influences. If there was a clear attribution explaining the experience, the psychotic symptom was rated as not present. Based on 75 videotaped interviews, the inter-rater reliability was computed as Fleiss' Kappa for assignment of children to each group based on life-time presence of PE symptoms. The inter-rater reliability was very good for both the grouping into children with or without PE (Fleiss Kappa = 0.95) and the further grouping into 1) healthy children (NonPE) 2) children with Psychotic Experiences but no delusional thoughts with paranoid content (PE-NonPa) and 3) children with Psychotic Experiences that include delusional thoughts with paranoid content Pa (Fleiss Kappa = 0.85) [44,45].

In Sample II PE were assessed using the screening question on AVH from the Auditory Vocal hallucination Rating Scale (AVHRS; [46]) and three items on delusional experiences from the Adolescent Psychotic Symptom Screener (APSS); [43]. The AVHRS is a structured 16-item interview evaluating experiences on AVH during a predetermined period (e.g. past month, past year). As opposed to the K-SADS applied in sample I, AVHRS only assess auditory Hallucinations. Each item consists of a compulsory question, followed by optional support questions. Items are scored on a 5-point scale, ordered in increasing severity, facilitating calculation of a severity score AVHRS [46]. The APSS items consist of questions on delusions (mind reading, persecutory delusions and receiving media messages). AVH were rated as: 0 (no) or 1 (yes) and were assessed at baseline over the past year and at follow-up over the five intervening years. Delusions were rated as: 0 (no), 1 (yes, likely) or 2 (yes, definitely) and were assessed over the lifetime [43]. A variable was constructed indicating presence of at least one (definite) delusion (hereafter: delusions). As in sample I, Pa was defined as any delusion of persecution, mind-reading and/or receiving messages from TV/radio. Based on the 337 children attending this part of the assessment, interrater reliability for AVH was good ($\kappa=0.88$).

Statistical analysis

Analyses were carried out using Stata 12 software (StataCorp LP, College Station, TX). Descriptive statistics were used to analyse sample characteristics. Group differences on demographic variables, ToM scores as well as the proxy measures of general cognitive ability were tested by chi-squared tests for categorical variables and by independent samples t-tests for continuous variables.

Logistic regression analyses were conducted with HyperToM, ToM total score, low mentalizing, gender and the proxy measures of general cognitive ability (BD respectively "school level") as independent variables. In each logistic regression analysis, the

Table 1. Demographic, ToM and PE data from sample I and sample II.

	Sample I	Sample II
N	1630	259
Age in months	137	159
Gender (% boys)	782 (48)	122 (47)
Low Socioeconomic status N(%)	382 (23)	80 (31)
General cognition		
Block Design (M, SD)	9.7 (3.9)	-
School Level - Lower vocational (N, %)	-	135 (55)
ToM score		
Mean (SD)	19.2 (4.2)	21.9 (4.6)
Range	3–33	12–33
Median	19	21
Mentalizing answers		
Mean (SD)	3.3 (1.5)	3.8 (1.7)
Range	0–8	0–8
Median	3	3
HyperToM	202 (12%)	21 (8%)
Psychotic Experiences (PE)	171 (10.5%)	156 (60%)
Hallucinations	68 (40%)	85 (55%)
Delusions	26 (15%)	22 (14%)
Both	77 (45%)	49 (31%)
Psychotic Experiences		
PE-NonPa	101 (59%)	85 (54%)
Pa	70 (41%)	71(46%)

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predictive effect of each of the ToM scale scores was estimated while adjusting for the proxy measures of general intelligence.

The logistic regression analyses were used to estimate 1) the risk of having a lifetime presence of PE (yes/no) for the group of children with low ToM compared to the group of children with high ToM in the two samples; and 2) the risk of a lifetime presence of PE (yes/no) for the group of children with HyperToM compared to those children without HyperToM in the two samples. The relative risk was calculated as odds ratio (OR) with 95% CI.

Finally, multinomial logistic regression analyses were used to estimate the dose-response relationship between HyperToM (yes/no) and having a lifetime history of paranoid delusions (Pa), a lifetime history of psychotic symptoms without paranoid delusions (PE-NonPa), and no lifetime history of PE. The hypothesis being tested was that the risk for Pa versus no PE when exposed to HyperToM would be higher than the risk for PE-NonPa versus no PE when exposed to HyperToM.

Thus, the estimated ORs express the risk of experiencing Pa relatively to no PE, and the risk of experiencing PE-NonPa relatively to no PE for children with HyperToM compared to the children without HyperToM. All analyses of risk of HyperToM status were repeated substituting HyperToM as predictor with each of the underlying dimensions of HyperToM, i.e. low ToM score and high mentalizing answers in order to be able to compare the OR of HyperToM to the OR of these variables. All multinomial logistic regression analyses were adjusted for gender. Post-estimation analysis was carried out to examine if the

estimated OR of HyperToM for Pa was significantly different from the OR of HyperToM for PE-NonPa.

Ethics

The Danish study (sample 1) was approved by The Danish Data Protection Agency (J.nr.2010-41-4438), the Capital Region of Denmark (J.nr. 2007-58-0015), and The National Committee on Health Research Ethics was consulted (J.nr.H-C-FSP-2010) in accordance with national guidelines. The written information for sample 1 clearly stated that 1) study participation is voluntary 2) consent can be withdrawn at any time and 3) all data will be de-identified. Parents and child agreed to participate by signing up for the face-to-face assessment of child at the hospital. This consent procedure was approved by the ethics committee.

In the Dutch study (sample 2) written informed consent was obtained from both parents and children, as approved by the local ethics committee.

Results

Sample 1

Psychotic Experiences. A total of 171 (10.5%) of the 1630 children reported lifetime PE. The further subgrouping of these 171 children based on the presence or absence of Pa yielded a Pa group of 70 (41%) children, and a PE-NonPa group of 101 (59%) children (Table 1). There were no significant differences regarding age or gender between either the PE and Non-PE groups, or between the Pa and PE-NonPa groups (Table 2).

Table 2. Between-group comparisons for differences in age, gender distribution and measures of cognition in children with psychotic experiences compared to children without and in children with paranoid delusions compared to children with psychotic experiences but without paranoid delusions.

	PE subsamples			Pa Subsamples		
	PE	Non-PE	Analysis	Pa	PE-NonPa	p
SAMPLE I	N = 171	N = 1459		N = 70	N = 101	
Gender (N, %boys)	77 (45)	715 (49)	$\chi^2(1) = 0.7794$	30 (43)	47 (47)	$\chi^2(1) = 0.2259$
Age in months (Mean, SD)	139 (4.7)	139 (4.7)	t (1628) = 1.04	140.1 (4.6)	139.8 (4.8)	t(169) = -0.3409
Block Design (Mean, SD)	9.3 (3.9)	9.8 (3.8)	t(1628) = 0.14	9.1 (3.9)	9.5 (3.9)	t(169) = 0.6346
SAMPLE II	N = 156	N = 103		N = 71	N = 85	
Gender (N, %boys)	73 (47)	47 (46)	$\chi^2(1) = 0.0812$	40 (56)	42 (49)	$\chi^2(1) = 0.7443$
Age in months (Mean, SD)	159 (5.9)	160 (5.8)	t (257) = 1.7254	159.4 (5.7)	158.4 (6.0)	t(154) = -1.0171
School(N, %preacademic)*	81 (52)	59 (57)	$\chi^2(2) = 2.0765$	33 (46)	54 (64)	$\chi^2(1) = 4.7688$

*missing data on 12 children.

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Theory-of-Mind Frederik. The median ToM score was 19 and the median for number of mentalizing answers was 3 (Table 1). Based on these numbers, a total of 827 (51%) were classified as having low ToM, and among these 202 (12%) children were classified as having HyperToM. There were no significant differences in neither gender (47% vs 48% boys $\chi^2(1) = 0.1310$, $p = 0.717$) nor age (139 vs 139 months $t(1628) = 1.0381$, $p = 0.2994$) between the groups with and without HyperToM.

Proxy General Intelligence: Block Design. There were no significant differences on BD score between the PE and NonPE groups, and similarly no differences between the Pa and PE-NonPa groups. The group of children with high ToM had a significantly higher BD Score than the children with low ToM (Table 2). The HyperToM group (mean = 9.1, SD = 3.7) had a significantly lower BD score than the Non-HyperToM group (mean = 9.8, SD = 3.8, $t(1628) = 2.6978$, $p = 0.007$). All subsequent analyses were adjusted for BD score.

Theory-of-Mind and Psychotic Experiences. The children with a low ToM score had an increased risk of having PE compared to the children with high ToM score (adjusted OR = 1.6, 95%CI 1.1–2.3, $\chi^2(4) = 12.42$ $p = 0.010$). The children with HyperToM compared to the children with no HyperToM also had an increased risk of PE (adjusted OR = 1.8, 95%CI: 1.2–2.7 $\chi^2(3) = 10.11$ $p = 0.006$). The estimated risks of PE for poor ToM and for HyperToM were within the same range with almost identical 95% CIs (Table 3).

The adjusted OR for Pa in the HyperToM group versus the group without HyperToM was 2.0 (95%CI: 1.1–3.7 $\chi^2(4) = 9.93$ $p = 0.021$), whereas the adjusted OR for having PE-NonPa was non-significant albeit directionally similar (Table 4). Post-estimation analysis confirmed that the OR for the children with HyperToM compared to those without HyperToM was significantly higher for Pa than for PE-NonPa ($\chi^2(2) = 7.96$, $p = 0.0187$).

Sample II

Psychotic Experiences. Of the 259 children in the case-control follow-up sample, 156 (60.2%) reported lifetime PE. The further subgrouping of these 156 yielded a Pa group of 71 children (46%) and a PE-NonPa group of 85 children (54%). Similar to sample I there were no significant differences in either age or gender between either the PE and Non-PE groups, or between the Pa and PE-NonPa groups (Table 2).

Theory of Mind Frederik. The median ToM score was 21, and the median number of mentalizing answers was 3 (Table 1). Applying the same criteria for HyperToM as in sample I (i.e. cut-offs: low ToM = ToM total score <19, and High mentalizing = number of mentalizing answers >3), 21 (8%) of the children in sample II were classified as having HyperToM. A significantly greater part of the group of children with HyperToM (81%) were girls compared to the group of children without HyperToM (51% $\chi^2(1) = 7.0293$ $p = 0.008$). There were no age-differences between the group with HyperToM (159 months) and without HyperToM (159 months $t(257) = 0.5699$ $p = 0.5692$).

Proxy General Intelligence: School level. Among the 247 children with existing data at school level, there were no significant differences in the percentages of the children attending pre-academic school in the PE compared to the NonPE group. However, significantly fewer children in the group of children with Pa (46%) compared to the group of children with PE-NonPa (64% $\chi^2(1) = 4.7688$ $p = 0.029$) (table 2). Significantly fewer children attended pre-academic education in (i) the low ToM (37%) compared to the High ToM group (64% $\chi^2(1) = 17.3139$ $p < 0.001$) and in (ii) the HyperToM (28%) compared to the non-HyperToM group (57%, $\chi^2(1) = 5.6594$ $p = 0.017$).

Table 3. Differences in frequency of Psychotic Experiences by ToM groups (and gender and measures of general cognition).

SAMPLE I	Odds Ratio for having PE			
	OR	95% CI	χ^2	p
MODEL 1				
Gender	1.2	0.8–1.6	$\chi^2(4) = 12.42$	0.361
Block Design	0.9	0.9–1.0	$\chi^2(4) = 12.42$	0.254
ToM Scores				
High Number of Mentalizing answers	1.6	1.1–2.6	$\chi^2(4) = 12.42$	0.011
Low ToM Score	1.6	1.1–2.3	$\chi^2(4) = 12.42$	0.010
MODEL 2				
Gender	1.2	0.8–1.6	$\chi^2(3) = 10.11$	0.347
Block Design	0.9	0.9–1.0	$\chi^2(3) = 10.11$	0.165
HyperToM	1.8	1.2–2.7	$\chi^2(3) = 10.11$	0.006
SAMPLE II	Odds Ratio for having PE			
	OR	95%CI	χ^2	p
MODEL 1				
Gender	1.1	0.7–1.8	$\chi^2(3) = 7.13$	0.755
ToM Scores				
High Number of Mentalizing answers	0.5	0.3–0.9	$\chi^2(3) = 7.13$	0.021
Low ToM Score	0.9	0.5–1.8	$\chi^2(3) = 7.13$	0.816
MODEL 2				
Gender	0.8	0.5–1.4	$\chi^2(2) = 7.56$	0.479
HyperToM	4.6	1.3–16.2	$\chi^2(2) = 7.56$	0.018

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To avoid having to exclude from the analyses the 12 children, of whom 8 had PE but missing data at school level, we first carried out both adjusted and non-adjusted analyses for the smaller sample of 247 children. As none of these analyses differed substantially in terms of estimated effects or level of significance, non-adjusted analyses were reported thus allowing inclusion of the full sample of 259.

Theory-of-Mind and Psychotic Experiences. The children with low ToM did not have a significantly increased risk of having PE compared to the children with high ToM. The children with HyperToM had an increased risk of PE compared to the children without HyperToM (OR = 4.6, 95%CI 1.3–16.2, $\chi^2 = (2)7.56$ $p = 0.018$) (Table 3). The OR for Pa in the HyperToM group versus the group without HyperToM was 6.2 (95%CI 1.7–23., $p = 0.002$), whereas the OR for having PE-NonPa was non-significant albeit directionally similar (Table 4). Post-estimation analysis confirmed that the OR for HyperToM was significantly greater for Pa than PE-NonPa ($\chi^2(2) = 7.96$, $p = 0.018$).

Discussion

Findings

The main finding of the present study was that HyperToM was associated more strongly with Pa than PE-NonPa. Confirming hypothesis 3, the OR was 2.0 for Pa in sample I and 1.6 for PE-NonPa, and in sample II the OR for Pa was 6.2 and 3.3 for PE-NonPa. Thus the study documents a clear, replicated relationship between an exaggerated theory of mind and paranoid symptoms in childhood.

Our first hypothesis on PE being more frequent in children with low ToM was confirmed in sample I as the odds for having PE was

1.6 times greater in the group of children with a low ToM score than in the group of children with a high ToM score. However, this was not the case in sample II, where no significant association was apparent.

Hypothesis two on PE being particularly frequent in children with HyperToM was confirmed, as the OR for having PE in both samples was higher for the HyperToM group than for the group without HyperToM. In sample I, the odds for PE was 1.8 times greater in the HyperToM group versus the Non-HyperToM group. In sample II, the corresponding estimate was a 4.6 times greater risk for PE in the HyperToM group versus the non-HyperToM group, while the risk of PE showed no significant association with poor ToM abilities measured as an overall low ToM score. Only in sample I, the odds of PE were within the same range, and with overlapping CIs, for children with poor ToM and for children with HyperToM.

ToM and development of psychosis

The results suggest that particularly the HyperToM type is associated with PE, and that this association is strongest for delusional ideas with paranoid content (Pa), i.e., delusions of persecution, mind-reading and/or receiving messages from TV/radio. These findings are in line with theories suggesting that while general alterations in ToM may be a vulnerability marker for psychosis, more specific types of alterations [29,47] may have a mediating role in the development of different types of specific symptoms.

Based on the work of Frith [48], it may be argued that development of ToM abilities, including the awareness of intentions of the self and others, is necessary in order to experience ideas of reference and symptoms like mind reading. Clearly,

Table 4. Differences in frequency of Psychotic Experiences without paranoid delusions and Psychotic Experiences with Paranoid delusions by ToM groups, gender and measures of general cognition.

STUDY	PE-NonPa			Pa		
	OR	95% CI	χ^2	p	OR	95% CI
MODEL 1						
Gender	1.1	0.7–1.6	$\chi^2(8) = 17.51$	0.707	1.3	0.8–2.1
Block Design	0.9	0.9–1.0	$\chi^2(8) = 17.51$	0.716	0.9	0.9–1.0
ToM Scores						
High number of mentalizing answers	1.2	0.8–1.9	$\chi^2(8) = 17.51$	0.387	2.3	1.4–4.0
Low ToM score	1.6	1.0–2.6	$\chi^2(8) = 17.51$	0.038	1.6	0.9–2.7
MODEL 2						
Block Design	0.9	0.9–1.0	$\chi^2(4) = 9.93$	0.504	0.9	0.9–1.0
HyperToM	1.6	0.9–2.8	$\chi^2(4) = 9.93$	0.073	2.0	1.1–3.7
STUDY II						
PE-NonPa			Pa			
N = 259	OR	95% CI	χ^2	p	OR	95% CI
MODEL 1						
Gender	0.8	0.5–1.5	$\chi^2(6) = 12.75$	0.524	1.1	0.6–1.9
ToM Scores						
High number of mentalizing answers	2.6	1.2–5.4	$\chi^2(6) = 12.75$	0.012	1.6	0.8–3.4
Low ToM Total score	0.9	0.4–1.9	$\chi^2(6) = 12.75$	0.755	1.3	0.6–2.8
MODEL 2						
Gender	0.8	0.4–1.4	$\chi^2(4) = 9.90$	0.365	0.9	0.5–1.7
HyperToM	3.3	0.8–13.1	$\chi^2(4) = 9.90$	0.098	6.2	1.7–23.6

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paranoid patients have intact ToM in the sense that they know that other people have mental states, but may perform poorly because of their difficulties in accurately monitoring other people's intentions [40,49].

HyperToM may in part be stress-induced. Increased stress responsiveness affects mentalizing capacity [50]. For example, a recent study [51] found that high cortisol-responding women make more mentalizing errors due to a tendency to develop HyperToM after stress induction, thus demonstrating that the environment, in the context of increased stress responsiveness, modulates the functioning of ToM abilities. Frith [4,48] suggested that whereas paranoid patients may have a normally functioning ToM when asymptomatic, during acute illness, reduced ToM functioning may lead to the belief that others have malevolent intentions [21]. Such combinations of trait and state-like qualities have been reported for other meta-cognitive mechanisms of psychotic symptoms such as a jumping-to-conclusions reasoning style [52].

Due to the cross-sectional design of the present study, etiological issues cannot be addressed. Future studies may examine how HyperToM develops, and how it may be related to maturational processes. HyperToM may be related to the inability to take perspectives as suggested by Langdon and colleagues [53] or to a tendency to overgeneralization of hypotheses, [29,32,34,54], but these theories have yet to be tested in longitudinal studies.

A retrospective study of young patients with schizophrenia [55] found an increased likelihood of delusional beliefs with age, indicating that the formation of these symptoms from preadolescence onwards depend on brain maturation and learning. Similarly, HyperToM may also depend on brain maturation and learning [56]. The immaturity of the more advanced aspects of ToM abilities in preadolescent children may increase the likelihood of social misinterpretation, anxiety and formation of paranoid and first-rank like delusional ideation that may ultimately result in the persistence of PE [55].

Strengths and limitations

A main strength of the study is the fact that the hypotheses were tested in two large, independent population-based samples from two different countries. PE and ToM were assessed using the same items and cut-offs. The age range was fixed around the onset of puberty and was roughly the same in the two samples. Mean age had no influence on any analysis.

There are, however, a few limitations that need to be considered. First, we were not able to control for general cognition with a measure of full IQ, but adjustment for appropriate proxy measures of IQ did not substantially change any of the results. Secondly, the psychometric properties of the ToM-F task have not yet been examined extensively. Nevertheless, the internal consistency

of the task was found to be fair and comparable across the samples, and the scores were close in range. Also, ToM-F is based on the ToM Storybooks for younger children, which have good psychometric qualities [39].

Finally, the cross-sectional design does not make it possible to determine the direction of the relationships. Longitudinal studies need to further explore the developmental trajectories of HyperToM in childhood and adolescence and to assess both the causal and temporal relationships between PE and HyperToM, and the stability of HyperToM over time.

Conclusion

The current study is the first to demonstrate patterns of association between specific alterations in ToM and psychotic symptoms in a population-based sample of children. The findings were replicated in a smaller, high prevalence study.

Our findings suggest that it may be productive to apply more differentiated measures of ToM instead of relying on an overall score based on number of correct answers. This could be helpful not only when conducting research on the development of PE and psychosis, but also when applying ToM tasks as part of a clinical assessment in child mental health service settings.

The results contribute to the understanding of the relationship between ToM and psychosis, which seems unlikely to be fully explained by an association between poor ToM and a state of psychosis. The current study points to the possibility of different alterations in ToM impacting on different stages of development of psychosis.

Supporting Information

Appendix S1 Rating Categories for ToM Storybook. (DOCX)

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Author Contributions

Conceived and designed the experiments: PJ AB EB AMS. Performed the experiments: LC. Analyzed the data: LC PJ JvO MV. Contributed reagents/materials/analysis tools: AB EB. Wrote the paper: LC PJ JvO AB MV AMS EB.

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Psychotic experiences and hyper-theory-of-mind in preadolescence – a birth cohort study

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Background. Knowledge on the risk mechanisms of psychotic experiences (PE) is still limited. The aim of this population-based study was to explore developmental markers of PE with a particular focus on the specificity of hyper-theory-of-mind (HyperToM) as correlate of PE as opposed to correlate of any mental disorder.

Method. We assessed 1630 children from the Copenhagen Child Cohort 2000 regarding PE and HyperToM at the follow-up at 11–12 years. Mental disorders were diagnosed by clinical ratings based on standardized parent-, teacher- and self-reported psychopathology. Logistic regression analyses were performed to test the correlates of PE and HyperToM, and the specificity of correlates of PE *v.* correlates of any Diagnostic and Statistical Manual of Mental Disorders, 4th edition (DSM-IV) mental disorder.

Results. Univariate analyses showed the following correlates of PE: familial psychiatric liability; parental mental illness during early child development; change in family composition; low family income; regulatory problems in infancy; onset of puberty; bullying; concurrent mental disorder; and HyperToM. When estimating the adjusted effects, only low family income, concurrent mental disorder, bullying and HyperToM remained significantly associated with PE. Further analyses of the specificity of these correlates with regard to outcome revealed that HyperToM was the only variable specifically associated with PE without concurrent mental disorder. Finally, HyperToM did not share any of the investigated precursors with PE.

Conclusions. HyperToM may have a specific role in the risk trajectories of PE, being specifically associated with PE in preadolescent children, independently of other family and child risk factors associated with PE and overall psychopathology at this age.

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Introduction

Hallucinations, delusions and thought disturbances in the absence of diagnosable psychotic illness, referred to as psychotic experiences (PE), are frequent in the general population with a median prevalence estimated at around 7% (Linscott & Van Os, 2013). PE are usually transitory, but longitudinal cohort studies have shown an association with later development of psychotic illness. Thus, PE may index psychometric risk for psychotic disorder (Poulton *et al.* 2000; Kaymaz *et al.*

2012; Kelleher *et al.* 2012; Linscott & Van Os, 2013). However, it is unclear if PE are a specific risk factor for psychotic disorder or represent risk for psychopathology in general (Kounali *et al.* 2014), as PE not only predict psychotic disorder, but also mark an increased risk for onset (Kaymaz *et al.* 2012; Jeppesen *et al.* 2015), as well as increased severity and poor prognosis of non-psychotic disorders (Kelleher *et al.* 2012; Wigman *et al.* 2012). Recent findings on the development of psychotic disorder suggest that the first stage may in fact be a diagnostically non-specific stage of potentially more severe psychopathology, which only later may acquire a degree of diagnostic specificity (Fusar-Poli *et al.* 2014).

PE are found to share demographic, familial, and developmental risk factors with psychotic disorders

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(Kelleher & Cannon, 2011), including: family liability to mental disorders (Mortensen *et al.* 2010; Polanczyk *et al.* 2010; Jeppesen *et al.* 2014), involvement in bullying for both victims and perpetrators (Lataster *et al.* 2006; Kelleher *et al.* 2008; Schreier *et al.* 2009; Kelleher & Cannon, 2010), lower socio-economic background (Polanczyk *et al.* 2010; Goldberg *et al.* 2011) and onset of puberty which is mediated in part by increased rate of emotional disorders (Jeppesen *et al.* 2015). Early developmental problems (such as emotional problems and interpersonal difficulties as well as impairments in neuromotor and cognitive development) are also associated with both psychotic illness and PE (Cannon *et al.* 2002). As in schizophrenia (Buckley *et al.* 2009; Achim *et al.* 2011), concurrent mental illness is very common in PE in children. Diagnoses appear across the spectrum (Nishida *et al.* 2008; Scott *et al.* 2009; Polanczyk *et al.* 2010; Jeppesen *et al.* 2015) but, as we have previously shown with data from the same sample as the current study, anxiety and depression may be particularly frequent (Jeppesen *et al.* 2015). Higher risk of PE in early adolescence has been reported in individuals with childhood neurodevelopmental non-psychotic disorder (ND) (Khandaker *et al.* 2014), which is also a frequent co-morbid disorder (Jeppesen *et al.* 2015). Lower intelligence quotient (IQ) is associated with schizophrenia (Woodberry *et al.* 2008; Khandaker *et al.* 2011) and may also be associated with PE in both non-clinical adult (Cannon *et al.* 2002; Johns *et al.* 2004) and child populations (Horwood *et al.* 2008; Polanczyk *et al.* 2010). However, these risk factors are to a large extent non-specific, and evidence supporting predictions as to which vulnerable individuals will develop which cluster of mental symptoms is sparse (Kounali *et al.* 2014).

A well-established risk factor for schizophrenia is impairments in theory-of-mind (ToM). However the nature (Bosco *et al.* 2009) and extent of the ToM impairments, and their role in the ontogenesis of psychosis, remain unclear. Furthermore, impairments in ToM are also prominent in patients across different diagnostic categories, including neurodevelopmental disorders, particularly autism spectrum disorder (ASD) (Brune, 2005) and bipolar disorder (Russell *et al.* 2006), suggesting that ToM impairments are not specific to schizophrenia (Marothi & Keri, 2014). ToM impairments are associated with PE in non-clinical adult (Versmissen *et al.* 2008; Langdon *et al.* 2010) and adolescent samples (Polanczyk *et al.* 2010; Barragan *et al.* 2011; Bartels-Velthuis *et al.* 2011; Clemmensen *et al.* 2014). Studies in both clinical and non-clinical adult and childhood populations have reported that ToM impairments may be associated with specific symptoms such as persecutory delusions rather than with diagnostic categories (Russell *et al.* 2006; Barragan *et al.* 2011).

Frith (1992, 2004) introduced the distinction between over- and undermentalizing; also referred to as, respectively, hyper-theory-of-mind (HyperToM) and hypo-theory-of-mind (HypoToM) (Abu-Akel, 1999). Whereas HyperToM can be defined as a social-cognitive process that involves making assumptions about other people's mental states that go so far beyond observable data that the average observer will struggle to see how they are justified (Frith, 2004; Montag *et al.* 2011), HypoToM refers to the prediction of behaviour on the basis of the actual state of the world rather than on beliefs or intentions and mental states of other people (Frith, 2004; Montag *et al.* 2011). This distinction between Hyper- and HypoToM is of potential importance (Fretland *et al.* 2015), as it might be contrasting positive schizophrenia on the one hand and negative schizophrenia and autism on the other (Abu-Akel & Bailey, 2000). Both Hyper- and HypoToM can lead to errors on standard ToM tasks, but these different strategies would lead to different kinds of error (Frith, 2004). According to the diametric model of the mind and mental illness, all mental disorders can be located along this dimension of ToM ranging from Hypo- to HyperToM (Crespi & Badcock, 2008; Badcock, 2011). It has been hypothesized that individuals with ASD and individuals with psychosis spectrum disorders (PSD) may be located at the extreme ends (Ciaramidaro *et al.* 2015). Individuals with ASD have low ToM skills regarding, for example, inferring intention or understanding false belief. They therefore can be positioned at the HypoToM side of the continuum. On the other hand, individuals with PSD can be typified as having HyperToM: patients with paranoid schizophrenia, for example, symptomatically over-interpret intention either positively, for example in erotomania (delusions that others are in love with the person), or negatively, for example in delusions of persecution. They also may display bizarre false beliefs about themselves and others, and generally exhibit excessive mentalism (Badcock, 2011).

Studies in both clinical (Montag *et al.* 2011) and general population (Fyfe *et al.* 2008) adult samples support the theory presented above. Various studies reported an association between HypoToM and autism and negative symptoms on the one hand and between HyperToM and psychotic disorders, positive symptoms of schizophrenia and schizo-affective disorder (Montag *et al.* 2011; Fretland *et al.* 2015) and delusions and paranoid delusions, in particular (Fyfe *et al.* 2008; Montag *et al.* 2011; Peyroux *et al.* 2014) on the other. One study (Russell *et al.* 2006) found that among individuals with schizophrenia and non-clinical controls, the paranoid subgroup of the former group tended to use more mental state terms than other groups to describe the movements of triangles moving around a

screen in 'random', 'goal-directed' or in 'ToM' conditions, the latter involving, for example, one triangle 'hiding from' or 'tricking' another. Patients with behavioural signs of schizophrenia and those with paranoid symptoms were poorer than patients with other symptoms, or controls, at describing the triangles' movements in the ToM condition. In addition, these results are consistent with the notion that ToM difficulties in paranoid patients are related to HyperToM (Fyfe *et al.* 2008). Using a similar methodology, one study (Blakemore *et al.* 2003) found perception of contingency when there was none in the animate non-contingent condition was associated with delusions of persecution across groups of: (1) patients with a diagnosis of schizophrenia; (2) patients with affective disorders; and (3) normal control subjects. Overall, previous findings suggest that HyperToM is specifically associated with psychotic symptoms/experiences and not with the overall diagnosis of schizophrenia. However, studies on HyperToM and PE all concern adult populations, and none included children. In a recent general population study of Danish children, based on data from the same sample as the present study, we showed that HyperToM was more strongly associated with PE than poor ToM in general, this being the case for paranoid ideation in particular (Clemmensen *et al.* 2014). Thus, while general impairments in ToM may be a vulnerability marker for psychotic disorder, more specific types of impairments such as HyperToM may be associated with development of specific psychotic symptoms such as paranoid delusions (Shamay-Tsoory *et al.* 2007; Montag *et al.* 2011).

The aim of the current study was to further examine the association between HyperToM (Clemmensen *et al.* 2014) and PE by exploring developmental markers of PE in preadolescence with a particular focus on the role of HyperToM as a factor that specifically makes an impact on the risk of having PE. To this end the specificity of HyperToM as a correlate of PE as opposed to a correlate of any mental disorder was studied.

The following hypotheses were tested:

1. HyperToM is independently associated with PE. That is, after adjusting for well-known risk factors: familial liability, concurrent mental disorders and symptoms, and early developmental problems, HyperToM is still significantly associated with PE.
2. HyperToM is specifically associated with PE rather than with any Diagnostic and Statistical Manual of Mental Disorders, 4th edition (DSM-IV) non-psychotic mental health disorder.
3. HyperToM is not associated with either neurodevelopmental disorder, anxiety or depression.

Method

Sample

The current study was conducted as part of the 11- to 12-year follow-up of The Copenhagen Child Cohort 2000 (CCC2000). CCC2000 is a general population birth cohort, consisting of 6090 children born in 16 municipalities in the Copenhagen County in the year 2000, followed prospectively from birth (Skovgaard *et al.* 2005). The cohort comprises 9% of all children born in Denmark that year, and is overall representative for children born that year in Denmark (Olsen *et al.* 2007).

The study was conducted from 1 May 2011 to 1 October 2012. In all, 4847 children were eligible for follow-up at the age of 11 or 12 years (see Fig. 1 for details and Clemmensen *et al.* 2014). The current sampling frame comprised a sample of 1630 children who attended the assessment at age 11–12 years [mean age 11.6 (s.d.=0.4) years; 34% of eligible children, 48% boys]. In the study of PE, participating children showed only minor differences on a number of socio-demographic and perinatal background characteristics compared with the rest of the cohort (those alive at age 11 years) with slightly lower frequencies of biological and psycho-social adversities among the participating children (Jeppesen *et al.* 2015).

Instruments

An overview of the variables is presented in Table 1.

Register data

Familial psychiatric liability and parental mental illness during early child development

Any diagnosed mental health disorder at any psychiatric hospital or centre in Denmark in any first-degree relative (including father, mother and siblings) was included from the Danish Psychiatric Central Register in order to detect a family history of mental health disorders. Details on included International Classification of Diseases (ICD)-8 and ICD-10 diagnoses are described elsewhere (Jeppesen *et al.* 2014).

Socio-economic status (SES)

Data on change in family income and on duration of mother's education were acquired from the Integrated Database for Labour Market Research and linked through the Danish Civil Registration System using the personal identification numbers of the CCC2000 children to describe SES. Low maternal education is consistently associated with poor mental health of the child (Boyle *et al.* 2011), and low family income is associated with several different lifetime

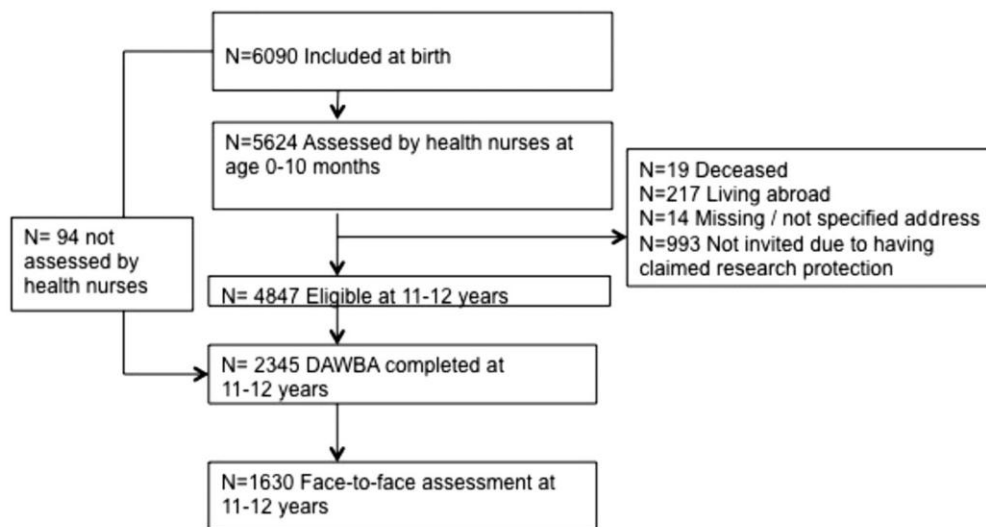


Fig. 1. Flow chart of participation. DAWBA, Development and Well-being Assessment.

mental disorders (Sareen *et al.* 2011). Change in family income was applied to best capture this condition over the full period with a single variable.

Assessment of early developmental problems

In Denmark, a community health nurse with specific training in infant health visits the same families regularly during the first year of life. For the CCC2000 study, a standardized record and manual were developed to record information on the health nurses' assessments prospectively from birth at four scheduled home visits conducted when the children were at the ages 1–5 weeks (visit 1), 2–3 months (visit 2), 4–6 months (visit 3) and 8–10 months (visit 4). Data recorded included information from the parents as well as the results and conclusions based on the health nurse's observations and assessments of the child. At each visit, the health nurse recorded whether the development of the child was normal or not, on a range of domains (overall development, feeding and eating, sleep and other regulatory functions; social interaction and communication and mother–child relationship). The domains were selected to cover social–emotional, cognitive and neurological development and to make it possible to record whether the function in each domain was within the normal range or not. Details of the standardized record are described elsewhere (Skovgaard *et al.* 2005).

Face-to-face assessments at the clinic at age 11 or 12 years

Bullying, puberty and cognition

Bullying was assessed with the Olweus Bully/Victim Questionnaire (Gothwal *et al.* 2013). Puberty was

assessed by Tanner staging based on self-reports (Coleman & Coleman, 2002). Performance on the block design (BD) subtest of the Wechsler Intelligence Scale for Children (WISC-III) was used as a proxy measure of children's general cognitive abilities. The BD subtest is highly correlated with full-scale IQ in the WISC-III (Kana *et al.* 2013).

PE

PE were assessed by a semi-structured interview using the Schedule for Affective Disorders and Schizophrenia for School-age Children – Present and Lifetime Version (K-SADS-PL) (Kaufman *et al.* 1997) screening section and the supplement on psychotic symptoms. Each of the 22 items of PE was scored: absent, likely present, or definitively present. PE were rated present (yes/no) if at least one psychotic symptom was scored as 'likely' or 'definitely' present within the last month and/or lifetime. Trained professionals, including two psychologists, three medical doctors, one psychology graduate student and one medical student, performed the interviews. All interviewers were trained by the senior researcher (P.J.) and participated in regular training seminars supported by videotaped interviews, as well as group discussions and supervision. The target was to obtain high inter-rater reliability in the observer-based ratings of the presence and severity of PE while taking into account attributions of symptoms to sleep, somatic disorders or toxic influences. If there was a clear attribution explaining the experience, PE was rated conservatively as not present. Based on 75 randomly selected videotaped interviews, the inter-rater reliability was very good for the grouping of the children into those with and without PE ($\kappa = 0.95$).

Table 1. Overview of familial and developmental variables in the study

Variables	Frequency	Description	Source of information	Distribution <i>n</i> (%)
Register data: the CCC2000 children and their first-degree relatives were linked via the Central Person Register numbers to the Danish Psychiatric Central Register and the family database				
Familial psychiatric liability	1614	Family history of mental disorders diagnosed at hospital. This measure was used as a proxy index of the genetic liability of any ICD mental disorder (ICD-8, and from January 1994, ICD-10), as well as any contact with a psychiatric hospital related to attempted suicide, self-harm, or abuse of alcohol or drugs. Included were all first-degree relatives (including father, mother and siblings). We included any registered diagnosis from the date of birth of the person or from April 1969 (whichever came last) and until the birth of the CCC2000 index child (for siblings until December 2010). Except for siblings, we included only diagnoses registered prior to the birth of the index child in order to avoid reverse causation	Psychiatric Central Register	No diagnosis 1383 (86) Any diagnosis 231 (14)
Parental mental illness during early child development	1630	Whether the mother or father had been diagnosed with a mental disorder during the first 3 years of the life of the child	Psychiatric Central Register	No 1550 (95) Yes 80 (5)
Changes in family composition years 2000–2010	1623	Changes in the family composition (whether the child lived together with both parents, one parent or new partners of the parent) were recorded annually throughout the observation period	The family database (Statistics of Denmark)	No changes 1258 (78) Changes 365 (22)
Change in family income years 2000–2010	1599	Based on the data available for the total sample, change in family income was divided into tertiles	The family database	1st (lowest) tertile: 425 (27) 2nd (middle) tertile: 510 (32) 3rd (highest) tertile: 664 (41)
Maternal education year 2010	1607	Length of the mother's education in 2010 in years	The family database	1–10 years: 171 (11) 11–14 years: 786 (49) 15+ years: 650 (40)
Assessments in infancy (child age 0–10 months)				
Infancy regulatory problems	1531	An overall variable of infancy regulatory problems was defined as the child having either feeding, sleeping or tactile (whether the child shows pleasure being touched and/or can easily be comforted in the parent's arms) problems; at least one visit	Measures of feeding and sleeping were only included from visit 2, 3 and 4 as most normally developing children establish a regular pattern of feeding and sleep at this age. Tactile reactivity was included at visit 1 and/or visit 2	Normal 1338 (87) Abnormal 193 (13)

Table 1 (cont.)

Variables	Frequency	Description	Source of information	Distribution <i>n</i> (%)
Mother–child relationship	1526	A rating of abnormal mother–child relationship was defined as deviances in the mothers in taking care of the child, handling, expectations, reactions and reciprocity	Health nurse records: visit 1, 2, 3 and 4	Normal 1434 (94) Abnormal 92 (6)
Infancy contact problems	1381	The overall variable of ‘child contact problems’ was defined as the child having problems within at least one of three domains: eye contact, contact smile, and contact babbling	In Denmark, a standardized test including contact and communication (the BOEL test) is carried out at the health nurse’s visit when the child is 8–10 months old	Normal 1313 (95) Abnormal 68 (5)
Assessment at age 11 or 12 years				
Pubertal stage	1630	Tanner stages 2–4 indicate onset of puberty	Pubertal stage was assessed by the child pointing out which of four diagrams of the Tanner stages best illustrated the child’s physical development	Pre-puberty: 1277 (78) Onset of puberty: 353 (22)
General cognition	1630	Performance on the BD was used as a proxy measure of children’s general cognitive abilities	WISC-III BD	Mean = 9.7, S.D. = 3.9, range 1–17
Bullying	1630	Whether the child was involved in bullying as either a victim or a perpetrator	The Olweus Bully/Victim Questionnaire (Gothwal <i>et al.</i> 2013) measuring physical, verbal and relational forms of bullying. Following Kowalski & Limber (2007) questions on cyber-bullying were added	Normal 1281 (78) Abnormal 359 (22)
HyperToM	1630	Whether the child has HyperToM or not	Theory-of-Mind Storybook Frederik	No HyperToM 1428 (88) HyperToM 202 (12)
PE	1630	Whether the child has PE or not	K-SADS-PL	No PE 1458 (89) PE 172 (11)
Any DSM-IV diagnosis	1614	Whether the child has a psychiatric diagnosis or not	DAWBA	No diagnosis 1383 (86) Diagnosis 231 (14)

CCC2000, Copenhagen Child Cohort 2000; ICD, International Classification of Disease; BD, block design; WISC-III, Wechsler Intelligence Scale for Children; S.D., standard deviation; HyperToM, hyper-theory-of-mind; PE, psychotic experiences; K-SADS-PL, Schedule for Affective Disorders and Schizophrenia for School-age Children – Present and Lifetime Version; DSM-IV, Diagnostic and Statistical Manual of Mental Disorders, 4th edition; DAWBA, Development and Well-being Assessment.

HyperToM

The ToM Storybook Frederik (ToM-F) (Blijd-Hoogewys & Bartels-Velthuis, 2007) was used to assess ToM. ToM-F is the Danish version of the Dutch ToM Storybook Freek (Blijd-Hoogewys & Bartels-Velthuis, 2007), aiming to test the understanding of second-order false belief, white lie, irony, double bluff and 'faux pas' (a socially awkward or tactless act) in 10- to 14-year-old children. The children are asked to respond to a total of 24 questions while listening to the storybook read aloud and at the same time being presented 16 pictures.

The internal consistency of ToM-F was good (Cronbach's $\alpha=0.7$). The task consists of 16 'test' and eight 'justification' questions. The test answers are scored 0 or 1; 1 is given for a correct understanding of the situation (range 0–16). The eight justification answers are classified according to 23 predefined categories (see Clemmensen *et al.* 2014 for the full set of categories) such as:

Desire: The answer refers to the protagonist's desire with respect to the situation. It involves wanting or desiring something.

Fact belief: The child refers to the protagonist's knowledge. It involves thinking, knowing, being sure of, expecting or recognizing.

Situational: Dwelling on the situation without reference to the mental state of the protagonist.

Based on these categories, the answers were scored ('0', '1', '2', and for some items '3') on an ordinal scale predefined for each situation, resulting in a justification sum score (range 0–20), that was summed with the test score ('0' or '1', range 0–16) to form the total scale score of ToM abilities (range 0–36). Scores on the justification items depend on the level and quality of references made to the thoughts, beliefs, feelings or intentions of the story characters or the child itself.

The eight justification answers were also scored on a dichotomous scale as a non-mentalizing ('0') or mentalizing ('1') type of answer, regardless of the classification of the answer as formally right or wrong in the context, resulting in a mentalizing scale score (range 0–8). Consistent with previous work, mentalizing answers were defined as those referring to beliefs, desires and similar inner states (Fyfe *et al.* 2008; Montag *et al.* 2012). Thus, the following 11 of the 23 categories were considered mentalizing: belief; desire; fact belief; value belief; mental state verb rest category; own frame of reference with mental state; emotion with empathy; emotion without empathy; perception with mental state; identification of first-order intention; identification of second-order intention (see Clemmensen *et al.* 2014 for a description of all categories). A high number of

mentalizing answers (high mentalizing) was defined as total score above the median.

HyperToM was defined on the basis of (i) total ToM scale score below the median combined with (ii) number of mentalizing answers above the median. Both measures were taken into account, as the aim was to capture children that had a low level of overall ToM abilities while making mental attributions frequently. Taking into account both measures, a categorical variable was constructed, capturing children who were among the top 50% with regard to number of mentalizing answers, while, at the same time, among the lowest 50% with regard to overall ToM abilities measured by the total scale score. These children showed a tendency to exaggerate and give aberrant mentalizing explanations, labelled HyperToM, in contrast to the children without HyperToM. The phenotype should not be conceptualized as somewhere between high and low levels of overall ToM abilities, but as another dimension of ToM skills that was measured as a dichotomized variable. ToM ratings were carried out in close collaboration with the Dutch authors of ToM-F. An initial training seminar was conducted. Thereafter consensus ratings on a subsample of 200 children were carried out by a Danish rating group headed by the first author (L.C.), and subsequently the remaining children were rated by the first author under supervision of the Dutch authors. A sample of 50 children was rated separately by one member of the Danish research group in order to measure the inter-rater reliability for assignment of children to each ToM group. The inter-rater reliability (computed as Cohen's κ) was very good for the categorizing of children as HyperToM ($\kappa=0.81$) (Altman & Gardner, 1991).

Web-based assessments

Psychiatric diagnoses

The Strengths and Difficulties Questionnaire (SDQ; Goodman, 2001) and the Development and Well-being Assessment (DAWBA; Goodman *et al.* 2000) were completed by parents, children and, if possible, teachers. The SDQ (Goodman, 2001) consists of 25 items covering psychopathology followed by the impact (Goodman, 1999). The SDQ scores were an integrated part of the DAWBA used for diagnosis.

The DAWBA is a highly structured interview designed to generate psychiatric diagnoses in children and adolescents according to DSM-IV and ICD-10 and covers child development, psychiatric symptoms, distress and social impairment. A computer algorithm generated the preliminary diagnoses, and subsequent clinical review by senior child psychiatrists determined the final DSM-IV diagnoses (Goodman *et al.* 2000). Inter-rater reliability of the DAWBA-based DSM-IV

diagnoses indexed by Cohen's κ was examined in a sample of 100 children and found to be high for any DSM-IV diagnosis ($\kappa=0.81$).

Illness category

Based on presence of PE (yes/no) and of any psychiatric diagnosis (yes/no), a variable 'illness category' was defined, consisting of the following four mutually exclusive groups: (1) no illness; (2) any psychiatric diagnosis (no PE); (3) PE (no psychiatric diagnosis); and (4) both (PE and a psychiatric diagnosis). This grouping enabled us to differentiate between associations to PE specifically, of any mental illness and of the combination. The category of 'both' may additionally be an expression of severity as having both PE and a psychiatric diagnosis may be considered more severe than having either (Kelleher et al. 2012; Wigman et al. 2012).

Statistical analysis

Analyses were carried out using Stata 12 software (StataCorp LP, USA). Associations between the family and developmental variables, and PE and HyperToM were tested using χ^2 tests for categorical variables and independent t tests for continuous variables. Logistic regression analyses were conducted including PE as the dependent variable, and all other variables as independent variables. This was done in order to analyse the independent association with HyperToM when adjusted for all other predictive variables. In order to answer the research question on the specificity of HyperToM as an associated variable to PE, multinomial logistic regression analyses were performed with illness category as the dependent variable, and the remaining variables as independent variables. Finally, associations between HyperToM and ND, anxiety and depression were tested using logistic regression analyses. In all regression analyses, variables were entered simultaneously as no predictions were made about the inter-dependence of variables. Entering the variables simultaneously made it possible to test which variables were significantly associated with PE and illness category, respectively, when adjusting for all other included variables.

Due to missing data (between seven and 249 cases) in seven variables (changes in family structure; change in family income 2000–2010; length of mother's completed education 2010; family mental illness liability; infancy regulatory problems; mother–child relationship; and child contact problems) imputations were performed using the STATA multiple imputation suite of commands (mi). Data were assumed to be missing at random, and gender and age were used to impute the missing values. All variables were imputed

30 times. This enabled us to use the full sample ($n=1630$) and not only the children without missing values ($n=1369$).

Results

HyperToM and PE and other mental illness

An overview of the correlations between all independent variables is shown in Table 2.

Familial risk and developmental variables: associations with PE and HyperToM

PE were significantly more prevalent in groups of children with: familial psychiatric liability (15.0% v. 9.8%); parental mental illness during early development (21.3% v. 10.0%); changes in family composition (13.7% v. 9.5%); change in family income (15.1% in the lowest tertile v. 9.8% in the middle and 7.8% in the highest tertile); regulatory problems (12.8% v. 9.2%); onset of puberty (11.4% v. 7.4%); having a psychiatric diagnosis (23.8% v. 8.3%); and being involved in bullying (19.5% v. 8.0%). None of these predictors of PE was associated with HyperToM. Only a low cognitive score on the WISC-III BD test was significantly associated with HyperToM (Table 3). This association could relate to not being autistic, rather than to low IQ. However excluding the participants with ASD from the analysis, BD score remained significantly lower in the group with HyperToM (mean = 9.0, S.D. 3.8) compared with the group without HyperToM (mean = 9.8, S.D. = 3.8, $t_{1589} = 2.6406$, $p = 0.0084$).

Independency of association with HyperToM

The regression analyses showed that HyperToM was significantly associated with PE after adjusting for all other included variables [odds ratio (OR) 1.81, 95% confidence interval (CI) 1.2–2.8, $p = 0.007$]. Apart from HyperToM, having a concurrent psychiatric diagnosis, being involved in bullying and lowest increase in family income remained significantly associated with PE (Table 4).

The specificity of the association of HyperToM with regard to PE v. other psychopathology

Multinomial regression analyses showed that HyperToM was the only variable exclusively associated with PE without concurrent mental illness (OR 1.71, 95% CI 1.0–2.8, $p = 0.034$) (Table 5). Involvement in bullying remained significantly associated with PE without mental illness (OR 2.37, 95% CI 1.6–3.7, $p < 0.001$) in a model including HyperToM, but involvement in bullying was also significantly associated with having any psychiatric diagnosis (OR 2.28, 95% CI 1.6–3.2, $p < 0.001$), and with

having both a psychiatric diagnosis and PE (OR 4.11, 95% CI 2.3–7.3, $p < 0.001$).

Looking specifically at the most prevalent concurrent diagnoses, HyperToM was not associated with either ND (OR 0.9, 95% CI 0.5–1.7, $p = 0.824$), anxiety (OR 0.57, 95% CI 0.27–1.19, $p = 0.132$) or depression (OR 1.66, 95% CI 0.72–3.83, $p = 0.234$).

Discussion

Hypothesis 1 on HyperToM being independently associated with PE was confirmed, as HyperToM was significantly associated with PE after adjusting for the following risk factors: gender; familial liability; having a concurrent mental disorder and parental mental illness during early child development; changes in family structure; change in family income 2000–2010; length of maternal education; regulatory problems; abnormal mother–infant relationship; infancy contact problems; onset of puberty; lower proxy measures of cognition and bullying. Hypothesis 2 was also confirmed, as HyperToM was exclusively associated with PE and not with either any psychiatric diagnosis (without PE) or with having both PE and a psychiatric diagnosis. HyperToM was the only variable being independently and specifically associated with PE. Bullying was associated with an increased risk of PE, but also with an increased risk of any mental disorder or problem including PE. This could indicate that bullying is a non-specific risk factor of general psychopathology, whereas HyperToM is a more specific index for psychosis proneness. HyperToM was also not associated with ND, anxiety or depression when these were examined separately. The current findings suggest that whereas the majority of the investigated variables are associated with a risk for psychopathology in general, HyperToM appears to be associated with a risk for PE in particular.

HyperToM may be considered not so much as a deficit but rather as a cognitive strategy or style (Sharp *et al.* 2011), that in part depends on brain maturation and learning (Abu-Akel, 2003). As the great majority of the sample did not express HyperToM at age 11–12 years, this may indicate a maturational delay in the children who do express this alteration in ToM. Thus, HyperToM at this age may be an expression of minor developmental delay and may predict a less severe instance of mostly transitory PE. The fact that HyperToM was only associated with PE without any co-morbidity, and not with having any mental illness and PE in combination, which may be viewed as more severe, seems to indicate so. However, it is also possible that the combination of HyperToM and PE expresses a different pathway to mental illness. These findings need to be replicated in different age groups,

Table 2. Zero-order correlations

	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	(10)	(11)	(12)	(13)
(1) Gender	1.00												
(2) Familial psychiatric liability	0.05	1.00											
(3) Parental mental illness during early child development	0.00	0.13*	1.00										
(4) Changes in family structure	0.03	0.06*	0.08*	1.00									
(5) Change in family income 2000–2010	–0.01	–0.11*	–0.07	–0.35*	1.00								
(6) Duration of the mother's education	0.07	–0.05	–0.01	0.05	0.29*	1.00							
(7) Regulatory problems	–0.00	–0.00	0.03	0.03	–0.05	–0.04	1.00						
(8) Abnormal mother–infant relationship	–0.04	0.01	0.07	0.02	–0.04	–0.01	0.22*	1.00					
(9) Infancy contact problems	0.01	–0.03	–0.02	0.01	–0.03	0.02	0.05	0.09*	1.00				
(10) Onset of puberty	0.09*	0.03	–0.00	0.01	–0.01	–0.03	0.02	–0.00	0.02	1.00			
(11) Block design	0.06*	–0.04	–0.01	–0.02	0.13*	0.21*	–0.05	–0.03	0.02	–0.01	1.00		
(12) Involvement in bullying	–0.04	0.09*	0.11*	0.04	–0.07*	–0.08*	–0.01	0.01	–0.02	0.02	–0.07*	1.00	
(13) Hyper-theory-of-mind	–0.00	0.01	–0.02	0.01	–0.00	–0.03	0.00	0.03	0.01	0.02	–0.07*	0.03	1.00

* $p < 0.05$.

Table 3. Univariable analyses of the associations between each of the familial and developmental variables and (1) psychotic experiences and (2) hyper-theory-of-mind

			Psychotic experiences				Hyper-theory-of-mind			
			<i>n</i>		Analysis		<i>n</i>		Analysis	
			—	+	χ^2 (df = 1) ^a	<i>p</i>	—	+	χ^2 (df = 1) ^a	<i>p</i>
Register data										
Gender	1630	Boys	704	77			684	97		
		Girls	754	95	0.7629	0.382	744	105	0.0010	0.974
Familial psychiatric liability	1630	—	1277	140			1244	184		
		+	181	32	5.1899	0.023	173	29	0.3372	0.561
Parental mental illness during early child development	1630	—	1395	155			1356	72		
		+	63	17	10.2007	0.001	194	8	0.4436	0.505
Changes in family composition	1623	—	1138	120			1105	153		
		+	315	50	5.2203	0.022	317	48	0.2548	0.614
Change in family income (2000–2010)	1599	1	361	64			373	52		
		2	460	50			445	65		
		3	612	52	14.8180 (df = 2)	0.001	584	80	0.1336 (df = 2)	0.935
Length of mother's education in years (2010)	1607	1–10	147	24			148	23		
		11–14	701	85			683	103		
		15+	590	60	3.4655 (df = 2)	0.177	576	74	1.1429 (df = 2)	0.565
Infancy variables										
Regulatory problems	1521	—	931	94			896	129		
		+	441	65	4.9163	0.027	442	64	0.0012	0.972
Abnormal mother–infant relationship	1526	—	1291	143			1258	176		
		+	78	14	2.5661	0.108	77	15	1.2829	0.257
Infancy contact problems	1369	—	1178	135			1187	166		
		+	61	7	0.000	0.997	12	4	2.3565	0.125
Face-to-face assessment at age 11 or 12 years										
Puberty	1630	≥2	326	26			314	39		
		0–1	1132	145	4.6252	0.032	1114	163	0.07502	0.386
Any DSM-IV diagnosis	1614	—	1268	115			1207	176		
		+	176	55	50.4271	0.000	205	26	0.3909	0.532
Block design	1630		Mean = 9.8	Mean = 9.2	$t_{1628} = 1.6896$	0.0913	9.8 (3.9)	9.0 (3.8)	$t_{1628} = 2.6914$	0.0072
Bullying	1630	+	1169	102			1120	151		
		—	289	70	39.0417	0.000	308	51	1.3946	0.238

df, Degrees of freedom; DSM-IV, Diagnostic and Statistical Manual of Mental Disorders, 4th edition.

^a Unless otherwise specified.

Table 4. Multivariable regression analysis of the independent effects of the familial and developmental variables on risk of PE (n = 1630)^a

	Risk for having PE		
	OR	(95% CI)	p
Gender	1.22	(0.9–1.7)	0.252
Length of the mother's education	0.96	(0.7–1.3)	0.768
Change in family income 2000–2010	0.79	(0.6–1.0)	0.044
Changes in family structure	1.08	(0.7–1.6)	0.699
Familial risk	1.30	(0.9–1.9)	0.164
Parental mental illness during early child development	1.49	(0.8–2.8)	0.204
Infancy contact problems	0.88	(0.4–2.1)	0.773
Regulatory problems	1.35	(0.9–1.9)	0.106
Abnormal mother–infant relationship	1.33	(0.7–2.5)	0.396
Onset of puberty	1.49	(1.0–2.3)	0.082
Involvement in bullying	2.21	(1.6–3.1)	<0.001
Psychiatric diagnoses of child	2.75	(1.9–4.0)	<0.001
Block design (intelligence)	1.00	(1.0–1.0)	0.848
Hyper-theory-of-mind	1.81	(1.2–2.8)	0.007

PE, Psychotic experiences; OR, odds ratio, CI, confidence interval.

^a This table shows the OR for each of the 14 variables for having PE when entered simultaneously in the model.

but the fact that HyperToM was the only factor that specifically increased the risk of having PE when children with other mental illness were excluded points to a subgroup that follows a pathway that to a lesser extent is preceded by early alterations.

The interpretation why the group with only PE represents a different pathway from the group with both PE and mental illness is supported by the fact that the latter was significantly associated with change in family income 2000–2010, abnormal mother–infant relationship and involvement in bullying. PE in this group of children may to a greater extent be a result of the concurrent disorder and related distress.

Mentalizing has known neural correlates (Hamilton *et al.* 2004) that may be affected more by environmental factors than previously assumed (Hughes *et al.* 2005). Whereas basic ToM skills may be more or less innate, later and more complex skills may be environmentally determined to a large extent (Hughes *et al.* 2005; Korver-Nieberg *et al.* 2013). Thus, exposure to chronic and episodic life stress as well as an invalidating, insecure context of attachment relationships may contribute to the development of HyperToM (Sharp & Venta, 2012). Considering previous research showing that patients with a psychotic disorder are more

reactive to stressors in normal daily life (Lardinois *et al.* 2011) and that an individual's sensitivity to everyday stressors (e.g. losing one's car keys) may be particularly important in the aetiology of psychosis (Palmier-Claus *et al.* 2012), a possibly productive future area of study is the relationship between HyperToM, stress reactivity and psychosis.

HyperToM does not necessarily constitute a problem in itself. However, in addition to an increased risk of PE, the presence of HyperToM may also increase the risk of persistence of PE over time. Following the proneness–persistence–impairment model of psychotic disorder (van Os *et al.* 2009), environmental risks for psychosis act additively in causing abnormal persistence which, in turn, increases the risk of subsequent transition to need for care (Cougnard *et al.* 2007).

The present study confirmed that many predictors of schizophrenia are also associated with PE. In addition, regulatory problems in the first year of life were also associated with PE. The fact that schizophrenia and PE share risk factors does not necessarily mean that these are specific for psychotic illness as risk factors are also associated with other psychiatric outcomes (Van Os *et al.* 1998; Kounali *et al.* 2014). However, our finding that HyperToM is more strongly associated with PE specifically than with any diagnosis supports the belief that HyperToM is aetiologically related to mechanisms underlying psychotic illness. In addition, the fact that HyperToM was only predicted by low IQ and not by any of the risk factors associated with PE indicates the possibility of a specific pathway to PE associated with HyperToM. Associations between childhood neurodevelopmental disorder, IQ and adolescent PE have been found (Khandaker *et al.* 2014). However, although HyperToM is associated with IQ in the present sample, there was no association with neurodevelopmental disorder. Thus this pathway may be different from the one leading to having both PE and a concurrent psychiatric diagnosis.

Strengths and limitations

A main strength of the study is the use of a large general population birth cohort sample with data from infancy to age 11–12 years. The data set included a broad range of variables from different sources.

However, the present study has several limitations. First, despite having data from the birth of the child until the age of 11–12 years, both HyperToM and PE were assessed cross-sectionally at age 11–12 years. Therefore, future longitudinal studies should further explore the causal and temporal relationships. Second, the psychometric properties of ToM-F have not yet been examined extensively. Nevertheless, the internal consistency of the task was found to be

Table 5. Multinomial regression analysis of the independent effects of the familial and developmental variables on risk of any psychiatric diagnosis without PE, PE without psychiatric diagnosis and concurrent PE and psychiatric diagnosis by familial risk, developmental deficits and HyperToM^a

	No illness (n = 1282) ^b	Any psychiatric diagnosis without PE (n = 176)			PE without psychiatric diagnosis (n = 117)			Both PE and psychiatric diagnosis (n = 55)		
		OR	(95% CI)	p	OR	(95% CI)	p	OR	(95% CI)	p
Gender	–	0.82	(0.6–1.1)	0.241	1.43	(1.0–2.1)	0.081	0.66	(0.4–1.2)	0.148
Familial psychiatric liability	–	1.55	(1.1–2.2)	0.020	1.53	(1.0–2.4)	0.056	1.49	(0.8–2.6)	0.173
Parental mental illness during early child development	–	1.29	(0.6–1.8)	0.496	1.16	(0.5–2.9)	0.746	0.44	(0.1–3.5)	0.431
Changes in family structure	–	1.69	(1.2–2.5)	0.007	1.44	(0.9–2.3)	0.121	0.92	(0.5–1.8)	0.802
Change in family income 2000–2010	–	0.98	(0.8–1.2)	0.827	0.82	(0.6–1.1)	0.168	0.68	(0.5–1.0)	0.050
Duration of the mother's education	–	1.09	(0.8–1.4)	0.507	1.02	(0.7–1.4)	0.908	0.95	(0.6–1.5)	0.833
Regulatory problems	–	0.73	(0.3–1.6)	0.411	1.53	(0.7–3.2)	0.258	0.66	(0.2–2.3)	0.516
Abnormal mother–infant relationship	–	1.24	(0.6–2.5)	0.536	0.73	(0.3–1.9)	0.531	4.77	(2.3–10.1)	<0.001
Infancy contact problems	–	1.31	(0.9–1.9)	0.141	1.29	(0.8–2.0)	0.236	1.77	(1.0–3.2)	0.057
Onset of puberty	–	1.19	(0.8–1.8)	0.404	1.69	(1.0–2.9)	0.063	1.37	(0.7–2.8)	0.398
Block design	–	0.95	(0.9–1.0)	0.010	0.95	(0.9–1.0)	0.072	1.05	(1.0–1.1)	0.252
Involvement in bullying	–	2.28	(1.6–3.2)	<0.001	2.37	(1.6–3.6)	<0.001	4.11	(2.3–7.3)	<0.001
HyperToM	–	0.74	(0.4–1.3)	0.267	1.71	(1.0–2.8)	0.034	1.48	(0.7–3.2)	0.98

PE, Psychotic experiences; HyperToM, hyper-theory-of-mind; OR, odds ratio; CI, confidence interval.

^a The table shows the OR for each of the 13 (psychiatric diagnoses of child is dependent in this model) variables for having either psychiatric diagnoses without PE, PE without psychiatric diagnoses and concurrent PE and Psychiatric diagnosis by familial risk, developmental deficits and HyperToM compared with having no illness when adjusted for each other.

^b Reference category.

good. In addition, ToM-F is based on the ToM Storybooks for younger children, which have good psychometric qualities (Blijd-Hoogewys *et al.* 2008; Bulgarelli *et al.* 2015). Finally, we were not able to control for general cognition with a measure of full IQ. Nevertheless, the BD test result, used as proxy measure of IQ, is strongly associated with full-scale IQ (Constantino *et al.* 2003). There is general consensus that neurocognition and social cognition (such as ToM) are related but different constructs, and there seems to be only a modest association between neurocognition and social cognition (Couture *et al.* 2006). Possibly, general cognitive abilities represent a necessary but not sufficient condition for adequate mentalization (Sprong *et al.* 2007).

Conclusion

This is the first study with data from infancy to age 11–12 years examining associations between HyperToM and PE, as well as other mental illness, familial liability to mental illness, demographic factors, and early developmental problems in preadolescent children from the general population. The findings suggest that a

wide range of family and child variables are associated with psychopathology in general, whereas HyperToM is specifically associated with PE. These findings indicate that the construct of HyperToM may be useful in delineating differential pathways to psychopathological outcomes, and the study of HyperToM may help us to understand more about mechanisms in the aetiology of psychotic illness.

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Declaration of Interest

None.

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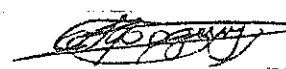
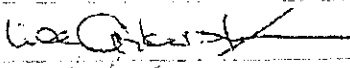
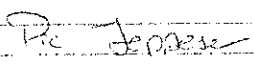
Title of PhD thesis:
Hyper-Theory-of-Mind in Children with Psychotic Experiences

This declaration concerns the following article:
Exploring a new Theory-of-Mind task for 8-14 year-old children

The PhD student's contribution to the article: (please use the scale (A,B,C) below as benchmark*)	(A,B,C)
1. Formulation/identification of the scientific problem that from theoretical questions need to be clarified. This includes a condensation of the problem to specific scientific questions that is judged to be answerable by experiments	C
2. Planning of the experiments and methodology design, including selection of methods and method development	B
3. Involvement in the experimental work	A
4. Presentation, interpretation and discussion in a journal article format of obtained data	C

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A. refers to:	Has contributed to the co-operation	0-33 %
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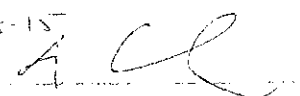
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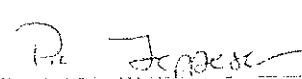
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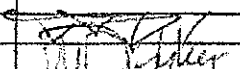
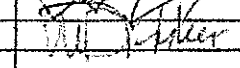
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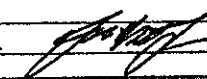


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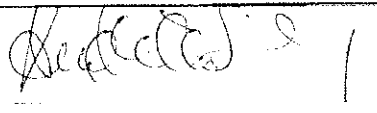
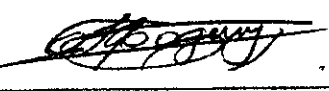
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Hyper-Theory-of-Mind in Children with Psychotic Experiences

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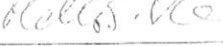
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