Social predictors of psychotic experiences in adolescence

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The role of social cognition, social functioning, parenting and religiosity in the emergence and course of adolescent psychotic experiences

Laura A. Steenhuis

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This dissertation is dedicated to my father, Egbert Steenhuis

Paranimfen
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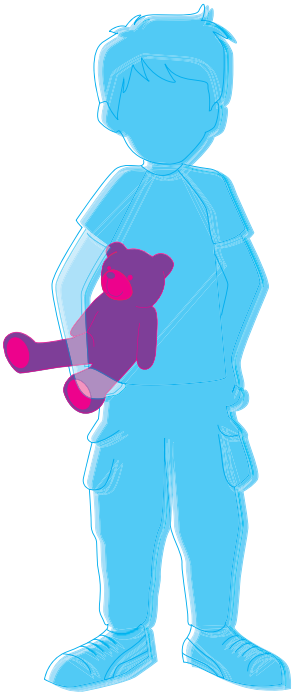
General introduction

CHAPTER 1



1.1 Psychotic Experiences

The lifetime prevalence of schizophrenia is estimated at about 1% (Saha, Chant, Welham, & McGrath, 2005) whereas the lifetime prevalence of all psychotic disorders has been estimated at 3% (Perälä et al., 2007). Psychotic disorders are often accompanied by both positive (e.g. hallucinations and delusions) and negative (e.g. affective flattening or apathy) symptoms (American Psychiatric Association, 2013), as well as disorganized thoughts and speech, cognitive symptoms (impairments of executive functioning, attention and memory) and mood symptoms (depression and mania) (American Psychiatric Association, 2013; Owen, Sawa, & Mortensen, 2016). Subthreshold forms of psychotic symptoms, such as psychotic experiences, are much more common in the general population than psychotic symptoms and psychotic disorders (van Os, Hanssen, Bijl, & Vollebergh, 2001). Psychotic experiences are 'attenuated' forms of psychotic symptoms (Yung, et al., 2005), as they are less frequent, severe, distressing and crystalized than psychotic symptoms, and do not meet clinical criteria. In addition, reality testing for hallucinatory experiences often remains intact, which means that when prompted, the individual realizes the experience may not have been real at the time (Kelleher & Cannon, 2011).

Lifetime prevalence rates of psychotic experiences in the general population have been estimated at around 7.2% in a relatively conservative meta-analysis, with a median annual incidence rate of 2.5% (Linscott & van Os, 2013). Prevalence rates during childhood and adolescence are often higher; the median prevalence rate for children between 9 and 12 years old lies around 17%, which declines to 7.5% between the ages of 13 and 18 years (Kelleher et al., 2012). Prevalence rates in other studies have been even higher, with 28% of adolescents aged between 13 and 17 years reporting hearing voices sometimes, whereas only 1.9% reported this always or nearly always (Yung et al., 2008). Importantly, the phrasing of the screening question whether an adolescent has a psychotic experience may influence prevalence rates (Kompus et al., 2015). The endorsement of the statement "I often hear a voice speaking my thoughts aloud" was 10.6% in a sample of adolescents aged between 16 and 19 years, but the endorsement of the statement "I have been troubled by hearing voices in my head" was 5.3% (Kompus et al. 2015). Overall, the prevalence rate of psychotic experiences in the general population differs according to the age groups and the screening question presented (Maijer, Begemann, Palmen, Leucht, & Sommer, 2017). The general consensus is that the prevalence rate of psychotic experiences is higher than the prevalence rate of diagnosable psychotic disorders in the general population, for children, adolescents and adults (e.g. 8% psychotic experiences and 3% psychotic disorders in adult populations; van Os, Linscott, Myin-Germeys, Delespaul, & Krabbendam, 2009; 7.5-17% psychotic experiences in children and adolescent samples; Kelleher, Connor et al., 2012).

The majority of mental disorders, such as substance abuse, mood disorders and psychotic disorders have an age of onset in young adulthood (Kessler et al., 2005). This makes it particularly interesting to examine whether the presence of psychotic experiences in adolescence can predict psychotic disorders in young adulthood. Previous research has attempted to examine whether psychotic experiences are predictive of psychosis specifically, finding evidence that there is an

increased risk for psychosis in adulthood when reporting psychotic experiences during childhood (Fisher et al., 2013; Poulton et al., 2000) and adolescence (Kaymaz et al., 2012; Welham et al., 2009; Dominguez et al., 2012). For example, the Dunedin longitudinal study demonstrated that children who had psychotic experiences (assessed as mind-reading, telepathy, paranoia, auditory hallucinations or bodily distortions) at age 11 years had an increased relative risk of 7.24 for developing schizophrenia at age 38 (Fisher et al., 2013). Moreover, a previous study demonstrated that one third of pre-clinical psychosis was preceded by psychotic experiences in adolescence (Dominguez, Wichers, Lieb, Wittchen, & Van Os, 2011). In line with these results, psychotic experiences have been previously criticized for not being specific enough for predicting psychosis (Paolo Fusar-Poli et al., 2016; Nieman & McGorry, 2015). However, a recent study demonstrated that ultra-high risk states for psychosis (characterized by sub-clinical psychotic experiences) are at an increased long-term risk for psychotic disorders, but not for other (non-psychotic) mental disorders (Fusar-Poli et al., 2017). Besides the risk for psychotic disorders, psychotic experiences are also associated with concurrent impaired social functioning and mental distress in adolescence (age 11 to 13 years; Kelleher et al., 2015), in addition to future poorer global functioning in young adulthood (age 11 to age 18 years; Healy et al., 2018). It therefore appears particularly relevant to identify predictors of the reporting, development and persistence of psychotic experiences during childhood and adolescence, given their association with concurrent and future lower functioning, and specific long-term predictive ability of psychotic disorders in young adulthood.

Auditory Vocal Hallucinations

Auditory vocal hallucinations (AVH) belong to the most commonly studied type of psychotic experiences. AVH are defined as hearing people talking, whispering, screaming, singing or muttering, in the absence of external stimuli. AVH are the most salient symptoms in psychotic disorders with prevalence rates in schizophrenia of about 60% to 70% (Andreasen & Flaum, 1991; Baethge et al., 2005). Currently, AVH are regarded as lying on a continuum, ranging from benign and often transient experiences in individuals in the general population, to distressing symptoms in clinical populations (Johns & Van Os, 2001; Larøi et al., 2012; van Os et al., 2009). AVH are common in psychotic illnesses and other mental disorders such as depression, and bipolar, dissociative and substance use disorders (Larøi et al., 2012), and also occur in the general population in children, adolescents and adults (Bartels-Velthuis, Wigman, Jenner, Bruggeman, & van Os, 2016; Bartels-Velthuis, van de Willige, Jenner, Wiersma, & van Os, 2012; Bartels-Velthuis, Jenner, van de Willige, van Os, & Wiersma, 2010; Maijer, Begemann, Palmen, Leucht, & Sommer, 2017; van Os et al., 2009).

The presence and persistence of AVH in children and adolescents may represent a risk factor for developing psychopathology later in life, though the risk is dependent on age (Jardri et al., 2014). To specify, the later the AVH is experienced in adolescence, the higher the risk of psychopathology. For example, AVH at age 7-8 years are more common but less associated with concurrent psychopathology, whereas incident and persistent AVH at age 12-13 years predicts three to five times higher odds of having clinical behavioral or emotional problems, within the same sample (Bartels-Velthuis, van de Willige, Jenner, Wiersma, et al., 2012; Bartels-Velthuis et al., 2010). Moreover, in a general population study of 11 to 16 year old adolescents, it was found that

the majority of adolescents with AVH had at least one lifetime mental disorder (Kelleher et al., 2012) and in a clinical sample of adolescents aged between 11 and 15 years, those who reported AVH were found to have on average three concurrent diagnosable DSM-IV disorders (Fujita et al., 2015; Kelleher, Cederlöf, & Lichtenstein, 2014). In addition, the risk of suicidal behavior was shown to be consistently associated with the presence of AVH in both clinical (Kelleher et al., 2012) and general population samples (Kelleher et al., 2013; Lindgren et al., 2017; Martin, Thomas, Andrews, Hasking, & Scott, 2015). Last, a proportion of AVH persists in adolescence (23.5%; Bartels-Velthuis, van de Willige, Jenner, van Os, & Wiersma, 2011; 27%; De Loore et al., 2011), and if so, the specific risk for psychotic disorders is five to six times higher than when AVH are transient (age 11 to age 26, Poulton et al., 2000; age 14 to age 21, Welham et al., 2009).

Regardless of whether AVH persist or not, the experience itself can be highly distressing and may warrant clinical attention. Raven et al. (2017) have shown that time to treatment of mental problems in children is substantial, so perhaps many children in the general population reporting AVH could actually meet clinical criteria. In support of these findings, a recent study (Maijer et al., 2018) demonstrated that one in four children aged 12-13 years in the general population with AVH may be in need of care. This was demonstrated by the fact that a quarter of the children from a general population sample (Bartels-Velthuis, et al., 2011; Bartels-Velthuis et al., 2010) reported similar AVH severity and problem behavior as a clinical sample of children who were in treatment for their AVH. Importantly, these children could have been identified five years earlier (at age 7-8 years) on the basis of parent-reported problem behavior. In addition, persistent mental health problems throughout adolescence were reported, as denoted by depressive symptoms and poorer school functioning at age 18-19 years (Bartels-Velthuis et al., 2016). Overall, the study shows that AVH can be regarded as a signal of a vulnerable population, which may be in need of care for a more diverse range of problems than AVH alone. It is therefore crucial to be able to predict and reliably asses the presence and course of AVH during childhood and adolescence, given the risk that AVH may present for concurrent and future psychopathology in young adulthood.

Assessment of Psychotic Experiences in Youth

There are a number of assessment tools available that examine psychotic experiences in childhood and adolescence, including the assessment of hallucinations, paranoia and delusions (e.g. the Adolescent Psychotic Symptom Screener, (Dolphin, Dooley, & Fitzgerald, 2015; Kelleher & Cannon, 2011); Specific Psychotic Experiences Questionnaire, (Ronald et al., 2014); Psychotic-Like Experiences Questionnaire for Children, (Laurens, Hobbs, Sunderland, Green, & Mould, 2012)). The majority of these measures broadly assess psychotic experiences and screen for the presence of, for example, hallucinations, using a single item (e.g. Fujita et al., 2015; Garralda, 2016), "Have you ever heard voices or sounds that no one else can hear". However, in addition to screening for the presence of a psychotic experience, it is important to assess the characteristics and qualities of this psychotic experience. For example, in AVH, the emotional valence, frequency of AVH, or lack of control over AVH could determine future psychopathology (Daalman et al., 2011), and may be relevant targets for (if necessary) the treatment of AVH. There are a few instruments that

assess the presence and (at least some) characteristics of AVH in childhood and adolescence, such as the Interview for Psychosis- Like Symptoms (Horwood et al., 2008) and the SOCRATES assessment (Kelleher & Cannon, 2014), but these are in an interview-based format and therefore time-consuming and costly. Currently, there is a need for a comprehensive self-report instrument that assesses both the presence and qualities of AVH, suitable for adolescent samples.

The Auditory Vocal Hallucination Rating scale (AVHRS; Bartels-Velthuis, van de Willige, Jenner, & Wiersma, 2012; Jenner & van de Willige, 2002) is a structured and validated interview for the assessment of characteristics and severity of AVH in both pediatric and adult populations (Bartels-Velthuis, et al., 2011; Bartels-Velthuis et al., 2016; Bartels-Velthuis et al., 2010). Given that there has been a shift from interview measures to self-report measures of AVH (Ratcliff, Farhall, & Shawyer, 2011), a short self-report version of the AVHRS has been developed, namely the AVHRS-Q(uestionnaire)(van de Willige, Bartels-Velthuis, & Jenner, 2010). This instrument is suitable for the assessment of AVH in adolescent and adult populations (useful for age 12 years and up), can be presented online, and takes on average only six minutes to complete. As such, the AVHRS-Q has the benefit of being inexpensive, time-efficient and does not require training of assessors. As a basis for potential widespread and international implementation, the AVHRS-Q requires formal validation.

Clinical Staging

A useful framework for research and intervention in the development of severe mental illness, is the clinical staging model of McGorry and colleagues (2010). The current thesis will use this clinical staging model as a framework to study the influence of social predictors on psychotic experiences in adolescence. The clinical staging model originated from general medicine and is most often applied to study medical diseases such as diabetes and arthritis. Clinical staging allows the differentiation of early and mild subclinical experiences from symptoms that signify mental illness progression and chronicity. This makes it useful for research in adolescence and young adulthood when the majority of mental disorders emerge. The model additionally enables clinicians to develop and deliver treatments which are relevant in early phases of illness, where it is hypothesized to be more effective than treatments applied at a later stage in illness. The clinical staging model has five stages (see table 1).

Table 1. Clinical staging model for psychotic disorders (McGorry et al., 2010)

Stage	Definition
0	Increased risk of psychotic disorder, without symptoms
1a	Mild or nonspecific symptoms (psychotic experiences), mild functional change or decline
1b	Ultra-High-Risk: moderate but subthreshold symptoms (psychotic experiences), with functional decline
2	First episode psychosis with moderate to severe symptoms and functional decline
3a	Incomplete remission
3b	Recurrence or relapse of psychotic disorder
3c	Multiple relapses
4	Severe, persistent, or unremitting illness

The current thesis will focus on the prodromal stage 1a (mild/non-specific symptoms in the general population) and 1b (ultra-high-risk (UHR) stage). Studying psychotic experiences in the general population (stage 1a) and the risk factors that influence their expression may be a crucial contribution to existing research which is often restricted to subjects with chronic psychosis (Verdoux & Van Os, 2002). In this way, it is possible to examine at which point risk factors may become evident, and when it may be possible and desirable to intervene and target them. Known risk factors for psychosis have been successfully identified in general population and childhood samples in relation to psychotic experiences, such as migration (Johns, Nazroo, Bebbington, & Kuipers, 2002; Laurens, West, Murray, & Hodgins, 2008), cannabis use (Henquet et al., 2004; Schubart et al., 2011) and social adversity (Bartels-Velthuis, van de Willige, Jenner, Wiersma, & van Os, 2012; Kelleher et al., 2008; Mackie et al., 2010). Therefore, studying predictors of psychotic experiences in childhood and adolescent samples can provide insight into which factors contribute to the development of psychosis and other mental disorders (Roddy et al., 2012).

The UHR for psychosis stage (stage 1b) has received a lot of attention over the last decade. This stage precedes the onset of a psychotic episode, most often presenting itself in adolescence or in early adulthood, and consisting of a period of instability and worsening of psychosocial deficits (Yung & McGorry, 1996). In order to accurately define those at UHR for a psychotic episode, three separate UHR criteria have been developed: (a) a genetic risk (b) brief limited intermittent psychotic symptoms (BLIPS; a brief period of distressing symptoms), and (c) attenuated positive symptoms (APS; a longer period of mild psychotic experiences), all occurring in the presence of a significant social impairment (Yung et al., 2005). Roughly, one third of individuals with UHR status

will develop a psychotic disorder within three years (Fusar-Poli et al., 2012). Studying additional risk factors, symptoms and outcomes in the UHR stage can refine the development of UHR criteria - and thus better predictions of psychotic disorders - and the development of new interventions to prevent progression to a psychotic disorder.

1.2 Social Predictors

Given the predictive ability of psychotic experiences for psychotic disorders (Fisher et al., 2013; Kaymaz et al., 2012) and poorer functioning (Kelleher et al., 2015) in young adulthood, it is important to understand what predicts the presence, frequency and course of psychotic experiences in adolescence. In this thesis, the emphasis lies on the exploration of social factors as predictors of psychotic experiences.

Impairments in social functioning are common in psychotic disorders (Couture, Penn, & Roberts, 2006). These impairments are not just considered an outcome of psychotic symptoms, but also as a risk factor for psychosis (Cornblatt et al., 2012; Davidson et al., 1999). Even before the first psychotic episode, individuals demonstrate signs of social withdrawal or a loss of role functioning (Cornblatt et al., 2012). In psychotic disorders, one factor responsible for an impairment in social functioning is a deficit in social cognition (Couture et al., 2006). To specify, if an individual has difficulty to accurately interpret the emotions from another person's face (Green & Horan, 2010) or to understand the intentions behind someone's actions (Frith, 1992), they will have more problems in functioning with other people in society and in fulfilling their expected social roles. This social cognitive deficit can be present before the first psychotic episode, as a "trait vulnerability" (Lavoie et al., 2013; Lee, Hong, Shin, & Kwon, 2015). If an impairment in social cognition is already present in childhood or adolescence, this may cause problems in social functioning in adolescence and early adulthood as a result. Thus, impaired social cognition as well as social functioning, and their inter-relations, will render the adolescent more vulnerable for psychosis in young adulthood. It is important to study whether social predictors of psychotic experiences can already be detected in adolescence, as a first step to determine when they can be intervened upon. In this thesis, social cognition (ToM and facial emotion identification) and social functioning (overall functioning and functioning specifically within the family environment) will be examined as social predictors of psychotic experiences. Besides these social factors, religiosity as a social construct will also be examined in relation to the reporting and course of auditory vocal hallucinations in adolescence.

1.3 Social Cognition

Social cognition can be defined as the psychological processes involved in the perception, encoding, storage, retrieval and regulation of social information about others and ourselves (Green, Horan, & Lee, 2015). Social cognition is a broad concept and often used as an umbrella term for different abilities. In the psychosis literature, the most commonly studied domains are social perception, attributional style, emotion perception and theory of mind (Green et al., 2015). Social cognition is often impaired in patients with a chronic psychotic disorder (Mehta

et al., 2013), but also in earlier phases of the illness. For example, social cognition is impaired in first episode psychosis (Andrew Thompson et al., 2012), the ultra-high risk phase of psychosis (Lee et al., 2015; Van Donkersgoed, Aleman, Wunderink, Nieboer, & Pijnenborg, 2015), and also in siblings of individuals diagnosed with a psychotic disorder (Bora & Pantelis, 2013). This has led to the hypothesis that social cognition may signify a trait vulnerability for the development of a psychotic disorder (Lavoie et al., 2013; Lee et al., 2015). However, when and how this vulnerability manifests itself remains unanswered. In this thesis, two domains of social cognition will be examined, namely theory of mind and facial emotion identification. How these two hypothetical 'trait vulnerabilities' may manifest itself and whether they may predict psychotic experiences in adolescence, will be explored.

Theory of Mind

Theory of mind (ToM) refers to the ability to represent human mental states and to make inferences about another person's intentions (Penn, Sanna, & Roberts, 2008). ToM includes understanding false beliefs (the understanding that others may have a wrong belief about reality) and faux pas (someone mistakenly saying something he should not have), but also for example the ability to understand hints, deception, metaphors, and irony. The idea that psychotic symptoms in psychotic disorders may be explained by a deficit in ToM was first raised by Frith (1992). According to his theory, a ToM deficit in psychotic disorders may explain (1) negative and disorganized symptoms, (2) delusions of alien control and voice-commenting hallucinations (a voice commenting on one's behaviour), and (3) delusions of reference and persecution. Since his theory emerged, a surge in research has examined how ToM may be implicated in psychotic disorders and how it is related to different symptoms. The general consensus is that ToM is significantly impaired in psychotic disorders, not only during acute episodes but also when patients are in remission (Herold, Tényi, Lénárd, & Trixler, 2002; Inoue et al., 2006). ToM is impaired in early phases of psychosis as well, during the first psychotic episode (Andrew Thompson et al., 2012), in the UHR for psychosis phase (Piskulic et al., 2016), and in siblings of individuals with a diagnosis of schizophrenia (Bora & Pantelis, 2013). Moreover, ToM does not seem to be associated with specific symptoms (e.g. paranoia), is impaired for both inpatients and outpatients, and is not explained by general cognitive functioning (Penn et al., 2008). Therefore, ToM may not be a state impairment, that is, it does not fluctuate with symptoms (Inoue et al., 2006). Instead, on the basis of the evidence, ToM ability might signify a trait deficit for psychosis.

Despite the emerging evidence that ToM may be a trait marker for psychosis (Horan et al., 2012), it remains unclear when ToM deficits first emerge (e.g. during childhood, adolescence or young adulthood). If ToM deficits are associated with a genetic or innate vulnerability for psychosis, individuals who later go on to develop schizophrenia may already have ToM deficits in childhood (Brüne, 2005b). On the other hand, it is possible that a genetic vulnerability only expresses itself after adolescence and that ToM development is normal during childhood in individuals who later develop schizophrenia (Brüne, 2005b; Corcoran, Malaspina, & Hercher, 2010; Ozguven et al., 2010). When comparing individuals with schizophrenia to individuals with autism, one often (though not always; Couture et al., 2010) finds that individuals with autism have lower

ToM performance than those with schizophrenia (Ozguven et al., 2010; Pilowsky 2000). This may be because in autism, a ToM impairment occurs earlier in development or certain aspects of ToM may not develop at all. Given that severe symptoms of schizophrenia often only emerge in adolescence or early adulthood (Paus, Keshavan, & Giedd, 2008), it is also possible that ToM first develops normally, followed by some neuropathological processes after puberty that break down ToM ability.

Currently, there is limited research about ToM ability in the context of psychotic experiences in childhood and adolescence. In some studies, ToM ability in relation to AVH and delusions in childhood has been examined. Bartels-Velthuis and colleagues (2011) examined the role of ToM ability in the development of delusion formation in 12-13 year old children with AVH, finding that better ToM skills protected against secondary delusion formation. However, they did not find that children with AVH had lower ToM skills than children without AVH. This is supported by a study of Sullivan and colleagues (2013) who found that ToM ability of children at age 12 was not related to psychotic experiences cross-sectionally. On the other hand, ToM ability at age 5 years has been found to be predictive of definite psychotic symptoms (without intact reality testing) at age 12 years (5.9% of a large birth cohort; Polanczyk et al., 2010). Whether preadolescent/childhood ToM ability has the potential to predict psychotic experiences at adolescence (when the emergence of a psychotic disorder is more likely), is a relevant and understudied question. Answering this question may shed more light on the development of psychosis (which often starts in adolescence or young adulthood) and as a first step may indicate when it could be possible to intervene on risk factors.

Facial Emotion Identification

Deficits in emotion processing have been considered important features of schizophrenia for more than a century (Bleuler, 1911). Meta-analyses demonstrate moderate to severe deficits in facial emotion identification ability in psychotic disorders (Chan, Li, Cheung, & Gong, 2010; Kohler, Walker, Martin, Healey, & Moberg, 2010), which have been confirmed at the neural level (Aleman & Kahn, 2005). Facial emotion identification (Green & Horan, 2010) refers to the ability of accurately identifying emotional expressions from another person's face, such as anger, disgust, fear, sadness, surprise and happiness (Ekman, 1999). The ability to recognize these basic emotions is essential to form emotional connections, to establish relationships and to communicate with others. Deficits in facial emotion identification have been hypothesized to play a role in the development of paranoia (an inability to understand others could feed negative interpretations; Combs, Michael, & Penn, 2006; Pinkham, Brensinger, Kohler, Gur, & Gur, 2011), delusions (an inability to correct faulty interpretations can cause and support delusional ideation; Bentall, Kinderman, & Kaney, 1994), and potentially hallucinations (continuous erroneous interpretation of social situations and others can lead to social stress, hyper vigilance, and hallucinatory experiences; Kohler, Bilker, Hagendoorn, Gur, & Gur, 2000). Generally, it is found that recognition of negative expressions (anger, fear, sadness and disgust) is impaired (Bediou et al., 2005; Janssens et al., 2012), but there is also some evidence for an impairment in recognizing positive expressions (Barkl, Lah, Harris, & Williams, 2014).

The deficit in facial emotion identification is hypothesized to be a trait deficit, given that a lowered emotion identification ability is found in chronic psychosis (Savla, Vella, Armstrong, Penn, & Twamley, 2013), first episode psychosis (Romero-Ferreiro et al., 2016), individuals at UHR for psychosis (Piskulic et al., 2016) and in siblings of individuals diagnosed with a psychotic disorder (Fett & Maat, 2013). If facial emotion identification is indeed a trait vulnerability for psychotic disorders, it is important to examine at which point this vulnerability can be detected, as to inform when early interventions can be delivered and are effective. In addition, examining the association between facial emotion identification at childhood without concurrent symptoms, and psychotic experiences in adolescence, will give a better idea whether facial emotion identification deficits are a true 'trait' or 'state' vulnerability. So far, few studies have examined whether facial emotion identification is prospectively associated with psychotic experiences in childhood and adolescence. One of these demonstrated that facial emotion identification in 8-year-olds was not associated with psychotic experiences at age 11 (Andrew Thompson et al., 2011). However, it could be that facial emotion identification was measured too early as full proficiency in the ability to perceive emotions from faces is usually acquired around age 10 (Durand, Gallay, Seigneuric, Robichon, & Baudouin, 2007; Walker-Andrews, 1997). To address this issue, Roddy and colleagues (2012) examined whether facial emotion identification at age 10-13 years was cross-sectionally associated with psychotic experiences, which was confirmed (especially for the emotion 'sad'). The next step would be to examine whether this association holds up longitudinally. In addition, given that adolescence is a developmental period when psychotic experiences may become more clinically relevant (Jardri et al., 2014), it is essential to examine how previous findings regarding early facial emotion identification ability and psychotic experiences in childhood (Thompson et al., 2011) or early adolescence (Roddy et al., 2012) manifest itself at later ages in adolescence (current thesis).

1.4 Social Functioning

Social functioning, which includes the ability to meet societal defined roles such, as being a homemaker, worker, student, spouse, family member or friend (Mueser & Tarrier, 1998), is commonly impaired in psychotic disorders (see review by Couture et al., 2006; Velthorst et al., 2016). Even though one may be inclined to perceive this impairment as a consequence of psychosis, it has been suggested that impaired social functioning may be a subclinical marker for psychosis (Cornblatt et al., 2012; Davidson et al., 1999). Support for this view comes from studies comparing social functioning of individuals at UHR for psychosis and of first-episode psychosis patients with healthy controls (Addington, Penn, Woods, Addington, & Perkins, 2008; Ballon, Kaur, Marks, & Cadenhead, 2007), demonstrating that social functioning appears to be impaired in early phases of the illness and even before the first psychotic episode.

Definitions of ultra-high risk (UHR) for psychosis include impaired social functioning (Yung, Phillips, Yuen, & McGorry, 2004). This impairment was found to be associated with a transition to the first psychotic episode in UHR individuals (Addington et al., 2017; Cornblatt et al., 2012; Mason et al., 2004). However, the exact nature of the association between social functioning

and the development of psychosis is complex, and the evidence of the predictive role of social functioning in the onset of a first psychotic episode is not always consistent (Brandizzi et al., 2015). A recent meta-analysis of 42 studies (Schultze-Lutter et al., 2015), showed that a social impairment does not significantly predict transition rates to a first psychotic episode in UHR samples, above the predictive contribution of positive symptoms. Therefore, the question remains whether social functioning can be considered a risk factor for psychopathology, or whether poor social functioning should be regarded as a consequence of symptomatology. Examining this association on a day to day basis for individuals separately (without averaging across groups), could reveal how this association forms in real life and could potentially aid in explaining previous inconsistent findings.

The family environment signifies an important context for social functioning during childhood and adolescence (DuBois, Eitel, & Felner, 1994). If impaired social functioning is indeed a subclinical marker for psychosis which is evident before the first psychotic episode (Cornblatt et al., 2012; Davidson et al., 1999), it is likely that this impairment is also evident within the family context. This may be expressed as lower family functioning, parental stress or more negative parenting styles. So far, the family environment has been studied extensively in more acute and chronic phases of psychotic disorders, finding that it is an important factor for the prognosis of the disorder once an individual has had their first psychotic episode (Butzlaff & Hooley, 1998; Carter, Schulsinger, Parnas, Cannon, & Mednick, 2002; Goldstein, 1985; Hooley, 2007; Tienari et al., 2004; Tienari & Wahlberg, 2008; Wahlberg et al., 2004). Important family environment factors that have been examined in the psychosis literature are expressed emotion (Butzlaff & Hooley, 1998; Hooley, 2007), the family rearing environment (Carter et al., 2002; Tienari et al., 2004) and family communication (Goldstein, 1985; Wahlberg et al., 2004). Prospective studies have shown that family members high in expressed emotion (over-involvement, high criticism, and negative affective style) greatly increase the risk of relapse in their relative diagnosed with a psychotic disorder (Butzlaff & Hooley, 1998; Weintraub et al., 2017). There is some evidence that the family environment can have both a protective and aggravating effect on psychotic symptoms from earlier phases of illness, before the first psychotic episode in the UHR phase (O'Brien et al., 2006; 2009). In addition, specifically expressed emotion appears predictive of the first psychotic episode in ultra-high risk samples (Haidl et al., 2018). Whether impairments in family functioning are predictive of the development and course of psychotic experiences (rather than a reaction towards clinical symptoms) in adolescents is unknown. The next step would be to examine whether family functioning in childhood can predict psychotic experiences in adolescence, before the emergence of the UHR phase or mental illness.

The Link between Social Cognition and Social Functioning

Given that impaired social functioning is prominent both in early and more chronic phases of psychosis (Addington et al., 2008; Ballon et al., 2007) and that it can have a significant negative impact on quality of life and outcome in psychosis (such as relapse and unemployment; Perlick, Stastny, Mattis, & Teresi, 1992), it is important to examine what underlies this impairment in social functioning. On the basis of a review of the literature, Couture and colleagues (2006) concluded

that the majority of studies concur that there is a clear and consistent association between lower social cognition and impaired social functioning in clinical samples with a psychotic disorder. Whether social cognition is associated with social functioning in adolescence is an unanswered question.

If social cognition is a trait impairment that is evident from early childhood, it is possible that a child with poorer social cognition will have more difficulty communicating and bonding with parents and peers, and thus functioning at home and at school. In turn, impaired social cognition and impaired social functioning in early adolescence, may render the individual vulnerable for developing a psychotic disorder. There is some evidence for this hypothesis in studies with clinical samples. To specify, ToM abilities are positively associated with community functioning (Pijnenborg et al., 2009), interpersonal skills (Pinkham & Penn, 2006), and role functioning (Ventura et al., 2015), and negatively associated with socially deviant behavior (Brüne, 2005a) in psychotic disorders. Also in the (earlier) UHR phase, a positive association between ToM ability and global functioning was found (Cotter et al., 2015). In addition, facial emotion identification was found to be associated with lower general social functioning, work functioning, independent living and interpersonal skills in psychotic disorders (Couture, Penn, & Roberts, 2006; Irani, Seligman, Kamath, Kohler, & Gur, 2012; Kee, Green, Mintz, & Brekke, 2003; Pinkham & Penn, 2006; Williams et al., 2009). It appears that both ToM ability and facial emotion identification abilities have a clear association with social functioning in adult clinical samples with a psychotic disorder and in samples with individuals who meet the UHR for psychosis criteria. The next step is to examine whether social functioning potentially mediates the relationship between social cognition and psychotic experiences in adolescence (see figure 1).

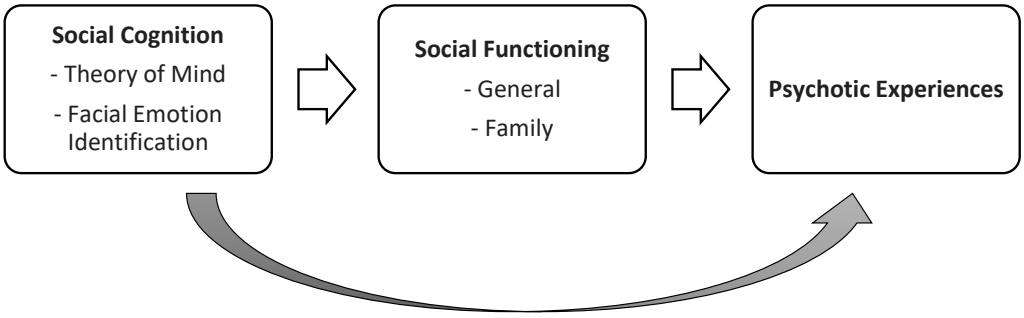


Figure 1. *Potential mediation model: social cognition (predictor), social functioning (mediator) and psychotic experiences (outcome) in adolescence.*

1.5 Religiosity

In this thesis, religiosity is termed a 'social' predictor, as religion is emotionally and connectively shared among others with the same religious beliefs (Beckford, 2004). Religion can therefore be considered as a social construct, through which we identify ourselves and connect with others and a 'supernatural' creator or God (Beckford, 2004). Religiosity is associated with a higher prevalence of psychotic experiences (Mohr, Brandt, Borras, Gilliéron, & Huguelet, 2006), both in adults in the general population (Aird, Scott, McGrath, Najman, & Al Mamun, 2010) and in clinical samples (Getz, Fleck, & Strakowski, 2001; Suhail & Ghauri, 2010). Explanations for these associations have ranged from religiosity representing a coping factor for psychopathology (Mohr et al., 2006), to religiosity representing an aggravator of psychopathology (Aird et al., 2010). The consensus is that religiosity can have both positive and negative influences on psychopathology in adults (Koenig, 2009; Pargament, Smith, Koenig, & Perez, 1998). How religiosity may influence psychotic experiences in adolescence is unclear.

The association between religiosity and mental health in adolescence has been examined for depressive episodes, behavioral problems, substance abuse and anxiety (12–21-year-olds, see review by Dew et al., 2008), but not for psychotic experiences in adolescence. Most studies conclude that religion has a positive impact on mental health of children and adolescents (see reviews by Dew et al., 2008 and Wong, Rew, & Slaikeu, 2010) though some report negative associations between mental health and religion (Exline, Yali, & Sanderson, 2000) whilst others report no associations (Evans et al., 1996). Given that religiosity can represent a source of comfort and hope for individuals with psychotic symptoms (as was demonstrated by Cottam et al., 2011 and Rosmarin, Bigda-Peyton, Öngur, Pargament, & Björgvinsson, 2013), adolescents with psychotic experiences may be more likely to report religious activity as a method of coping and social belonging. On the other hand, given that religiosity can also be experienced negatively for individuals with psychotic disorders (see a review by Koenig et al., 2009), it could also aggravate psychotic experiences and be associated with an increased severity of symptoms in adolescence.

1.6 Dissertation Content and Main Research Questions

This thesis starts out with the investigation of a self-report assessment tool of auditory vocal hallucinations (AVH), followed by four studies that examine social predictors (social cognition, social functioning and religiosity) of psychotic experiences in adolescence:

In Chapter 2 the aim is to examine whether AVH can be reliably assessed in a self-report manner. As such, the Auditory Vocal Hallucination Rating Scale (Questionnaire) (AVHRS-Q) will be investigated in two patient samples with AVH. The internal reliability and (convergent and divergent) validity of the AVHRS-Q will be addressed.

In **Chapter 3** and **Chapter 4** it is assessed whether social cognition is predictive of psychotic experiences in adolescence, and whether this might be mediated by social functioning. As such, these chapters describe whether the 'trait vulnerability' of social cognition for psychosis can already be detected in early adolescence. Specifically, the aim of **Chapter 3** is to study whether ToM ability in early adolescence (age 12-13 years) can predict psychotic experiences 6 years later (age 18-19 years). In addition, it is explored whether social functioning mediates this relationship. The aim of **Chapter 4** is to examine whether facial emotion identification and family functioning (age 11) can predict psychotic experiences five years later (age 16 years). It is also explored whether family functioning mediates the relationship between facial emotion identification and psychotic experiences. As such, **Chapter 4** will additionally address the question whether the family environment is predictive of psychotic experiences in adolescence.

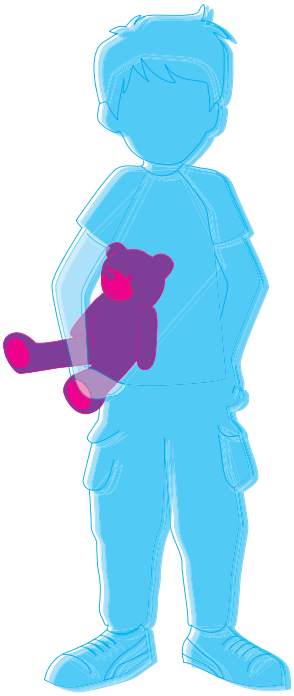
Chapter 5 describes the idiographic associations between social functioning and psychotic experiences in daily life in four individuals at ultra-high risk (UHR) for psychosis. Using a time-series analysis, the aim of this chapter is to study the directionality, temporal dynamics and statistically causal effects of the association between social functioning and psychotic experiences for each individual separately. The question is whether this association is heterogeneous amongst participants, thus providing some insight into previous inconsistent findings regarding the role of social functioning in psychosis.

Chapter 6 depicts whether religiosity is associated with psychotic experiences (specifically AVH) in adolescence. In a sample of young adolescents of 12-13 years, the associations between AVH, delusions and religiosity are explored. This may shed light on the role of religiosity in psychotic experiences in adolescence and whether these may be viewed as a protective or risk factor.

In **Chapter 7** the aims and findings outlined in each chapter will be summarized and integrated. This chapter will also be dedicated to the critical and strong points of the research, and the clinical relevance of the findings. This chapter will finish with future perspectives and concluding remarks of the research presented in this thesis.

The Development, Validity and Reliability of the Auditory Vocal Hallucination Rating Scale Questionnaire (AVHRS-Q)

CHAPTER 2



Steenhuis, L. A., Pijnenborg, G. H. M., van der Willige, G., Visser, E., Nauta, M. H., Aleman, A. & Bartels-Velthuis, A. A. (2019)

The Development, validity and reliability of the Auditory Vocal Hallucination Rating Scale self-report questionnaire (AVHRS-Q)

Social Psychiatry and Psychiatric Epidemiology
https://doi.org/10.1007/s00127-019-01692-z

Abstract

Purpose

The Auditory Vocal Hallucination Rating Scale Questionnaire (AVHRS-Q) is a short self-report measure assessing several characteristics of auditory vocal hallucinations (AVH) that was derived from a validated clinical interview (The Auditory Vocal Hallucination Rating Scale; AVHRS). This study investigated the internal reliability, convergent validity and divergent validity of the AVHRS-Q using two clinical samples.

Methods

In sample I, 32 psychiatric patients with AVH were recruited from an academic hospital service and assessed with the AVHRS and the AVHRS-Q. Data for sample II was retrospectively retrieved from a pseudonymised Routine Outcome Monitoring (ROM) database collected in the context of mental healthcare at the same academic hospital service. Data from 82 psychiatric patients with AVH were retrieved, who completed the AVHRS-Q, and measures of psychological distress (the Outcome Questionnaire; OQ-45, and the Symptom Checklist; SCL-90) and quality of life (the Manchester Short Assessment of Quality of Life; MANSA).

Results

The AVHRS-Q showed good internal consistency in both samples. Severity scores of the AVHRS-Q were strongly correlated to the severity scores of the AVHRS ($r = .90$, $p<0.01$). The AVHRS-Q and AVHRS did not differ in the identification of mild and severe voice-hearers ($X2 (1, N = 32) = 15.71$). AVHRS-Q severity scores had moderate correlations with measures of psychological distress (OQ-45, $r = .43$, $p<0.01$; SCL-90, $r = .50$, $p<0.05$) and quality of life (MANSA, $r = -.22$,$p<0.01$).

Conclusions

The AVHRS-Q demonstrated good reliability, convergent validity and divergent validity, suggesting it can be applied in both clinical and research settings for a quick and reliable assessment of AVH.

2.1 Introduction

Auditory vocal hallucinations (AVH) are prevalent in children, adolescents and adults, both in clinical settings and in the general population (Bartels-Velthuis, et al., 2011; de Leede-Smith & Barkus, 2013; Kelleher et al., 2012; Linscott & van Os, 2013). AVH are common in psychotic illnesses and other mental disorders such as depression, bipolar -, dissociative -, and substance use disorders (Larøi et al., 2012). AVH severity may be predictive of (amongst others) social problems (Bartels-Velthuis et al., 2010; Frederick & Killeen, 1998), suicidal ideation (Kelleher et al., 2014) or substance abuse (Spencer, Castle, & Michie, 2002) and a reliable assessment of AVH is therefore very important. Given that voice-hearing is an internal experience which cannot be directly observed or measured, investigating AVH relies on the report of individual experiences. The most reliable manner to do this is by using structured interviews and self-report instruments.

In 2012, Bartels-Velthuis and colleagues validated the AVHRS, a structured interview to gain insight into the characteristics of voices (Bartels-Velthuis, van de Willige, Jenner, & Wiersma, 2012) and from which a severity measure of voice-hearing can be derived. The AVHRS distinguishes itself from other measures for AVH, as besides the qualitative characteristics and severity of AVH, it also assesses the form and content of voices (in contrast to the BAVQ-R; Chadwick, Lees, & Birchwood, 2000) and the number of voices (in contrast to the PSYRATS; Haddock, McCarron, Tarrier, & Faragher, 1999) (see the validation paper by Bartels-Velthuis, van de Willige, Jenner, & Wiersma, 2012 for a more elaborate description). Given that there has been a shift from interview measures to self-report measures of AVH (Ratcliff et al., 2011), a questionnaire version of the AVHRS was warranted and has now been developed. Indeed, self-report measures have the benefit of being inexpensive and time-efficient and do not require training of assessors. This is especially useful when quick or frequent assessment of AVH is required. For example, in clinical practice this may be necessary for routine outcome monitoring (ROM) or for clinical intakes. Self-report measures may also be useful for research on clinical therapies, to examine to what extent or at which time-point, the occurrence, characteristics and severity of AVH are changing.

A number of self-report measures for AVH are available (Ratcliff et al., 2011). These questionnaires are usually tailored to measure a specific aspect of AVH, for example beliefs about AVH (e.g. BAVQ-R; Chadwick et al., 2000), interpretations and attitudes towards AVH (e.g. VPD; Birchwood, Meaden, Trower, Gilbert, & Plaistow, 2000), coping with AVH (RAHQ; Mann & Pakenham, 2006), and mindfulness of AVH (SMVQ; Paul Chadwick, Barnbrook, & Newman-Taylor, 2007). There are some questionnaires on AVH that have a wider focus and are also quite brief (13 items, Hamilton Program for Schizophrenia Voices Questionnaire (HPSVQ); Van Lieshout & Goldberg, 2007; 10 items, The Delusion and Voices Self-Assessment (DV-SA); Pinto, Gigantesco, Morosini, & La Pia, 2007). However, these questionnaires do not incorporate items on the form of address (1st, 2nd or 3rd person), the location of voices, separate or simultaneous voices, severity of negative content, or whether the voices make them anxious. The DV-SA specifically does not enquire about the duration or loudness of voices, or whether negative voices are present. Overall,

compared to previous measures the AVHRS-Q ensures a comprehensive assessment of AVH, encompassing multiple qualitative aspects of AVH (e.g. negative voices, distress, interference with thinking and daily functioning) in a set of 17 items.

The aim of this study is to validate a self-report version of the Auditory Vocal Hallucination Rating Scale (AVHRS; Bartels-Velthuis, van de Willige, Jenner, & Wiersma, 2012; Jenner & van de Willige, 2002), called the AVHRS-Q(uestionnaire). In this validation study, the internal consistency, convergent validity and divergent validity of the AVHRS-Q will be examined. It is expected that the AVHRS-Q will correlate highly with the interview version (AVHRS; Bartels-Velthuis, van de Willige, Jenner, & Wiersma, 2012), demonstrating good convergent validity. As greater severity of AVH is related to both increased psychological distress and a lower quality of life (de Jesus et al., 2011), it is expected that the severity measure of the AVHRS-Q will correlate with measures of psychological distress (the Outcome Questionnaire, OQ-45; Lambert et al., 1996 and the Symptom Checklist, SCL-90; (Derogatis, Rickels, & Rock, 1976) and quality of life (the Manchester Short Assessment of Quality of Life, MANSA; Priebe, Huxley, Knight, & Evans, 1999). However, given that the AVHRS-Q specifically measures AVH characteristics and severity and not general psychological distress or quality of life, the correlations between these measures are expected to be no more than moderate, indicative of divergent validity.

2.2 Methods

Participants and Procedures

For the current study data of two clinical samples (for demographics see table 1) were used. Inclusion criteria consisted of receiving treatment for AVH, being between 18-65 years old, and having a good command of the Dutch language. Exclusion criteria consisted of having an organic brain disorder. Approval for the study with Sample I was obtained from the Medical Ethics Committee of the University of Medical Center Groningen (ref: M13.146159). The sample size for sample I was calculated a priori by a statistician. It was determined that at least 31 people were required to obtain a two-sided confidence interval with minimum length of 0.1 for a correlation of 0.9. Thirty-two patients with AVH were recruited for Sample I at the Voices Outpatient Department of the University Medical Center Groningen (the Netherlands). Patients were approached by their therapist or by the research coordinator of the Voices Outpatient Department, and received both verbal and written information about the research study, including an informed consent form. Upon providing written informed consent, participants were contacted by the researcher and completed the AVHRS-Q and were interviewed with the AVHRS. During the study, participants alternately started with the self-report version of the AVHRS (AVHRS-Q) or with the interview (AVHRS) in order to rule out selective memory biases for one of the measurements. Data collection for Sample I took place from February 2011 until December 2015.

Data for sample II was retrospectively retrieved from a pseudonymised Routine Outcome Monitoring (ROM) database collected in the context of mental healthcare at the Voices Outpatient Department of the University Medical Center Groningen (the Netherlands). All patients who are referred for treatment to the University Medical Center Groningen take part in ROM assessments and are informed that their data may be used for research purposes whilst having the option to opt-out. Given that this data was collected in the context of treatment and not for research purposes - therefore not requiring the patient to change their behavior for the research - no additional ethical approval for the data is required according to Dutch legislation. Sample II consisted of 82 patients with AVH receiving treatment at the Voices Outpatient Department of the University Medical Center Groningen (the Netherlands). At the start of their treatment, they completed the AVHRS-Q, the MANSA and either the OQ-45 (n = 62) and/or the SCL-90 (n = 24) (depending on which instrument their therapist selected) through the ROM service. The requested ROM data was collected from October 2011 until February 2017. As the current study took part in the Netherlands, all questionnaires and interviews were completed in Dutch language.

Table 1. *Demographics of sample I and II*

	Sample I (n=32)	**Sample II (n=82)**
Female (n, %)	18 (56)	44 (54)
Age (*M*, SD)	38 (11)	39 (12)
Duration of AVH in years (*M*, SD)	12 (11)	N.A.
Psychotic disorder[$] (n, %)	29 (91)	60 (73)
Also diagnosed with a comorbid disorder	8 (28)	24 (40)
Other disorder (e.g. mood disorder, personality disorder, anxiety disorder)	3 (9)	22 (27)
Also diagnosed with a comorbid disorder	0 (0)	8 (36)

Note.
AVH; Auditory Vocal Hallucinations. N.A.; Not Available.
[$] Psychotic disorders in these samples consisted of Schizophrenia, Schizoaffective disorder and Psychotic disorder not otherwise specified.

Measures

The AVHRS and Development of the AVHRS-Q. The AVHRS (Bartels-Velthuis, van de Willige, Jenner, & Wiersma, 2012; Jenner & van de Willige, 2002) is a structured 16-item interview, administered by an experienced therapist to evaluate AVH during a period of one month. The AVH are rated on 4- and 5-point scales in terms of frequency, duration, loudness, negative content, distress, anxiety, control, and interference with thinking and daily life. Scores range from 0 (not applicable) to 3 or 4 (most applicable).

The AVHRS-Q (Van de Willige et al., 2010) is the self-report version of the AVHRS, designed to be administered without the presence of an interviewer, therapist or researcher. A full version of the AVHRS-Q can be downloaded at http://www.rgoc.nl/#home/downloads (see table 2 for a summary of the items). The AVHRS-Q has 17 items, 15 of which are assessed with a 4- and 5-point scale and two on a 10-point scale. For the 4- and 5- point scales, scores range from 0 (not applicable) to 3 or 4 (most applicable). For the 10-point scales, scores ranging from 1 (not at all/never) to 10 (extremely/always). The items of the AVHRS-Q were based on the items of the AVHRS, but adapted somewhat for the purpose of self-report administration. The first version of the AVHRS-Q was evaluated by ten patients with AVH. Based on their feedback and input from experts in the field, ten questions from the original AVHRS were refined and one item was expanded into two items. To specify, some items of the AVHRS-Q received more answer options in comparison to the interview version (see Table 2, items 3, 4, 7, 8, 10, and 15). For example, the item assessing duration of voices has four answer options in the interview version (seconds, minutes, one hour, and several hours to continuously) in comparison to five options in the questionnaire (see table 2, item 4). Moreover, the wording of some items were reformulated to be more simple and unambiguous (see table 2, item 12 and 13). Additionally, the AVH frequency and intensity of suffering in the AVHRS-Q (see table 2, item 16 and 17) are rated on a ten-point scale instead of a five-point scale in the AVHRS, as to be more sensitive to subtle changes over time.

In accordance with the AVHRS and previous publications with this measure (Bartels-Velthuis, et al., 2011; Bartels-Velthuis et al., 2016; Bartels-Velthuis, van de Willige, Jenner, Wiersma, et al., 2012; Bartels-Velthuis et al., 2010), a severity index can be composed from the individual items of the AVHRS-Q. Items regarding the number of voices, localization of voices and hypnagogic/hypnopompic hallucinations are not included in the severity index (see previous publications; (Bartels-Velthuis, van de Willige, Jenner, & Wiersma, 2012). The answers to individual items are recoded to '0' (none to mild consequences) or '1' (considerable to severe consequences). Subsequently, a sum score of the recoded items is created, ranging from 0 to 14. In addition to the AVHRS-Q providing an overall severity measure of AVH, the individual items can also be used to yield specific information on characteristics of AVH (see table 2).

Table 2. Summary of individual items of the AVHRS-Q and construction of the severity index

AVHRS-Q Item	Options	Severity Index (point awarded per option)
1. Number of voices	Always one voice	-
	More than one voice	
2. Separately or simultaneously	Speaking separately	0
	Speaking separately and together	1
	Always speaking together	1
3. Frequency	Not more than once a month	0
	Once a week	0
	Once a day	0
	Once an hour	1
	More than once an hour	1
4. Duration	A few seconds	0
	A few minutes	0
	A few minutes to about 15 minutes	0
	15 minutes to about an hour	1
	One hour to almost constantly	1
5. Hypnagogic and/or hypnopompic voices	Voices when falling asleep	-
	Voices when waking up	
	Voices both when falling asleep and when waking up	
	Voices occur at all times	

6.	Location	Inside my head	-
		Inside my head and from the outside environment	
		From the outside environment (in the immediate vicinity)	
		From the outside environment, further away	
7.	Form of address	The voices say what I am thinking (1st person)	0
		The voices speak to me (2nd person)	0
		The voices speak to me and about me (2nd and 3rd person)	1
		The voices speak about me (3rd person)	1
8.	Loudness	Soft whisper or murmuring	0
		More quiet than own voice	0
		As loud as own voice	0
		Louder than own voice	1
		Much louder than own voice (yelling, shouting, screaming)	1
9.	Positive or Negative Content	Always positive	0
		Mostly positive but occasionally negative	0
		Mostly neutral or equally positive and negative	0
		Mostly negative	1
		Always negative	1

10. Severity of Negative Content	Negative, but not about myself or others	0
	Negative about what I or others do	0
	Negative about how I am or how others are	1
	Threatening commands or orders	1
11. Anxiety	Never	0
	Occasionally	0
	Half of the time	1
	Most of the time	1
	All of the time	1
12. Interference with Daily Functioning	Never	0
	Occasionally	0
	Half of the time	0
	Most of the time	1
	All of the time	1
13. Interference with thoughts	Never	0
	Occasionally	0
	Half of the time	1
	Most of the time	1
	All of the time	1

14. Control	Always	0
	Most of the time	0
	Half of the time	0
	Less than half of the time	1
	Never	1
15. Attribution of Origin	The voices only concern myself	0
	The voices mostly concern myself	0
	Equally concern myself as outside influences	1
	Mostly caused by outside influences	1
	Fully caused by outside influences	1
16. Frequency of distress (1= never, 10=always)	0-6	0
	7-10	1
17. Intensity of distress (1= not at all, 10=extremely)	0-6	0
	7-10	1
Total:		Minimum=0 Maximum=14

Note.
AVHRS-Q; Auditory Vocal Hallucination Rating Scale-Questionnaire.
This table represents a summary of the questionnaire and is not suitable for assessments.
The full questionnaire can be downloaded at: http://www.rgoc.nl/#home/downloads.

Quality of Life. Quality of life was assessed with the Manchester Short Assessment of Quality of Life (MANSA; Priebe et al., 1999, a 16-item self-report measure consisting of four objective items and 12 subjective items (satisfaction with life, accommodation, housemates (or living alone), leisure activities, physical health, psychological health, personal safety, friendships, relationship to family, (absence of) romantic relationship, sex life and financial circumstances). Items are rated on a 7-point Likert scale, ranging from 1 'could not be worse' to 7 'could not be better'. The summary score consists of the mean of the twelve subjective items, with higher scores indicating better quality of life.

Psychological Distress. Psychological distress was assessed with either the Outcome Questionnaire (OQ-45) or the Symptom Checklist (SCL-90). Given that the data was collected through ROM assessments for treatment purposes, the therapist was free to choose which assessment measure was administered to the patient on the basis of the therapists own preference and familiarity with the instrument. For the current study, both questionnaires were selected, as using only one would have led to a loss of information. The OQ-45 (Lambert et al., 1996) is a 45-item self-report measure assessing clinical outcome in terms of symptom distress, interpersonal relations and social role performance. For this study, the symptom distress subscale was used consisting of 25 items. Each item is scored on a 5-point rating scale, from never '0' to almost always '4'. A sum score denoting psychological distress was computed by adding up all items, with high scores pointing to more distress. The SCL-90 (Derogatis et al., 1976) is a 90-item self-report measure, assessing a variety of psychopathology. Each item is rated on a 5-point rating scale, from '1' (never) to '5' (almost always). The items are clustered in nine dimensions: Somatization, Obsessive-Compulsive, Interpersonal Sensitivity, Depression, Anxiety, Hostility, Phobic Anxiety, Paranoid Ideation and Psychoticism. A sum score denoting psychological distress was computed by adding up all items. Higher scores suggest a lower level of psychological and physical functioning.

Statistical Analyses

Analyses were carried out using SPSS version 23 for Windows (IBM, 2014). In sample I, two severity groups were created separately for both the AVHRS and AVHRS-Q: those with 'severe AVH' (scoring in the highest quartile of the severity index, i.e. in our study 10 or higher) and with 'mild AVH' (scoring 0-9).

In order to examine convergent validity in sample I, Pearson correlation coefficients between total severity scores and separate items of the AVHRS and AVHRS-Q were computed. A paired samples t-test was performed to examine the differences in the mean AVH severity score between the AVHRS-Q and the AVHRS. An exact McNemar's test was used to examine the distribution of mild and severe AVH groups between the two measures. Internal consistency of both instruments was determined by calculating Cronbach's alpha (Cronbach, 1951).

In order to examine divergent validity in sample II, Pearson correlation coefficients between the total severity score of the AVHRS-Q and total score of the MANSA, the SCL-90 and OQ-45, were computed.

2.3 Results

Descriptives

In Sample I, the AVHRS-Q took an average of 5.8 minutes to be completed (SD: 2.72, range: 2-15), whereas the AVHRS took an average of 14.3 minutes to administer (SD: 4.69, range: 8.3-27).

Internal Consistency

In sample I, Cronbach's alpha of both the AVHRS-Q and the AVHRS was 0.87. In sample II, Cronbach's alpha of the AVHRS-Q amounted to 0.78.

Convergent Validity

The average severity scores and severity groups for both the AVHRS-Q and AVHRS for sample I are given in table 3. The severity measure of the AVHRS and AVHRS-Q were highly correlated. This correlation did not differ for participants who started with the AVHRS ($r = .90$, $p<0.01$) and those who started with the AVHRS-Q ($r = .89$, $p<0.01$). The Pearson correlation coefficients between individual corresponding items of both measures ranged from 0.44 (moderate) to 0.82 (high), with a median of .72 (see table 4). The mean AVH severity measure and the distribution of severity groups did nog differ significantly between the AVHRS-Q and the AVHRS.

Table 3. *Average AVH severity score and distribution of severity groups for the AVHRS-Q and AVHRS (Sample I, N = 32)*

		AVHRS-Q	AVHRS	Pearson's *r*	Paired Samples t-test	Exact Mc Nemar's test
AVH Severity score (*M, SD*)		6.91 (3.15)	7.38 (3.66)	*r*=.90**	*t*(31)=-.55	
AVH Severity Group (*N, %)*	Mild	24 (75%)	22 (68.8%)			X^2 (1, N = 32) = 15.71
	Severe	8 (25%)	10 (31.3%)			

Note:
*p<0.05, **p<0.01
AVH; Auditory Vocal Hallucinations, AVHRS-Q; Auditory Vocal Hallucination Rating Scale-Questionnaire, AVHRS; Auditory Vocal Hallucination Rating Scale.

Table 4. *Correlations between Individual items of the AVHRS-Q and AVHRS*

AVHRS-Q Item	Pearson correlation with corresponding item on AVHRS
1. Number of voices	.86**
2. Separately or simultaneously	.84**
3. Frequency	.73**
4. Duration	.70**
5. Hypnagogic and/or hypnopompic voices[$]	
6. Location	.71**
7. Form of address	.56**
8. Loudness	.78**
9. Positive or Negative Content	.85**
10. Severity of Negative Content	.57**
11. Anxiety	.74**
12. Interference with Daily Functioning	.46**
13. Interference with thoughts	.52**
14. Control	.82**
15. Attribution of Origin	.84**
16. Frequency of distress	.44*
17. Intensity of distress	.70**

Note.
**p<0.05, **p<0.01*
AVHRS-Q; Auditory Vocal Hallucination Rating Scale-Questionnaire, AVHRS; Auditory Vocal Hallucination Scale, $could not be computed as all participants consistently reported option 4 'at all times of the day'.

Divergent Validity

Descriptives of sample II are given in table 5. In sample II, the AVHRS-Q severity score was moderately correlated with the psychological distress (OQ-45 and SCL-90) and the quality of life (MANSA) scores. AVH severity was not significantly different between those who did and did not complete the OQ-45 ($t(80) = .46$, $p>0.05$) and SCL-90 ($t(80) = -.48$, $p>0.05$)

Table 5. *Comparison of average AVH severity scores (AVHRS-Q) with measures of Quality of Life (MANSA) and Psychological Distress (OQ-45 and SCL-90) (Sample II)*

	M (SD)	MANSA (n=82)	SCL-90 (n=24)	OQ-45 (n=62)
AVH Severity score (Pearson's *r)*	7.66 (2.69)	-0.22**	.50*	.43**

Note.
**p<0.05, **p<0.01*
AVH; Auditory Vocal Hallucinations, AVHRS-Q; Auditory Vocal Hallucination Rating Scale-Questionnaire, AVHRS; Auditory Vocal Hallucination Rating Scale, MANSA; the Manchester Short Assessment of Quality of Life, SCL-90; Symptom Checklist, OQ-45; Outcome Questionnaire.

2.4 Discussion

The current study shows that the Auditory Vocal Hallucination Rating Scale Questionnaire (AVHRS-Q) (Van de Willige et al., 2010) is a reliable and valid self-report instrument to assess the characteristics and severity of auditory vocal hallucinations (AVH). The findings demonstrate that the AVHRS-Q converges highly with the interview measure on which it was based (the AVHRS; Bartels-Velthuis, van de Willige, Jenner, & Wiersma, 2012). In addition, the AVHRS-Q is shown to be a specific measure of AVH and not a general measure of psychological distress (OQ-45; Lambert et al., 1996) and SCL-90; Derogatis et al., 1976) or quality of life (MANSA; Priebe et al., 1999). Internal reliability of the AVHRS-Q was found to be good and comparable to the reliability of the AVHRS.

The AVHRS-Q severity scores correlate highly with the corresponding severity scores of the interview version (AVHRS). In addition, the AVHRS-Q and the AVHRS did not identify a different proportion of patients as having 'mild' or 'severe' AVH. This implies that the already validated and widely used AVHRS (Bartels-Velthuis, Blijd-Hoogewys, & van Os, 2011; Bartels-Velthuis, van de Willige, Jenner, & Wiersma, 2012; Maijer, Palmen, & Sommer, 2017; Steenhuis et al., 2016) can now also be used in the self-report version for the same (research or clinical) purposes. Importantly, the individual items of the AVHRS-Q also corresponded highly to the items of the AVHRS, with

the exception of four moderately correlating items. Given that the AVHRS-Q had to be short and not (too) cognitively demanding, explanations and examples of items were not included in the self-report questionnaire. This may have resulted in discrepancies (and therefore moderate correlations) between four specific items of the AVHRS-Q and AVHRS. It is therefore important to keep in mind that whilst the AVHRS-Q can be used to reliably achieve a quick overall severity measure of AVH (similar to the interview-based AVHRS), one should be cautious when only interpreting single items of the AVHRS-Q (specifically the items on form of address, severity of negative content, interference with daily functioning, interference with thoughts). Moreover, the AVHRS-Q severity scores were only moderately related to measures of quality of life and psychological distress, which indicates that the AVHRS-Q specifically measures characteristics and severity of AVH. Overall, the AVHRS-Q demonstrates good convergent and divergent validity in this study.

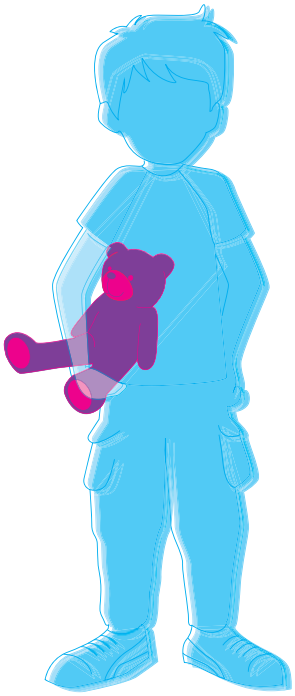
An important feature of the AVHRS-Q is that it takes only six minutes on average to complete. This makes it exceptionally suitable for quick and frequent assessments, for instance in research on the effectiveness of treatments or for frequent monitoring in a clinical context, such as Routine Outcome Monitoring (ROM) assessments. Currently, ROM assessments for patients with psychosis often consist of more global outcome measures for positive symptoms, such as the Positive and Negative Syndrome Scale (PANSS) (Egger et al., 2016; Kay, Fiszbein, & Opler, 1987; Tasma et al., 2016). One PANSS item assesses the severity of hallucinations, but does not inquire about, for example, whether the patient has separate or simultaneous voices, whether the patient has negative or positive voices, or even how AVH interfere with daily functioning. All these aspects may be potentially relevant for treatment or in signifying the nature of distress. Currently, the AVHRS-Q is being utilized in the ROM protocol of the Voices Outpatient Department of the University Medical Center Groningen.

The current study has some limitations. First, in contrast to the HPSVQ (Van Lieshout & Goldberg, 2007) and the DV-SA (Pinto et al., 2007), the AVHRS-Q does not enquire about the social circumstances of AVH, or whether the command hallucinations are obeyed. However, the AVHRS-Q does enquire about the interference with daily functioning and the presence of command hallucinations, which can be further explored during therapy. Second, similar to the validation study on the AVHRS interview (Bartels-Velthuis, van de Willige, Jenner, & Wiersma, 2012) we did not measure sensitivity to change. As all patients were in therapy for their voices and the AVHRS-Q is incorporated in treatment, retest data would likely be confounded with therapeutic effects. In order to assess this in an unbiased manner, a control group not receiving treatment for their AVH should have been included. However, given that all patients had quite severe AVH for a substantial amount of years, this was deemed unethical. Third, the current study recruited two reasonably chronic patient samples, implying the current findings may be less generalizable to healthier populations. However, the AVHRS-Q has already been administered in a general population sample, supporting its use in less chronic samples (Bartels-Velthuis et al., 2016).

One important strength of the current study is that the AVHRS-Q is based on an existing measure, the AVHRS, which has already been deemed to have good psychometric properties (Bartels-Velthuis, van de Willige, Jenner, & Wiersma, 2012) and was used in multiple research projects (Bartels-Velthuis, et al., 2011; Bartels-Velthuis, van de Willige, Jenner, Wiersma, et al., 2012). A second strength is that the AVHRS-Q was evaluated by patients with AVH and that their feedback was used to improve the AVHRS-Q into its current form.

To conclude, the AVHRS-Q is a quick self-report version of a validated interview on auditory hallucinations already in use, the AVHRS. The current study demonstrates that the AVHRS-Q has good internal consistency, convergent validity and divergent validity. The AVHRS-Q can very well be applied in both clinical practice and research, where it is required to assess AVH in a quick and reliable manner.

Childhood Theory of Mind Does Not Predict Psychotic Experiences and Social Functioning in a General Population Sample of Adolescents



CHAPTER 3

Steenhuis, L. A., Pijnenborg, G.H.M., van Os, J., Aleman, A., Nauta, M.H. & Bartels-Velthuis, A. A. (2019)

Childhood theory of mind does not predict psychotic experiences and social functioning in a general population sample of adolescents

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Abstract

Aims

Theory of Mind (ToM) is often impaired in early and chronic phases of psychosis and it is often suggested that poor ToM is a trait vulnerability for psychosis. The aim of this study was to examine in an adolescent sample whether childhood ToM abilities can predict psychotic experiences over a period of six years and whether this is mediated by social functioning. To examine whether ToM is a specific predictor for psychosis, symptoms of depression and anxiety were also examined.

Materials and Methods

A baseline case-control sample (T0: age 7-8 years) with and without auditory vocal hallucinations (AVH) in the general population was assessed after five years (T1: age 12-13 years) on ToM ability (ToM Storybook Frank), and after eleven years (T2: age 18-19 years) on psychotic experiences (Community Assessment of Psychic Experiences; CAPE), depressive and anxiety symptoms (Depression Anxiety and Stress Scale; DASS-21), and social functioning (Groningen Questionnaire on Social Behaviour; GVSG-45). Analyses were conducted on a subsample of 157 adolescents aged 18-19 years (T2) who had data available on ToM ability at T1.

Results

ToM at T1 was not predictive of psychotic experiences after six years (from age 12-13 to age 18-19) and social functioning was also not a mediator. ToM was not associated with psychopathology in general (depressive and anxiety symptoms) over six years (from age 12-13 to age 18-19).

Conclusions

The current study found no evidence for a longitudinal association between ToM ability and psychotic experiences, social functioning, and symptoms of depression and anxiety, in adolescence.

3.1 Introduction

Psychotic disorders often co-occur with deficits in social cognition (Penn et al., 2008), which are found to contribute considerably to the impairment in social functioning associated with these disorders (Brüne, 2005a). Theory of Mind (ToM) is a domain of social cognition (Premack & Woodruff, 1978), and is defined as the ability to represent human mental states or making inferences about someone else's intentions or emotions (Couture et al., 2006). Since Frith (1992) (Frith, 1992) hypothesized that ToM deficits may account for the development of (amongst others) delusions and third-person auditory hallucinations, ToM has been investigated extensively in psychotic disorders (Bora, Yucel, & Pantelis, 2009). There is evidence that ToM is impaired in multiple phases of psychosis, such as in acute psychosis (Bora & Pantelis, 2013), first episode psychosis (Andrew Thompson et al., 2012), individuals at risk for psychosis (Green et al., 2012; Piskulic et al., 2016) and first-degree relatives of individuals with schizophrenia (Bora & Pantelis, 2013). In addition, ToM ability often does not necessarily fluctuate with symptoms (Piskulic et al., 2016), suggesting that a deficit in ToM may be a trait marker for psychosis rather than a state-related factor (Bora & Pantelis, 2013; Lee et al., 2015), though not all evidence is consistent with this (Pinkham, 2014). It is important to investigate when the ToM vulnerability for psychosis can be 'detected' as to examine, as a first step, whether and when early interventions may be possible and effective. Given that psychotic experiences are prevalent in samples of youth (Bartels-Velthuis et al., 2010; Kelleher et al., 2012; Maijer, et al., 2017), and may signify a precursor to psychotic disorders (Fisher et al., 2013), it is fruitful to examine whether poorer ToM is associated with psychotic experiences during adolescence.

Currently, there is limited research on ToM ability in association to psychotic experiences in childhood and adolescence. A previous cross-sectional study found that ToM ability at age 12 years was not associated to psychotic experiences (Sullivan et al., 2013), whilst another study found that ToM ability at age five years was prospectively associated with definite psychotic symptoms at age 12 years (Polanczyk et al., 2010). Whether ToM ability in childhood is associated with psychotic experiences at later ages (18-19 years) in adolescence is a relevant and understudied question. Given that psychotic experiences occurring late in adolescence are more predictive of mental health problems in adulthood (Jardri et al., 2014), answering this question might shed more light on the role of ToM in the development of psychosis.

Impaired social cognition, including ToM ability, has been hypothesized to be the underlying driving source of impaired social functioning in psychotic disorders (Couture et al., 2006). So far, the link between ToM and social functioning has been explored mostly in studies with clinical samples. Findings imply that impaired ToM is strongly associated with several domains of social functioning (Couture, Granholm, & Fish, 2011). ToM abilities in patients diagnosed with schizophrenia were positively associated with social functioning (Pijnenborg et al., 2009) and interpersonal skills (Pinkham & Penn, 2006), and negatively associated with socially deviant behaviour (Brüne, 2005a). In addition, a positive association between ToM and global functioning in an ultra-high-risk (UHR) sample was found (Cotter et al., 2015), indicating the association

may already be present before the first psychotic episode. Despite the emerging evidence that ToM may be a trait marker for psychosis (Green et al., 2012), it remains unclear whether a ToM vulnerability for psychosis can be detected during childhood and adolescence. If a ToM deficit represents a vulnerability for psychosis, individuals who later go on to develop schizophrenia may already have poor ToM ability during childhood (Brüne, 2005b), which could influence their early social interactions with parents and peers. In line with this idea, one might expect children and adolescents with poorer ToM ability to function worse as well, rendering them more liable for psychotic experiences.

Social functioning, which includes the ability to meet societal defined roles such as being a homemaker, worker, student, spouse, family member or friend (Mueser & Tarrier, 1998), is commonly impaired in psychotic disorders (Couture et al., 2006; Velthorst et al., 2016). It has been suggested that a decline in social functioning may be a subclinical marker for psychosis (Cornblatt et al., 2012; Davidson et al., 1999). Support for this view comes from studies comparing social functioning of individuals at UHR for psychosis and of first-episode psychosis patients with healthy controls (Addington et al., 2008; Ballon et al., 2007), demonstrating that social functioning appears to be impaired in early phases of psychotic disorders and even before the first psychotic episode. In fact, a decline in social functioning has been shown to be predictive of a transition to the first psychotic episode in UHR individuals (Mason et al., 2004). We hypothesize that an individual with increasing social functioning difficulties may have less positive social experiences and may develop less social skills, potentially rendering an individual more vulnerable to the development of paranoia (Green & Phillips, 2004) and delusional ideation (Garety, Kuipers, Fowler, Freeman, & Bebbington, 2001). The question remains when this deficit in social functioning first becomes apparent. There is already some evidence that an increase in peer problems and a decline in prosocial behavior precede psychotic experiences during early adolescence (Sullivan et al., 2013). As deficits in ToM may predict impaired social functioning (Couture et al., 2006) and poor social functioning may predict enhanced psychotic experiences (Addington et al., 2008), it is warranted to examine whether social functioning potentially (and partially) mediates the relationship between ToM and psychotic experiences.

The current study aims to examine in a general population sample of adolescents whether poorer ToM ability at age 12-13 years is associated with the frequency of psychotic experiences at age 18-19 years. In addition, it will be examined whether social functioning mediates the relationship between ToM ability and the frequency of psychotic experiences. Given that recent studies have noted that risk factors may not be specific for psychosis but predictive of psychopathology in general (Fusar-Poli, Yung, McGorry, & van Os, 2014), we will also examine the association between ToM ability and symptoms of depression and anxiety.

3.2 Materials and Methods

Participants

A baseline case-control sample (n = 694) was recruited eleven years earlier from a population-based survey on AVH in almost all 7- and 8-year-old children (n = 3870) in the province of Groningen, the Netherlands (Bartels-Velthuis et al., 2010). Data from this case-control sample was available at age 7/8 years (T0, (Bartels-Velthuis et al., 2010)), age 12/13 years (T1, (Bartels-Velthuis, et al., 2011) and age 18/19 years (T2, (Bartels-Velthuis et al., 2016)) (Fig 1). For a full description of the samples at baseline and each follow-up study, see previous publications on this sample (Bartels- Velthuis, et al., 2011; Bartels-Velthuis et al., 2016; Bartels-Velthuis et al., 2010). Given that not all participants in the second follow up assessment had completed the ToM task at the first follow up assessment, the current study was conducted on a subsample of 157 adolescents aged 18 - 19 years (54% of the 293 participants at T2).

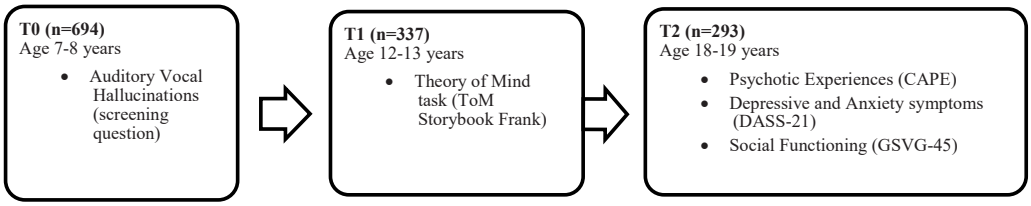


Figure 1. Measurement waves (T0, T1, & T2) of the case-control study.
Sample size, age and measures are displayed at each measurement wave. Note that the total sample size studied (n=157) in the current study differs from the N's displayed in the table. CAPE, Community Assessment of Psychotic Experiences; ToM, Theory of Mind; DASS-21, Depression Anxiety and Stress Scale; GVSG-45, Groningen Questionnaire on Social Behaviour.

Measures

Theory of Mind (ToM). ToM was assessed at T1 using the ToM Storybook Frank for children aged 10- 14 years (Bartels-Velthuis, et al., 2011; Blijd-Hoogewys & Bartels-Velthuis, 2007). A validation study in a Danish child and adolescent sample demonstrated that the Storybook Frank task has good psychometric properties (Clemmensen et al., 2016). The task consists of multiple domains: first- and second-order false beliefs, deception paradigm, white lie, irony, double bluff and faux-pas. Children are presented with 20 pictures whilst the storybook is read aloud by the interviewer. Children answer 22 'test' and 10 'justification questions'. The 'test' answers are coded with a 1 (correct understanding of the situation) or 0 (incorrect understanding of the situation), yielding a range of 0 to 22. The 'justification' questions (e.g. Why does Frederik think that?) are coded on an ordinal scale ranging from 0 to 1, 2 or 3 (different predefined scale for each tested situation), with a total score ranging from 0 to 25. Scores for each question 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 'test' and 'justification' scores are summed together in a total score (maximum score = 47, higher scores indicate better ability). ToM ability at T1 was dichotomized into relatively low (children scoring equal to, or below the mean of 27.19, SD = 4.87) or high ability (children scoring above the mean) in this sample (in line with earlier publications on the T1 sample; (Bartels-Velthuis, et al., 2011)). The low ToM ability group had a mean ToM ability of 23.57 (SD = 2.89) and the high ToM ability group had a mean ToM ability of 31.54 (SD = 2.74).

Psychotic Experiences. Psychotic experiences were assessed at T2 with the Community Assessment of Psychic Experiences (CAPE; (Konings, Bak, Hanssen, Van Os, & Krabbendam, 2006; Peters, Day, Mckenna, & Orbach, 1999), a 42-item self-report questionnaire to assess the frequency and distress of psychotic experiences in general population samples. The CAPE has previously shown to have good discriminant and convergent validity and good psychometric properties (Hanssen et al., 2003; Konings et al., 2006). In this study, psychotic experiences were assessed using the frequency of positive psychotic experiences (20 items, rated on a four-point scale: 0 'never', 1 'sometimes', 2 'often' and 3 'nearly always'). A total score was created by adding up the 20 frequency items, with a higher score indicating a higher frequency of psychotic experiences.

Given that at least part of the adolescents in this sample were previously selected on auditory vocal hallucinations (AVH) in childhood (Bartels-Velthuis et al., 2010), the analyses in this study will control for this. At baseline (T0), the presence of AVH was assessed with the following question: 'In the past five years, have you heard one or more voices that only you and no one else could hear?' ('yes/no'; Bartels-Velthuis et al., 2010).

Depressive and Anxiety symptoms. Symptoms of depression and anxiety were assessed at age 18-19 (T2) with the Depression Anxiety and Stress Scale (DASS-21; Lovibond & Lovibond, 1995; Dutch translation: de Beurs, van Dyck, Marquenie, Lange, & Blonk, 2001). The DASS is a 21-item self- report measure of symptoms of anxiety, depression and stress, which has shown to have good reliability and validity in a sample of non-clinical adolescents (Hall, 2010). Each of the three subscales of the DASS-21 contains seven items. A 4-point severity scale measures the extent to which each state has been experienced over the past week. For comparability with the 42-item DASS, scores were doubled in accordance with the makers of the scale (Lovibond & Lovibond, 1995). A sum score was created for the depression subscale and for the anxiety subscale, by adding the scores of all seven items of each subscale, with a higher score indicating a higher severity of symptoms of depression and anxiety.

Social Functioning. Social functioning was assessed at T2 with the 45-item self-report questionnaire Groningen Questionnaire on Social Behaviour (in Dutch: de Groningse Vragenlijst over Sociaal Gedrag (GVSG-45; de Jong & van der Lubbe, 2001). Ten items enquiring about the participants' functioning as a parent were omitted as our sample consisted of adolescents. The remaining 35 items assess functioning with parents ("Lately I have avoided (one of my) parents"), a significant other ("I discussed my personal issues with my boyfriend/girlfriend"), friends/acquaintances ("I enjoyed spending time with my friends/acquaintances"), education

("I was late at school (in the classroom/lecture hall)"), vocation ("I was able to finish my work on time"), household chores ("I found it difficult to adhere to the daily rules of the household"), and hobbies ("I was able to relax in my free time"), each consisting of five items with a 4-point scale ('never', 'sometimes', 'often', 'always'). A mean score of positive responses (scores 1-4) was created for the overall social functioning scale (max 35 items), with a higher mean score indicating better social functioning. The social functioning items showed good internal consistency in this study (Cronbach's alpha: 0.83). Due to a technical error, three questions pertaining to the 'hobby' domain were not administered, resulting in a total of 32 questions for the overall social functioning scale.

Education. Education was assessed at T2 in a separate sociodemographic questionnaire (see previous publication, Bartels-Velthuis et al., 2016) assessing the level of current education. Answer options included (1) primary education, (2) lower vocational education, (3) higher general secondary education (4) pre-university secondary education, (5) intermediate vocational education, (6) higher vocational education and (7) university education. In line with a previous study using this sample (Bartels-Velthuis et al., 2016), education level was dichotomized into low levels of education (options 1, 2, 3, and 5) and high levels of education (options 4, 6 and 7).

Procedures

This study was approved by the Medical Ethical Committee of the University Medical Center Groningen, the Netherlands (ABR number NL42619.042.12). For the first follow-up, written informed consent was obtained from both parents and children. For the child, the explanation of the study was adapted to their developmental level. The ToM task was administered by trained interviewers at the child's home in absence of the parent(s) (Bartels-Velthuis, et al., 2011). For the second follow-up, participating adolescents sent a written informed consent form by post. After receipt of the consent, an email was sent with a link to online questionnaires, assessing demographic information, psychotic experiences, psychopathology and social functioning (Bartels-Velthuis et al., 2016). For all assessment points, participants had (and were informed of) the right to withdraw from the study at any point.

Statistical analyses

Statistical analyses were conducted using SPSS 23 (IBM, 2014). Significance tests were two-tailed with alpha set at 0.05. In order to explore whether social functioning at T2 mediates the possible association between ToM at T1 and the frequency of psychotic experiences at T2, the computational procedure PROCESS (Hayes, 2012) was utilized. A 'simple mediation model' was computed, which includes the direct effect of ToM ability (T1) on the frequency of psychotic experiences (T2), with the indirect effect operating through social functioning (T2). The direct and indirect effects of ToM (T1) on the frequency of psychotic experiences (T2) were obtained from three linear regression models (Baron & Kenny, 1986; Preacher & Hayes, 2004). The Sobel test was used as an inferential method to test hypotheses about the indirect effect (Preacher & Hayes, 2008). In addition, bias-corrected bootstrap confidence intervals using 10,000 bootstrap samples are computed. Mediation is established if the confidence interval for an indirect effect does not include zero.

To examine specificity of ToM ability for psychotic experiences, two longitudinal linear regression models were computed to examine the predictive ability of ToM at T1 on symptoms of depression and anxiety at T2. All analyses in this study were adjusted for AVH at baseline (T0), and educational level at T2 (dichotomized into low and high).

3.4 Results

The 157 participants at T2 had a mean age of 18.9 years (SD = 0.35, range 18.2–19.9). At baseline, 76 reported AVH and 81 did not (X^2 = 0.05, p = 0.83). Significantly more females participated in this study (57.3%) compared to males (X^2 = 12.2, p = 0.001), but there were no significant differences between males and females in ToM ability at T1 (males: M = 26.60, SD = 5.01, females: M = 27.18, SD = 5.01, t(155)=.519, p=.605) and in the frequency of psychotic experiences at T2 (males: M = 4.12, SD = 4.42, females: M = 4.44, SD = 4.36, t(149) = .630, p = .530).

Data on ToM ability at T1 in addition to CAPE scores at T2 was available for 52% of the 293 T2 participants (n=151; 6 individuals did not complete the CAPE). Missing values on T1 ToM ability were a result of: (i) the ToM task at T1 being optional and some participants choose not to partake in the assessment (N = 78 of T1 adolescents (23%), resulting in n = 54 of T2 adolescents (18%), and (ii) 88 participants (30%) in the current follow-up not partaking at T1 but having the option to re-enter the study at T2. Participants at T2 who had data of the ToM task at T1 did not significantly differ in the frequency of psychotic experiences or average social functioning, from participants at T2 who did not take part at the ToM task at T1.

Data on baseline AVH, ToM ability at T1, and depressive and anxiety symptoms, the frequency of psychotic experiences and average social functioning at T2, can be found in Table 1.

Table 1. Data on baseline AVH, ToM ability at T1, and depressive and anxiety symptoms, frequency of psychotic experiences and social functioning at T2 (n = 157)

		Frequency (%) or Mean (S.D.)	Range
(T0)			
AVH	No	81 (51.6)	
	Yes	76 (48.4)	
(T1)			
ToM ability	Low	82 (52.2)	
	High	75 (47.8)	
(T2)			
Educational level	Low	66 (49.6)	
	High	67 (50.4)	
Frequency of Psychotic Experiences		4.09 (4.59)	0-60
Depressive symptoms		6.11 (6.32)	0-42
Anxiety symptoms		4.75 (4.59)	0-42
Social Functioning		3.31 (.33)	1-4

Note.
AVH, Auditory Vocal Hallucinations; ToM, Theory of Mind.

Mediation Analysis: ToM ability at T1 predicting the Frequency of Psychotic Experiences at T2, as Mediated by Social Functioning at T2

See Table 2 for a summary of the mediation analysis computed with PROCESS. It can be seen that the direct effect of ToM ability at T1 on psychotic experiences at T2 was not significant. The 95% confidence interval of the bootstrap results revealed that the indirect effect of ToM ability at T1 on psychotic experiences at T2 through social functioning at T2 included zero, indicating that social functioning was not a mediator of the association between ToM ability and psychotic experiences. This was supported by the Sobel test, demonstrating no mediation in the model ($z = 1.00$, $p=0.32$). Notably, the combination of all variables in the model (ToM ability, social functioning and control variables) explained a significant proportion of variance in the frequency of psychotic symptoms ($R^2 = 16\%$, $F(3, 147) = 5.99$, $p = 0.001$).

Table 2. *Mediation analysis: ToM ability at T1 predicting the frequency of psychotic experiences at T2, as mediated by social functioning at T2 (n=151)*

	B	B S.E.	t	p-value	95% C.I. Lower	Upper
Effect of ToM T1 on social functioning T2	-.07	.06	-1.06	.29	-.19	.06
Effect of social functioning T2 on psychotic experiences T2	-3.91	.96	-4.08	.00	-5.81	-2.01
Effect of ToM T1 on psychotic experiences T2	1.14	.66	1.72	.09	-.17	2.45
Bootstrap result for indirect effect of ToM T1 on psychotic experiences T2 through social functioning T2	0.26	0.30			-.14	1.09
R^2 = 16%						
Sobel test: z = 1.00, p=0.32						

Note.
All analyses are corrected for voice hearing at baseline and educational level at T2.
ToM, Theory of Mind; T1, first follow-up at age 12-13 years; T2, second follow-up at age 18-19 years.

Specificity of ToM for Psychosis: the Longitudinal Relationship between ToM ability at T1 and Symptoms of Depression and Anxiety at T2

See Table 3 for a summary of the two regression models. ToM ability at T1 was not significantly associated with symptoms of depression or anxiety at T2. The variance of symptoms of depression and anxiety that was explained by the model, was small and insignificant (depression: R^2 = 3%, F(3, 147) = 1.41, p = 0.24, anxiety: R^2 = 3%, F(3, 147) = 1.46, p= 0.23).

Table 3. *Longitudinal Linear Multiple Regression models to predict depressive and anxiety symptoms at T2, with ToM ability at T1 (N=151)*

	Depression							Anxiety						
						95% C.I.							95% C.I.	
	B	SE B	β	t	p	Lower	Upper	B	SE B	β	t	p	Lower	Upper
Constant	3.63	2.32		1.57	.12	-.95	8.22	5.23	1.70		3.08	.00	1.86	8.60
Education	-.64	1.16	-.05	-.56	.58	-2.94	1.65	-1.26	.85	-.13	-1.47	.14	-2.94	.44
AVH (T0)	1.17	1.14	.09	1.03	.31	-1.08	3.42	1.08	.84	.11	1.30	.20	-.57	2.74
ToM ability T1	2.04	1.16	.16	1.75	.08	-.27	4.34	.78	.86	.08	.91	.37	-.92	2.47
R^2 of model	3%							3%						

Note.
ToM, Theory of Mind; T2, second follow-up at age 18-19 years; T1, first follow-up at age 12-13 years; AVH, Auditory Vocal Hallucinations; T0, baseline at age 7-8 years.

Post-hoc Exploration: 10% of Individuals with Lowest Scores on ToM Ability at T1

To investigate whether a specific subsample with the lowest ToM abilities are at risk for psychotic experiences, we conducted a post-hoc exploration. The group with the 10% lowest scores (mean ToM T1 ability: 20 or lower) were compared with the rest of the group (top 90% of ToM T1 scores) on psychotic experiences at T2. A Mann Whitney U test showed no significant difference between the group of 10% lowest scores (Mdn = 2) and the remaining scorers on the ToM task at T1 (Mdn = 3), on the frequency of psychotic experiences at T2 (U = 1346, p = .11). It was also examined whether there were differences between the group with the lowest 10% of scores (Mdn = 3.47) and the group of remaining scorers on the ToM task at T1 (Mdn = 3.31), on social functioning at T2. No significant differences were found (U = 800, p = .10).

Post-hoc Exploration: Continuous Measure of ToM ability at T1

To investigate whether the dichotomization of ToM ability at T1 was responsible for the lack of an association between ToM ability at T1 and the frequency of psychotic experiences at T2, a post-hoc exploration was conducted using the sum score of ToM ability at T1. See table 4 for a summary of the regression model. The continuous measure of ToM ability at T1 was also not significantly associated with the frequency of psychotic experiences at T2.

Table 4. *Longitudinal Linear Multiple Regression model to predict the frequency of psychotic experiences at T2, with a continuous measure of ToM ability at T1 (N = 151)*

	Frequency of psychotic experiences						
						95% C.I.	
	B	**SE B**	**β**	**t**	**p**	**Lower**	**Upper**
Constant	2.81	1.96		1.44	.15	-1.07	6.69
Education	-1.37	.70	-.18	-1.96	.05	-2.75	.02
AVH (T0)	-.07	.68	-.01	-.10	.92	-1.41	1.28
Sum score of ToM ability T1	.11	.07	.15	1.69	.10	-.02	.25
R^2 of model	4%						

Note.
ToM, Theory of Mind; T2, second follow-up at age 18-19 years; T1, first follow-up at age 12-13 years; AVH, Auditory Vocal Hallucinations; T0, baseline at age 7-8 years.

3.5 Discussion

In line with the idea that poor ToM ability may represent a vulnerability for developing psychosis (Bora & Pantelis, 2013; Lee et al., 2015), the current study examined in a general population sample of adolescents whether poorer ToM ability at age 12-13 years was associated with the frequency of psychotic experiences at age 18-19 years. In addition, it was examined whether social functioning at age 18-19 years mediates this relationship. Contrary to our expectations, we did not find evidence that poorer ToM ability in childhood was longitudinally associated to increased psychotic experiences in adolescence over a period of six years. This was confirmed in a post-hoc exploration when examining the bottom 10% of scorers on the ToM task, again establishing no evidence for increased psychotic experiences. Social functioning was therefore not identified as a mediator between ToM ability and psychotic experiences. Similarly, ToM ability did not predict symptoms of anxiety or depression over six years' time. The findings imply that in the current adolescent general population sample, ToM ability was not a vulnerability factor for psychotic experiences, social functioning, or for depression and anxiety.

Given that the literature is quite consistent in the hypothesis that ToM ability might represent a vulnerability factor for the development of psychosis (Bora & Pantelis, 2013; Green et al., 2012; Lee et al., 2015), we were surprised not to find an association between early ToM ability at age 12-13 years and the frequency of psychotic experiences at age 18-19 years. On the basis of our findings, we speculate that the group of poorer scorers on the ToM task (those scoring equal to, or below the mean; roughly half of the sample) may not be a proxy of an at 'risk' or 'vulnerability' group, and therefore is not impaired enough to detect differences in psychotic experiences. In our post-hoc exploration we selected 10% of the lowest scorers on the ToM task, which we considered to have impaired levels of ToM ability (similar to ToM scores in a high functioning autism spectrum disorder group; 40). However, this impaired sub-group did not report a higher frequency of psychotic experiences in comparison to adolescents who performed higher on the ToM task. Our findings are supported by a recent study (Mollon, David, Zammit, Lewis, & Reichenberg, 2018) indicating that an increasing developmental (verbal and non-verbal) cognitive deficit between infancy and adulthood is only present for individuals who develop a psychotic disorder, with only weak evidence for individuals with psychotic experiences. As most adolescents in this sample will not develop a psychotic disorder (prevalence in general population samples 1%, (van Os et al., 2001); prevalence for adolescents with psychotic experiences 7.5%, (Linscott & van Os, 2013)), it may be difficult to detect a ToM vulnerability for psychosis in this adolescent sample. Larger samples with a longitudinal design may yield more power to examine the development of the ToM vulnerability for psychosis during childhood and adolescence. In addition, including a later follow-up assessment including clinical diagnostic information could verify our speculations that perhaps only those adolescents who go on to develop a psychotic disorder will have demonstrated early signs of a ToM vulnerability in adolescence.

It is important to emphasize that that the current findings are based on a general population sample of adolescents with mild psychotic experiences. Although the current sample was recruited as a case-control cohort from the general population on auditory vocal hallucinations 11 years earlier, most adolescents no longer heard voices at age 18-19 years (only 15; Bartels-Velthuis et al., 2016) and were therefore considered to meet similar levels of psychotic experiences as in a random sample from the general population. Indeed, the average number of psychotic experiences in the current sample was lower than an UHR of psychosis sample (Mossaheb et al., 2012; our sample: 1.2, vs. UHR sample: 1.6 - 1.9) and therefore cannot be viewed as meeting clinical levels. Moreover, although psychotic experiences have the ability to predict psychotic disorders (Linscott & van Os, 2013), the majority of psychotic experiences disappear over time (Bartels-Velthuis et al., 2016; Kelleher et al., 2012). Therefore, perhaps this sample was not suitable to detect a ToM vulnerability for psychotic experiences. When comparing our findings to earlier studies, it has previously been found that ToM ability of children at age 12 was not associated with psychotic experiences cross- sectionally (Sullivan et al., 2013). On the other hand, ToM ability at age five years has been found to be predictive of definite (more clinical) psychotic symptoms at age 12 years (Polanczyk et al., 2010). This is supportive of the idea that ToM ability may not be related to psychotic experiences in adolescence more broadly, but only to clinical psychotic symptoms or disorders.

In our study, ToM ability at age 12-13 years was not associated to social functioning at age 18-19 years, and social functioning was not a mediator between ToM ability and the frequency of psychotic experiences. When examining adolescents who scored in the bottom 10% of the sample on ToM ability at T1, there was no evidence for poorer social functioning in comparison to adolescents who scored higher on the ToM task. We therefore found no evidence that ToM ability was longitudinally associated with social functioning in this general population sample of adolescents. In clinical samples it is often found that ToM is an important predictor for several domains of social functioning (e.g. Couture et al., 2011). However, a study on a young UHR sample found that although ToM deficits were present, they were not associated with social functioning with parents (specifically experiences of the caregiving relationship; Tomlinson, Onwumere, & Kuipers, 2014). Similarly, a recent study found that ToM was not predictive of social functioning in individuals with recent-onset psychosis (Simons et al., 2016). We speculate that ToM ability only affects social functioning when ToM is below a certain threshold, one that is only reached during more acute phases of psychosis (Pijnenborg et al., 2009). Above this threshold, an individual may be able to compensate poorer ToM ability with other factors (e.g. cognitive abilities, motivational strategies or personality) in order to retain effective social functioning.

The current study has some limitations. First, the current sample was a sub-sample of a larger sample, of whom not all participants took part in the previous ToM task. We therefore have an opportunistic sample that may be biased as we only studied the adolescents who were willing and able to participate in a ToM task. However, when comparing adolescents who did and did not participate in the ToM task on psychotic experiences and social functioning, we did not find any significant differences. Second, it is possible that some participants were or had been in care for

mental health problems, as their health care consumption was not assessed at the time. However, this was purposely done in order to avoid pathologizing auditory hallucinations. Third, perhaps an association between ToM ability and the frequency of psychotic experiences would become evident when changing the threshold of 10% to an even lower level (e.g. 5% lowest scorers). However, larger sample sizes are required to have enough power to detect such differences. In addition, one could speculate that the dichotomization of ToM ability was responsible for a loss in data and therefore the null-findings in this study. However, when checking our analysis using continuous measures in the post-hoc exploration, the same (null-) result was found. Fourth, the ToM task has been validated in a Danish sample and in a shorter form (Clemmensen et al., 2016), thus we cannot confirm that the psychometric properties will be identical in the current sample. Fifth, the utilized sub-sample consisted of significantly more females than males. Given that gender differences exist in how psychosis develops (Abel, Drake, & Goldstein, 2010), future research should aim to include equal numbers of males and females in their study. Last, in contrast to the first assessments (at T0 and T1) in this sample, assessments at T2 took place in a self-report form in an online format. This may limit comparability of findings to previous assessment points in the current longitudinal sample and other studies examining similar questions. Nevertheless, we also believe there is a benefit in online and self-report assessments, as there may be a lower chance of social desirability bias and perceived stigma in the reporting of psychotic experiences.

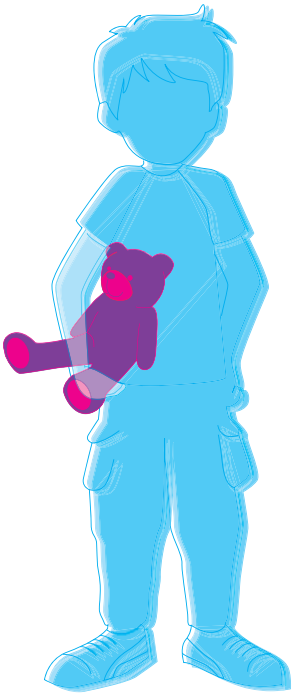
Future research should examine the same associations using different domains of social cognition, such as emotion identification, given that other social cognitive domains are also impaired in early phases of psychosis (Green et al., 2015) and are consistently associated with social functioning (Couture et al., 2006). This might be especially relevant as a review (Healey, Bartholomeusz, & Penn, 2016) demonstrated that deficits in emotion recognition were found to be consistently impaired in first episode psychosis, especially in lower level abilities (e.g. face and voice emotion recognition), whereas some domains of ToM remained intact (first-order ToM abilities). Therefore, it is possible that deficits in social cognitive domains other than ToM, such as emotion identification, are more sensitive to be picked up on at earlier stages before the first psychotic episode. So far there are only few studies which have examined whether emotion identification is prospectively associated with psychotic experiences in childhood and adolescence. One of these studies (Thompson et al., 2011) did not find an association between facial emotion identification at age 8 and psychotic experiences at age 11. Given that emotion identification, a lower-level social cognitive ability, may not be associated with psychotic experiences in childhood, it may also be unlikely that ToM ability (a higher-level social cognitive ability) is associated with psychotic experiences. To explore these speculations further, research is required to prospectively examine multiple domains of social cognition, and their inter-relations, in association to psychotic experiences in childhood and adolescence.

To conclude, although it has been suggested that a deficit in ToM may be a vulnerability marker for psychosis, the current study found no longitudinal evidence for an association between ToM ability and the reporting of psychotic experiences in adolescence. It was also demonstrated that ToM ability was unrelated to social functioning, and to symptoms of depression and anxiety

in adolescence. Based on our findings and in the context of the presented literature (Mollon et al., 2018; Polanczyk et al., 2010; Sullivan et al., 2013), we speculate that ToM deficits may only be associated with clinical psychotic symptoms or psychotic disorders, and not psychotic experiences more broadly.

The Longitudinal Association between Preadolescent Facial Emotion Identification and Family Factors, and Psychotic Experiences in Adolescence (The TRAILS Study)

CHAPTER 4



Steenhuis, L.A., Pijnenborg, G.H.M., van der Stouwe, E.C.D., Hartman, C.A., Aleman, A., Bartels-Velthuis, A.A., & Nauta, M.H.

The longitudinal association between preadolescent facial emotion identification and family factors, and psychotic experiences in adolescence (The TRAILS study)

Submitted

Abstract

Aims

An impairment in facial emotion identification could signify a vulnerability for the development of psychosis, which may be mediated by family functioning. The current study examines whether facial emotion identification and family factors at preadolescence (age 11) predict psychotic experiences five years later during adolescence (age 16).

Materials and Methods

Data was obtained from the epidemiological cohort TRAILS (TRacking Adolescents' Individual Lives Survey; N=2059). At preadolescence, a facial emotion identification test and three questionnaires to assess family functioning, perceived parenting styles and parenting stress, were administered. At adolescence, a questionnaire on psychotic experiences was administered. Data were analyzed using multiple linear regression models

Results

Facial emotion identification at preadolescence was not associated with psychotic experiences at adolescence, and the mediational role of family functioning was not further explored. Increased overprotective parenting at preadolescence was associated with a higher frequency of psychotic experiences and delusions at adolescence, while the other family factors (parenting stress, family functioning, and rejective and warm parenting) at preadolescence were not significantly associated with psychotic experiences at adolescence.

Conclusions

While clinical symptoms in early and chronic psychosis have been associated with facial emotion identification deficits, this association was not present in the current adolescent cohort. Conversely, perceived overprotective parenting was prospectively associated with psychotic experiences, possibly either due to a vulnerability for psychosis, a natural reaction towards a vulnerable child, or a shared genetic liability in both parents and adolescents. Future research may examine the mechanism behind the role of overprotective parenting on psychotic experiences during adolescence.

4.1 Introduction

Psychotic disorders have often been associated with social cognitive impairments (Penn et al., 2008). One of the domains of social cognition is facial emotion identification (Green & Horan, 2010), which refers to the ability to accurately identify emotional expressions from another person's face. The 'basic' set of emotions (anger, disgust, fear, sadness, surprise and happiness) as proposed by Ekman and colleagues are each characterized by a distinct facial expression, physiology and evolutionary purpose (Ekman, 1999). The ability to accurately recognize these emotions is crucial in facilitating emotional connections and communicating effectively with others. In psychotic disorders, recognition of positive expressions (happiness) is preserved and recognition of negative expressions (anger, fear, sadness and disgust) is impaired (Bediou et al., 2005; Combs et al., 2006; Janssens et al., 2012; Kohler et al., 2003), although some studies report impairments for both positive and negative emotions (Barkl et al., 2014).

Recent studies demonstrated that impairments in the identification of facial affect are not only found in chronic psychosis (Savla, Vella, Armstrong, Penn, & Twamley, 2013), but also in first episode psychosis (Romero-Ferreiro et al., 2016), the ultra-high risk phase of psychosis (Piskulic et al., 2016; Van Donkersgoed et al., 2015), and in siblings (Fett & Maat, 2013). The evidence suggests that early impairment may show up for specific emotions, rather than as a general deficit (Romero-Ferreiro et al., 2016). Deficits in facial emotion identification have been hypothesized to play a role in the development of psychotic experiences. To specify, facial emotion identification deficits could give rise to paranoia (an inability to understand others could feed negative interpretations; Combs et al., 2006; Pinkham, Brensinger, Kohler, Gur, & Gur, 2011), delusions (an inability to correct faulty interpretations can cause and support delusional ideation; Bentall et al., 1994), and potentially hallucinations (continuous erroneous interpretation of social situations and others can lead to social stress, hyper vigilance, and hallucinatory experiences; Kohler, Bilker, Hagendoorn, Gur, & Gur, 2000) (see also a review by Couture, Penn, & Roberts, 2006). Overall, an impairment in facial emotion identification may be a trait vulnerability for psychosis, rather than a consequence of the disorder. It is important to investigate at which point facial emotion identification impairments can be 'detected' as to examine when early interventions may be possible and effective. Given that psychotic experiences are prevalent in samples of youth (Bartels-Velthuis, Jenner, van de Willige, van Os, & Wiersma, 2010; Kelleher et al., 2012; Maijer, Begemann, Palmen, Leucht, & Sommer, 2017), and may signify a precursor to psychotic disorders (Fisher et al., 2013), it is fruitful to examine whether reduced facial emotion identification in preadolescence is associated with psychotic experiences during adolescence.

Social cognitive impairments have been found to contribute to diminished social functioning in psychotic disorders (Brüne, 2005a). If deficits in facial emotion identification are present from childhood, this may already lead to problems in the development of socially competent behaviors and interactions. Given the importance of the family environment for children and adolescents' functioning (DuBois et al., 1994), it is possible that children with poor facial emotion identification skills have more difficulty functioning in the family environment as

well. For example, children with poor facial emotion identification skills may perceive parenting as more negative, either due to inaccurate identification of emotions of their parents, or due to an accurate perception of more rejective or overprotective parenting as a reaction to their lower social cognitive abilities. Therefore, if facial emotion identification abilities predict psychotic experiences throughout adolescence, it may be especially interesting to explore the possibility whether this association might be mediated, at least partially, by family functioning.

The family context has gained much attention in psychosis studies, mostly in more acute and chronic phases of illness (Butzlaff & Hooley, 1998; Carter et al., 2002; Goldstein, 1985; Hooley, 2007; Tienari et al., 2004; Tienari & Wahlberg, 2008; Wahlberg et al., 2004). There is a strong indication that family factors such as expressed emotion (Butzlaff & Hooley, 1998; Hooley, 2007), the family rearing environment (Carter et al., 2002; Tienari et al., 2004) and family communication (Goldstein, 1985; Wahlberg et al., 2004) are important predictors of the prognosis of psychosis once an individual has transitioned to a first psychotic episode. Several prospective studies have found that patients with family members who are high in expressed emotion (over-involvement, high criticism, and negative affective style) are at an increased risk of relapse in schizophrenia over a period of nine to twelve months (Butzlaff & Hooley, 1998; Weintraub, Hall, Carbonella, Weisman de Mamani, & Hooley, 2017). Also in children with elevated mental health problems, parental styles (such as communication deviance , expressed emotion or affective style), significantly predicted schizophrenia spectrum disorders in adulthood in a 15 year prospective longitudinal study (Fisher et al., 2013), although it is important to note that this sample was limited in its size (n=50). In the ultra-high risk phase of psychosis (before the first psychotic episode), family functioning (a positive warm environment) has been shown to be protective (Brien et al., 2006, 2009), both for reducing negative and disorganized symptoms, and improvement in functioning over a period of three (Brien et al., 2006) and six (Brien et al., 2009) months. Whether the family environment and parenting styles are predictive of the development and course of psychotic experiences (rather than a reaction towards clinical symptoms) during adolescence, remains understudied so far.

The aim of the current study is to examine whether a) facial emotion identification and b) family factors at preadolescence (age 11) predict psychotic experiences five years later during adolescence (age 16). We expect that both lower facial emotion identification abilities and more negative family functioning in preadolescence will predict a higher frequency of psychotic experiences at adolescence. If confirmed that facial emotion identification abilities are associated with psychotic experiences in adolescence, we will further explore whether functioning in the family environment (at least partially) mediates the relationship between facial emotion identification and psychotic experiences. Given that childhood mental health is associated with parenting behaviors at preadolescence (Marsman, Oldehinkel, Ormel, & Buitelaar, 2013) and is likely to predict adult mental health, the current study will control for pre-adolescent mental health problems (internalizing and externalizing behaviors).

4.2 Method

Sample

Data used in the current study were collected as part of the longitudinal 'TRacking Adolescents Individual Lives Survey' (TRAILS), a prospective cohort study which aims to elucidate the etiology of mental health problems during adolescence (Oldehinkel et al., 2015; Ormel et al., 2012). The National Dutch Medical Ethical Committee approved this study and the research has been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments. Written consent was obtained from all adolescents and their parents. As done in previous studies in this cohort (Zandstra et al., 2015), we merged data from two TRAILS samples, a large population-based birth cohort (n=2230) and a smaller parallel clinic-referred cohort (n=543), in order to acquire a large sample with a wide variation in mental health. Data of the first and third data collection waves with mean ages of around 11 (T1) and 16 (T3) years were used for the current study. Participants were included if they at least completed the assessment on psychotic experiences at T3 (n=2059). Due to missing data, N varies between 1956 and 2059 in the total sample.

Full details on the sampling procedure, descriptive statistics, response rates and selective attrition have all been provided in previous studies (De Winter et al., 2005; Ormel et al., 2012). In summary, to obtain the population cohort, TRAILS approached 135 primary schools in five municipalities in the north of the Netherlands, of which 90.4% agreed to participate. After contacting eligible preadolescents and their parents, 2230 participants (76% of those that were contacted) were enrolled in the study at T1 (mean age = 11.1 years, SD = .56; 49.2% boys). Five years later, 81% of them participated at T3 (N = 1816; mean age, 16.3 years, SD = 0.7; 48% boys). The two data waves included in this study ran from March 2001 to July 2002 (T1), and from September 2005 to August 2007 (T3). The clinic-referred cohort contained preadolescents who had been referred to the Groningen University Child and Adolescent Psychiatric Outpatient Clinic at any point in their life. At T1, 543 participants (43% of those that were contacted) participated in the study (mean age = 11.1 years, SD = 0.50; 65.9 % boys). In total 416 (76.6%) of them completed measurements at T3. The data waves in the clinic-referred cohort started two years after the population cohort: from September 2004 to December 2005 (T1), and from and September 2009 to February 2011 (T3). The same design and instruments were used for both cohorts.

Measurements

Facial Emotion Identification. To assess facial emotion identification at T1, we used the Identification of Facial Expressions Task, which is part of the Amsterdam Neuropsychological Tasks program (ANT; de Sonneville, 1999). This task is a reliable and valid instrument with acceptable test-retest reliability, and construct, criterion, and discriminant validity (de Sonneville, 1999; Günther, Herpertz-Dahlmann, & Konrad, 2005; Rowbotham, Pit-ten Cate, Sonuga-Barke, & Huijbregts, 2009). Trained undergraduate psychologists assessed each participant individually. The task consists of six parts of 40 trials each, divided over 20 target and 20 non-target trails. Each part focusses on a specific emotion (happy, sad, angry, fear, surprise and disgust) and lasts five

minutes in total. Participants were instructed to press the yes-button for a target emotion and the no-button if a different emotion was displayed. For our study, we selected all emotions except surprise, as we focused explicitly on positive and negative emotions and surprise is considered as neither positive nor negative (Fontaine, Scherer, Roesch, & Ellsworth, 2007). Each emotion was examined separately, as early impairment may show up for specific emotions, rather than a general deficit (Romero-Ferreiro et al., 2016). For each emotion the error proportion (EP) and reaction time (RT) was calculated. EPs were calculated as the mean proportion of misses and false alarms, using the subsequent equation: EP = ((misses/(misses + hits)) + (false alarms/(false alarms + correct rejections)))/2. RTs were calculated by the mean RT across hits and correct rejections. EPs and RTs that were more than four standard deviations above the mean (Stevens, 2009) as well as participants performing at chance level of accuracy (50% or more errors) were considered missing (Vrijen, Hartman, & Oldehinkel, 2016). In addition, outliers in one outcome parameter were also noted missing for the other, as EP and RT may influence each other. For each emotion, standardized Z-scores were created for both the RTs and EPs. It is important to examine both the EPs and RTs of emotions, as both aspects could reveal distinct and independent associations with the development of psychotic experiences (Barkhof, de Sonneville, Meijer, & de Haan, 2015). Therefore, 10 variables of facial emotion identification were constructed: EP happy, EP sad, EP angry, EP fear, EP disgust, RT happy, RT sad, RT angry, RT fear and RT disgust.

Family Functioning. To assess family functioning at T1, a modified version of the General Functioning Scale of the McMaster Family Assessment Device (FAD; (Epstein, Baldwin, & Bishop, 1983)) was administered to the primary parent. The FAD has shown to have adequate test-retest reliability, good divergent and convergent validity, in addition to adequate sensitivity and specificity (Miller, Epstein, Bishop, & Keitner, 1985). The scale includes six dimensions of family functioning, consisting of communication, problem solving, affective responsiveness, affective involvement, roles and behavior control. The scale comprises twelve items with a 4-point scale, ranging from 1 (totally disagree) to 4 (totally agree). A sum score was computed by adding up all items (a higher score indicates lower family functioning).

Perceived Parenting Style. To assess perceived parenting style at T1, the EMBU-C (Markus, Lindhout, Boer, Hoogendijk, & Arrindell, 2003) was administered, which is the child version of the EMBU (English translation: My Memories of Upbringing; (Perris, Jacobsson, Linndström, von Knorring, & Perris, 1980)). The EMBU-C has good psychometric properties and convergent validity (Markus et al., 2003). The questionnaire contains the following three scales: Rejection (12 items), Emotional Warmth (18 items), and Overprotection (12 items). Items are assessed using a 4-point scale, ranging from 0 (no, never) to 4 (yes, almost always). Responses of fathers and mothers were highly correlated for rejection ($r = 0.68$, $p < 0.001$), emotional warmth ($r = 0.79$, $p < 0.001$) and overprotection ($r = 0.81$, $p < 0.001$), and therefore, in line with previous TRAILS papers (Bouma, Ormel, Verhulst, & Oldehinkel, 2008; Kay, Wolkenfeld, & Murrill, 1988; Marsman et al., 2013; Oldehinkel, Veenstra, Ormel, de Winter, & Verhulst, 2006), scores were combined (averaged) for both parents. If information for only one parent was present, the score for the one parent was used.

Parental Stress. To assess parental stress at T1, a short Dutch form of the Parental Stress Index (PSI; (Abidin, 1982)) was administered. The Dutch version has been found to have good psychometric properties and construct validity (Egberink, Frima, & Vermeulen, 1996). It is a 25-item questionnaire to assess the magnitude of stress in the parent-child relationship. Items are rated by the parent on a 6-point scale from 1 (disagree very much) to 6 (agree very much). The instrument contains two subscales, assessing the child's characteristics (11 items) and the parents' characteristics in the parenting context (14 items). A previous study (Janssens, Oldehinkel, & Rosmalen, 2009) conducted a factor analysis of this measure in the current TRAILS sample, and discovered that one item did not load on either the child or the parent factor (item 24: "I feel confident about the future upbringing of my child"). Therefore, this item was excluded in the TRAILS cohort. For the purpose of this study, only the parent subscale was used to obtain a measure of perceived stress for the parent.

Childhood Mental Health. To assess childhood mental health at T1, the Youth Self-Report (YSR; Achenbach, 1991) was administered. The YSR has a good test-retest reliability and discriminative validity (Achenbach, 1991). In this 112-item questionnaire, descriptions of emotions and behaviors are rated on a three-point scale (not true (0), somewhat or sometimes true (1) and very often true (2)). These items assess two broad dimensions of behavior problems: internalizing (anxious/depressed, withdrawn/depressed and somatic complaints) and externalizing (aggressive behavior and rule-breaking behavior) problems. For the current study, a total score of all problem behaviors was computed based on 105 items (in line with Achenbach & Dumenci, 2001).

Psychotic Experiences. To assess psychotic experiences at T3, the Community Assessment of Psychic Experiences (CAPE; Konings et al., 2006; Peters et al., 1999) was used. The CAPE is a self-report questionnaire with good psychometric properties, discriminative validity (Hanssen et al., 2003) and test-retest reliability (Konings et al., 2006). The positive experiences subscale has 20 items assessing the frequency and distress of positive experiences (e.g. delusions and hallucinations) separately. The frequency/distress of each item is assessed on a four-point scale ((1) never/no distress, (2) sometimes/a bit distressed, (3) often/quite distressed, and (4) nearly always/very distressed). For the current study, the frequency of positive experiences was used. Based on a factor analysis, Wigman and colleagues (2011) found five underlying dimensions of the CAPE that are differently associated with risk of future psychopathology. Their study (Wigman et al., 2011) demonstrated that hallucinations, delusions and paranoia, but not grandiosity and paranormal beliefs, were mostly associated with distress and future psychopathology. For the current study these three risk sub-domains were separately identified by calculating a sum score of delusions (8 items) and paranoia (5 items), and a categorical score of hallucinations as either absent or present (0/1). Given the low endorsement rate of hallucinations in this sample, adolescents received a 'present' score on the hallucination variable if they endorsed at least one (or more) of the three hallucination items.

Statistical Analysis

Analyses were carried out in SPSS (IBM, 2014). To examine whether the hypothesized predictors were related to the outcomes of our study, Pearson's correlations were first computed between facial emotion identification variables (RTs, EPs), psychotic experiences (total frequency, hallucinations, delusions and paranoia), and family factors (family functioning, overprotective, warm and rejective parenting, and parental stress). With the relevant associations identified, a number of multiple linear and logistic regression models were run to examine our hypotheses in a step-wise approach. All assumptions of these analyses (e.g. homoscedasticity and normality of residuals) were checked beforehand. First, psychotic experiences (age 16) were predicted by facial emotion identification variables (age 11) (linear and logistic regression models). Second, psychotic experiences (age 16) were predicted by family factors at preadolescence (age 11) (linear and logistic regression models). Third, family factors were predicted by facial emotion identification (both at age 11) (linear regression models). Findings were corrected for multiple testing with the Bonferroni-Holmes correction, thus correcting the p-value per step off, starting with the lowest p-value (Holm, 1979). All analyses were controlled for age, sex and pre-adolescent mental health problems. If our first hypothesis was met, we aimed to explore whether family functioning (age 11) mediates the relationship between the relevant facial emotion identification variable (age 11) and psychotic experiences (age 16). This was done with the computational process PROCESS (Hayes, 2012), for which a 'parallel multiple mediation model' was computed, where X (the causal variable: facial emotion perception), was modeled to influence Y (the outcome variable: psychotic experiences) directly, as well as indirectly, through multiple mediator variables (the mediators: family functioning, overprotective, warm and rejective parenting, and parental stress).

4.3 Results

Descriptives

Characteristics of the sample and assessments outcomes are given in table 1. Of all psychotic experiences, the most endorsed symptom was paranoia (89%), followed by delusions (52%) and hallucinations (15%). In the identification of facial emotions task, positive emotions were easier to recognize than negative emotions, as denoted by lower reaction times ($t(2641) = 76.32$, $p<0.01$) and lower proportion of errors ($t(2641) = 57.29$, $p<0.01$). In table 2, correlations between all variables are displayed.

Table 1. Characteristics of the sample and assessments outcomes

	N	Mean (SD)/ Frequency (%)	Range
Age	2059	16.17 (.69)	14.42-18.36
Sex (% female)	2059	1018 (49.4)	
T1			
Mental health (YSR: Total Problems)	2018	.36 (.19)	0.00-1.18
Facial Emotion Identification (IFE task)			
EP			
Happy	2030	3.31 (3.45)	0-17.50
Sad	2033	12.88 (9.41)	0-45
Angry	2020	8.34 (6.18)	0-35
Fear	2020	7.74 (6.84)	0-37.50
Disgust	2026	6.16 (5.53)	0-30
RT			
Happy	2030	880 (206)	458-1750
Sad	2033	1210 (286)	528-2449
Angry	2020	1116 (257)	581-2188
Fear	2020	1113 (280)	552-2323
Disgust	2026	1062 (250)	546-2091
Family Functioning (FAD)	1956	1.79 (.38)	1.00-4.00
Parental Stress (PSI)	1959	1.93 (.89)	1.00-5.60

		N	Mean (SD)/ Frequency (%)	Range
Parenting Behavior (EMBU-C)				
	Warm Parenting	2047	3.22 (.49)	1.17-4.00
	Rejective Parenting	2046	1.51 (.32)	1.00-3.44
	Overprotective Parenting	2046	1.86 (.37)	1.00-3.44
T3				
Psychotic Experiences (CAPE)				
	Total Frequency	2059	1.28(.23)	1.00-2.85
	Hallucinations (N, %)	2051	299 (14.6)	
	Delusions	2037	1.20(1.73)	0.00-17.00
	Paranoia	2039	2.61(1.77)	0.00-10.00

Note.
IFE, Identification of Facial Expressions Task; EP, Error Percentage (raw); RT, Reaction Time (raw); FAD, Family Assessment Device; PSI, Parental Stress Index; EMBU-C, My Memories of Upbringing; CAPE, Community Assessment of Psychic Experiences. T1, Age 11; T3, Age 16.

Table 2. *Correlations between psychotic experiences (frequency, hallucinations, delusions and paranoia), facial emotion identification (happy, sad, angry, fear and disgust) and family factors (family functioning, parental stress, warm, rejective and overprotective parenting). (N = 1956-2059)*

Questionnaire/ Task	Variables	1.	2.	3.	4.	5.	6.	7.	8.	9.	10.	11.	12.	13.	14.	15.	16.	17.	18.	19.
IFE task	1. RT Happy	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	2. RT Sad	.68**	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	3. RT Angry	.65**	.72**	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	4. RT Fear	.60**	.64**	.71**	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	5. RT Disgust	.61**	.67**	.71**	.73**	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	6. EP Happy	.74**	-.04	-.03	-.04*	-.03	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	7. EP Sad	.61**	.10**	.10**	.09**	.09**	.29**	-	-	-	-	-	-	-	-	-	-	-	-	-
	8. EP Angry	.02	-.01	.05*	.05**	.03	.29**	.43**	-	-	-	-	-	-	-	-	-	-	-	-

Questionnaire/ Task	Variables	1.	2.	3.	4.	5.	6.	7.	8.	9.	10.	11.	12.	13.	14.	15.	16.	17.	18.	19.
	9. EP Fear	.06**	.03	.04*	.17**	.07**	.23**	.36**	.43**	-	-	-	-	-	-	-	-	-	-	-
	10. EP Disgust	.01	-.03	-.02	-.01	.06**	.28**	.32**	.38**	.32**	-	-	-	-	-	-	-	-	-	-
FAD	11. Family Functioning	.02	.02	.01	.01	.03	.44*	.05*	.03	.01	.04*	-	-	-	-	-	-	-	-	-
PSI	12. Parental Stress	.04*	.04*	.03	.03	.06**	.01	.07**	.06**	.07**	.08**	.43**	-	-	-	-	-	-	-	-
EMBU-C	13. Warm Parenting	-.08**	-.06**	-.06**	-.05*	-.07**	-.03	-.09**	-.08**	-.05**	-.08**	-.15**	-.12**	-	-	-	-	-	-	-
	14. Rejective Parenting	.04*	.04	.04	.02	.06**	.00	.05*	.02	.02	.03	.12**	.22**	-.32**	-	-	-	-	-	-
	15. Overprotective Parenting	-.01	-.01	-.01	.01	.02	.01	.01	-.02	.02	-.02	.02	.09**	.19**	.45**	-	-	-	-	-
CAPE	16. Total Frequency	.04	.02	.01	.01	.03	-.01	-.05*	-.05*	-.01	-.04	.01	.06**	.03	.07**	.14**	-	-	-	-
	17. Hallucinations	.06**	.04	.05*	.03	.05*	-.03	.03	-.01	-.01	.02	.01	.04*	-.02	.04	.07**	.59**	-	-	-
	18. Delusions	.04	.03	.01	.01	.03	.03	-.01	-.01	.00	.00	.02	.05*	-.01	.05*	.11**	.80**	.48**	-	-
	19. Paranoia	.04	.01	.00	-.00	.01	-.04	.06*	-.05*	-.01	-.04	.02	.05*	.03	.09**	.13**	.75**	.28**	.43**	-

Note.

**p<0.05, **p<0.01; IFE, Identification of Facial Expressions Task; RT, Reaction Time (standardized); EP, Error Proportion (standardized); FAD, Family Assessment Device; PSI,, Parental Stress Index; EMBU-C, My Memories of Upbringing; CAPE, Community Assessment of Psychic Experiences.*

1. Associations between Facial Emotion Identification Abilities at Preadolescence (age 11) and Psychotic Experiences at Adolescence (age 16)

Facial emotion identification abilities at age 11 were not significantly associated with delusions at age 16, and thus not further examined in the regression models (see table 2). Table 3 demonstrates both linear and logistic regression models, in which frequency of psychotic experiences, hallucinations and paranoia is predicted by facial emotion identification (EPs and RTs), after adjustment for confounders. The results demonstrate that facial emotion identification abilities at age 11 were not significantly associated with psychotic experiences at age 16. In the absence of an association, mediation by family factors was not explored.

2. Associations between Family Factors at Preadolescence (age 11) and Psychotic Experiences at Adolescence (age 16)

Table 4 shows the results from four regression models (both linear and logistic) predicting psychotic experiences (frequency, hallucinations, delusions and paranoia) with family factors, after correcting for confounders. Findings demonstrate that overprotective parenting at age 11 was positively associated with both the frequency of psychotic experiences and delusions at age 16.

3. Associations between Facial Emotion Identification Abilities and Family Factors at Preadolescence (age 11)

Overprotective parenting was not significantly associated with family factors at age 11, and thus not further examined in the regression models (see table 2). Table 5 shows the results from four linear regression models, predicting family factors (family functioning, parental stress, warm and rejective parenting) by facial emotion perception (EPs and RTs), after correcting for confounders. The results demonstrate that facial emotion perception abilities were not significantly associated with family factors at age 11.

Table 3. *Results of linear and logistic regression analyses of psychotic experiences (frequency, hallucinations, delusions and paranoia) at age 16 on facial emotion identification reaction times at age 11. (n=2020-2059)*

	Frequency of psychotic experiences					**Hallucinations**		**Delusions**					**Paranoia**				
	B (95% C.I.)	**SE B**	**β**	**t**	**p**	**OR (95% C.I.)**	**p**	**B (95% C.I.)**	**SE B**	**β**	**t**	**p**	**B (95% C.I.)**	**SE B**	**β**	**t**	**p**
Family Functioning (FAD)	-.01 (-.04-.02)	.02	-.02	-.78	.44	1.18 (.81-1.73)	.40	-.04 (-.27-.18)	.11	-.01	-.38	.70	-.02 (-.24-.20)	.11	-.00	-.18	.86
Parental Stress (PSI)	.01 (.00-.03)	.01	.06	2.22	.03	1.09 (.93-1.28)	.29	.08 (-.02-.18)	.05	.04	1.66	.10	.07 (-.03-.17)	.05	.04	1.46	.15
Warm Parenting (EMBU-C)	.01 (-.01-.04)	.01	.03	1.19	.23	.73 (.54-.99)	.05	-.09 (-.27-.10)	.09	-.03	-.94	.35	.19 (.01-.34)	.09	.05	2.03	.05
Rejective Parenting (EMBU-C)	-.03 (-.07-.01)	.02	-.04	-1.42	.16	.77 (.45-1.34)	.35	-.25 (-57-.07)	.17	-.05	-1.51	.13	.02 (-.30-.34)	.16	.00	.14	.89
Overprotective Parenting (EMBU-C)	.06 (.02-.09)	.02	.09	3.36	**.00**	1.66 (1.08-2.55)	.02	.47 (.21-.72)	.13	.10	3.57	**.00**	.26 (.01-.51)	.13	.06	2.03	.04

Note.
All effects were adjusted for sex, age, and preadolescent mental health problems. OR, Odds Ratio; RT, Reaction Time (standardized); EP, Error Proportion (standardized); C.I., Confidence Interval.

Table 4. Results of linear and logistic regression analyses of psychotic experiences (frequency, hallucinations, delusions and paranoia) at age 16 on family factors at age 11. (n=2037-2059)

	Frequency of psychotic experiences					**Hallucinations**		**Delusions**					**Paranoia**				
	B (95% C.I.)	**SE B**	**β**	**t**	**p**	**OR (95% C.I.)**	**p**	**B (95% C.I.)**	**SE B**	**β**	**t**	**p**	**B (95% C.I.)**	**SE B**	**β**	**t**	**p**
Family Functioning (FAD)	-.01 (-.04-.02)	.02	-.02	-.78	.44	1.18 (.81-1.73)	.40	-.04 (-.27-.18)	.11	-.01	-.38	.70	-.02 (-.24-.20)	.11	-.00	-.18	.86
Parental Stress (PSI)	.01 (.00-.03)	.01	.06	2.22	.03	1.09 (.93-1.28)	.29	.08 (-.02-.18)	.05	.04	1.66	.10	.07 (-.03-.17)	.05	.04	1.46	.15
Warm Parenting (EMBU-C)	.01 (-.01-.04)	.01	.03	1.19	.23	.73 (.54-.99)	.05	-.09 (-.27-.10)	.09	-.03	-.94	.35	.19 (.01-.34)	.09	.05	2.03	.05
Rejective Parenting (EMBU-C)	-.03 (-.07-.01)	.02	-.04	-1.42	.16	.77 (.45-1.34)	.35	-.25 (-57-.07)	.17	-.05	-1.51	.13	.02 (-.30-.34)	.16	.00	.14	.89
Overprotective Parenting (EMBU-C)	.06 (.02-.09)	.02	.09	3.36	**.00**	1.66 (1.08-2.55)	.02	.47 (.21-.72)	.13	.10	3.57	**.00**	.26 (.01-.51)	.13	.06	2.03	.04

Note.
All effects were adjusted for sex, age, and preadolescent mental health problems. P-values in bold indicate significance after Bonferroni-Holm correction. OR, Odds Ratio; C.I., Confidence Interval; FAD, Family Assessment Device; PSI,, Parental Stress Index; EMBU-C, My Memories of Upbringing.

Table 5. *Results linear regression analyses of family factors on facial emotion identification reaction times at age 11. (n=1956-2059)*

	Family Functioning					**Parental Stress**					**Warm Parenting**					**Rejective Parenting**				
	B (95% C.I.)	**SE B**	**β**	**t**	**p**	**B (95% C.I.)**	**SE B**	**β**	**t**	**p**	**B (95% C.I.)**	**SE B**	**β**	**t**	**p**	**B (95% C.I.)**	**SE B**	**β**	**t**	**p**
EP Happy	.00 (-.01-.02)	.01	.01	.48	.63	-.05 (-.09--.01)	.02	-.05	-2.4	.02	.01 (-.00-.04)	.01	.03	1.57	.12	-.01 (-.02-.00)	.01	-.03	-1.85	.07
EP Sad	.01 (-.00-.03)	.01	.04	1.49	.14	.02 (-.02-.06)	.02	.02	.94	.34	-.02 (-.05--.00)	.01	-.05	-2.14	.03	.01 (-.00-.02)	.01	.03	1.75	.08
EP Angry	.01 (-.01-.03)	.01	.02	.72	.47	.02 (-.02-.07)	.02	.03	1.07	.29	-.02 (-.04-.00)	.01	-.04	-1.73	.08	.01 (-.01-.02)	.01	.02	.80	.42
EP Fear	-.01 (-.03-.01)	.01	-.03	-1.17	.24	.04 (.00-.09)	.02	.05	1.96	.05	-.00 (-.03-.02)	.01	-.01	-.33	.74	-.00 (-.02-.01)	.01	-.01	-.51	.61
EP Disgust	.01 (-.01-.02)	.01	.02	.70	.48	.044 (.00-.09)	.02	.05	2.11	.04	-.02 (-.05--.00)	.01	-.05	-2.10	.04	.00 (-.01-.02)	.01	.01	.38	.70

RT Happy	.01 (-.02-.03)	.01	.02	.73	.47	.03 (-.03-.08)	.03	.03	.95	.34	-.03 (-.06--.00)	.02	-.06	-2.24	.03	.00(-.01-.02)	.01	.01	.44	.66
RT Sad	-.00 (-.03-.02)	.01	-.01	-.23	.82	.02 (-.05-.07)	.03	.02	.48	.63	-.00 (-.03-.03)	.02	-.01	-.15	.88	-.00 (-.02-.02)	.01	-.00	-.12	.91
RT Angry	-.01 (-.04-.01)	.01	-.04	-1.07	.29	-.03 (-.09-.03)	.03	-.03	-.94	.35	-.01 (-.05-.02)	.02	-.02	-.69	.49	-.00 (-.02-.02)	.01	-.00	-.07	.94
RT Fear	-.00 (-.03-.02)	.01	-.00	-.12	.91	-.03 (-.09-.03)	.03	-.04	-1.04	.30	.01 (-.02-.04)	.02	.02	.70	.48	-.02 (-.03-.00)	.01	-.05	-1.63	.10
RT Disgust	.02 (-.01-.04)	.01	.04	1.21	.23	.04 (-.02-.10)	.031	.04	1.17	.24	-.00 (-.03-.03)	.02	-.00	-.07	.95	.02 (.00-.04)	.01	.06	2.09	.04

Note.
All effects were adjusted for sex, age, mental health problems at age 11. C.I., Confidence Interval; RT, Reaction Time (standardized); EP, Error Proportion (standardized).

4. Post-hoc Exploration: the 5% Lowest Scores on Facial Emotion Identification Abilities and the Frequency of Psychotic Experiences

We hypothesized that perhaps only adolescents who scored very poorly on facial emotion identification at preadolescence were more vulnerable for developing psychotic experiences at adolescence. Therefore, to investigate whether a specific subsample, namely preadolescents with the lowest scores (highest 5% of EPs and longest 5% of RTs) on the facial emotion identification task are at an increased risk for psychotic experiences in adolescence, we conducted a post-hoc exploration. The group of 5% lowest scorers on the emotion perception task had an average EP (%) of 13.67 (SD: 1.64), 38.46 (SD: 3.42), 24.00 (SD: 4.59), 27.20 (SD: 4.76) and 20.62 (SD: 3.41), for the emotions happy, sad, angry, fear and disgust respectively. The mean in RT (ms) for this group were 1431 (SD: 126), 1990 (SD: 157), 1805 (SD: 139), 1840 (SD: 173), 1719 (SD: 138), for the emotions happy, sad, angry, fear and disgust, respectively. We compared the lowest 5% with the remaining 95% of scores of EPs and RTs on all emotions (happy, sad, angry, fear and disgust) at preadolescence on the frequency of psychotic experiences at adolescence using independent samples t-tests, finding no significant differences between the groups (see table 6).

Table 6. *Independent samples t-test between highest (5%) and lowest (95%) scores on facial emotion identification task on the frequency of psychotic experiences (n=2020-2059)*

	Mean (SD) frequency of psychotic experiences		**Independent samples t-test**
	95% bottom scores	**5% highest scores***	
EP happy	1.28 (.23)	1.29 (.21)	t(2057)=-.36, p=.72
EP sad	1.29 (.23)	1.25 (.23)	t(2057)=1.56, p=.11
EP angry	1.29 (.23)	1.27 (.24)	t(2057)=1.08, p=.28
EP fear	1.28 (.23)	1.30 (.22)	t(2057)=-.59, p=.55
EP disgust	1.28 (.23)	1.30 (.26)	t(2057)=-1.08, p=.28
RT happy	1.28 (.23)	1.32 (.23)	t(2057)=-1.61, p=.11
RT sad	1.28 (.23)	1.29 (.23)	t(2057)=-.58, p=.56
RT angry	1.28 (.23)	1.31 (.25)	t(2057)=-1.56, p=.12
RT fear	1.28 (.23)	1.28 (.21)	t(2057)=.04, p=.97
RT disgust	1.29 (.23)	1.28 (.23)	t(2057)=.62, p=.54

Note.
**Higher scores indicate worse facial emotion identification abilities (more errors and longer reaction times); RT, Reaction Time (standardized); EP, Error Proportion (standardized).*

4.5 Discussion

Reduced social cognition has often been identified as a trait marker for psychosis, as it is compromised in early phases of psychosis (Romero-Ferreiro et al., 2016), as well as in siblings of individuals diagnosed with a psychotic disorder (Fett & Maat, 2013). We examined whether diminished facial emotion identification can be identified as a vulnerability marker for subsequent psychotic experiences in a young adolescent sample. The results did not confirm our hypothesis that facial emotion identification abilities at preadolescence were associated with psychotic experiences at adolescence. When examining a sub-sample of preadolescents scoring the lowest performance on the facial emotion identification task, we still found no vulnerability for psychotic experiences associated with impaired identification of facial affect in adolescence. In absence of an association, mediation by family factors was not explored. As a main effect, increased overprotective parenting at preadolescence was associated with a higher frequency of psychotic experiences as well as delusions in adolescence, after adjustment for preadolescent mental health. There was no indication that parenting stress, family functioning, and rejective and warm parenting were associated with psychotic experiences, indicating these factors may not pose a vulnerability for psychotic experiences.

In the broader adolescent population, when individuals are not recruited for their high risk status or previous episode of psychosis, facial emotion identification does not seem to be predictive of the development of psychotic experiences. Thus, it is possible that the association between facial emotion identification and psychotic experiences is not present in a large and relatively healthy sample. We speculated that perhaps this association would be detectable in a subgroup of adolescents with demonstrably lowered performance in facial emotion identification. However, a post-hoc examination based on this subsample also showed no indication of a vulnerability for psychotic experiences over time. Although the reporting of psychotic experiences may increase the risk of developing a mental illness (Fisher et al., 2013; Kaymaz et al., 2012; Poulton et al., 2000; Welham et al., 2009), the large majority of psychotic experiences are transient and benign during adolescence (Bartels-Velthuis et al., 2016). Therefore, perhaps an impairment in facial emotion identification is not predictive of psychotic experiences in adolescence, but it may be predictive of clinical psychotic symptoms in young adulthood. This reasoning would be in line with findings of a recent study (Mollon et al., 2018) which reported that developmental cognitive deficits between infancy and adulthood are only found in those who develop a psychotic disorder, with only weak evidence for individuals who have psychotic experiences. The same might hold for the association between facial emotion identification abilities and family functioning, which perhaps becomes evident only at levels of actual impairment.

In the current study, perceived overprotective parenting at preadolescence was predictive of the frequency of psychotic experiences at adolescence, after controlling for early existing mental health problems. It should be noted first that we need to be cautious about the clinical relevance of this finding: the effect of overprotective parenting on the frequency of psychotic

experiences was relatively small (denoted by the small, but significant correlation and regression coefficient). Second, we need to be cautious about the interpretation. It is possible that when parents overly protect their child, the child is less able to form its own coping mechanisms towards daily stressors. As a result, the child may be less resilient to negative events in life, rendering them more vulnerable to develop psychotic experiences and/or delusions. Another explanation may be that overprotection by the parent is a natural reaction towards a child that is more vulnerable, and requires extra support and care. The parent may sense that the child is sensitive towards certain experiences, and the overprotective parenting may then be an attempt of preventing negative outcomes. However, given that the association was corrected for preadolescent mental health problems, this explanation could be less likely. Overprotective parenting may be a trans-diagnostic risk factor, as previous studies have also found overprotective parenting to be predictive of substance abuse (Creemers et al., 2011; Visser, De Winter, Vollebergh, Verhulst, & Reijneveld, 2013), anxiety (Van Oort, Greaves-Lord, Ormel, Verhulst, & Huizink, 2011), and internalizing and externalizing problems (Sentse, Lindenberg, Omvlee, Ormel, & Veenstra, 2010). Such a risk factor may actually be genetically mediated, which leaves a third explanation that genetic background is causal in both overprotective parenting and in offspring liability to mental health problems. Future research should aim at furthering our understanding of the mechanisms shaping the association.

We expected that rejective parenting, parenting stress, lower family functioning and a lack of warm parenting would also predict psychotic experiences in adolescence, but we did not find evidence for this in the current study. It is possible that overprotective parenting is specifically relevant for the development of psychotic or internalizing problems, whereas rejective parenting may be more relevant for, for example, aggressive problems (Sijtsema, Oldehinkel, Veenstra, Verhulst, & Ormel, 2014). An alternative explanation could be that the negative impact of family factors during preadolescence can be compensated with protective factors in adolescence, such as a strong social network of peers. Indeed, previous findings demonstrate that although negative parenting (specifically dominant and harsh parenting) is predictive of externalizing behaviors in adolescence, the association was attenuated by good quality friendships and peer group affiliation (Lansford, Criss, Pettit, Dodge, & Bates, 2003). In contrast, overprotective parenting often renders a child placid, cautious and sensitive (Olweus, 1993), making them less attractive to peers, and more often at risk of peer victimization (Smith & Myron-Wilson, 1998). Future research could examine whether the protective effect of peer relationships on negative parenting in preadolescence is less strong (or perhaps not evident) for overprotected children.

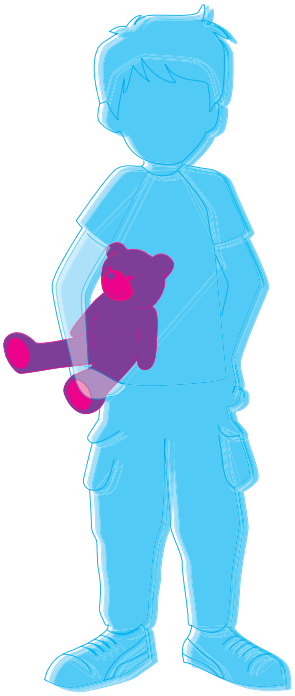
This study has a number of limitations. The Facial Expressions Task (ANT, de Sonneville, 1999) is not suited to assess biases in facial emotion identification. An emotional bias is a qualitative deviation in emotional processing (Dondaine et al., 2014), such as for example, the under-attribution of happiness when labelling neutral faces (Kohler et al., 2003). Given that previous studies have found that emotional biases are present and important in psychosis (Premkumar et al., 2008; Weiss et al., 2007) our study would have been more comprehensive to assess biases in

addition to the ability to identify emotions per se. In addition, the inclusion of neutral faces would have yielded more information, as processing of neutral faces (a socially ambiguous stimulus) has reported to be abnormal in individuals with a psychotic disorder (Derntl & Habel, 2017). Last, in the ideal design, we would have assessed psychotic experiences at age 11 (rather than general problem behavior), as well as emotion identification at age 16, which would have allowed us to examine concurrent associations that aid in the interpretation of our null findings across these five years. This study also has a number of strengths. First, we used a longitudinal design to examine whether facial emotion identification and family factors would predict psychotic experiences in adolescence, where most studies utilize cross-sectional designs (or shorter follow-up periods) and examine these associations in older samples or in samples with individuals who already have psychotic experiences or symptoms, thus limiting the examination of cause-consequence associations. Second, our study has a large sample size and a follow-up period of five years. To the best of our knowledge, we were the first to examine in a longitudinal way whether preadolescent facial emotion identification abilities and family factors have the potential to predict psychotic experiences in adolescence.

The current study examined whether facial emotion identification and family factors at preadolescence (age 11) were predictive of psychotic experiences five years later at adolescence (age 16). Facial emotion identification at preadolescence was not associated with psychotic experiences at adolescence. This may suggest that a facial emotion identification vulnerability for psychosis cannot be detected in early adolescence. Alternatively, it may only be evident in subgroups of individuals who ultimately develop a psychotic disorder, indicating that psychotic experiences in adolescence are still too mild or have little specificity for the subsequent psychotic disorder. Overprotective parenting at preadolescence predicted the frequency of both psychotic experiences and delusions, after adjusting for preadolescent mental health. Possibly, overprotective parenting at a young age results in a lack of self-reliance, autonomy or coping skills in adolescents, making them especially vulnerable to psychotic experiences as a reaction to life stressors. However, it could be that overprotection by parents is a natural reaction towards a child that is more vulnerable, and requires extra support and care. Likewise, overprotection by parents and their children's vulnerability for psychotic experiences could have a shared background, for example, a shared genetic liability. Future research is needed to examine the mechanism behind the role of overprotective parenting on psychotic experiences during adolescence.

The Dynamic Association between Social Functioning and Paranoia in Individuals at Ultra-High Risk for Psychosis

CHAPTER 5



Steenhuis, L.A., Booij, S.H., Nauta, M.H., Bartels-Velthuis, A.A., Aleman, A., Vos, M., Pijnenborg, G.H.M. & Wigman, J.T.W. (2019)

The dynamic association between social functioning and paranoia in individuals at ultra-high risk for psychosis

Submitted for publication

Abstract

Aim

Social functioning is often impaired during the ultra-high risk (UHR) phase for psychosis, yet this does not always predict a transition to psychosis. The aim of this study was to investigate in four UHR individuals separately whether changes in social functioning preceded changes in psychotic experiences (specifically paranoia), or the other way around.

Methods

Four individuals at UHR for psychosis completed a diary application every evening for 90 days. Two items on social functioning ('time spent alone' and 'experienced social support') and two items on paranoia ('suspiciousness' and 'feeling disliked by others') were selected. Time series (T = 90) of each individual were analyzed using vector auto regression analysis (VAR), to estimate the lagged (over 1 day) effect of social functioning on paranoia, and vice versa, and their contemporaneous associations.

Results

There was substantial heterogeneity in the association between social functioning and paranoia for the four individuals, both for the direction and sign (negative or positive). The most consistent finding was that increases in paranoia on a previous day resulted in increases in social functioning on the current day.

Conclusions

The association between social functioning and paranoia differs amongst four UHR individuals. For three out of four individuals, social functioning appeared to manifest itself as a coping mechanism. Therefore, social functioning may not only represent a 'risk factor' for psychotic experiences in UHR individuals, but it may also represent a 'protective factor' in daily life.

5.1 Introduction

Social functioning is often impaired in individuals with psychosis, both in early and more chronic phases (Addington et al., 2008; Couture et al., 2006). Even before a first psychotic episode, during the ultra-high risk (UHR) phase for psychosis, social functioning can be impaired (Addington et al., 2008; Ballon et al., 2007). Importantly, impaired social functioning was found to be predictive of a first psychotic episode (Cannon et al., 2008; Nelson et al., 2013; Velthorst et al., 2009; Yung et al., 2008). However, the exact nature of the association between social functioning and the development of psychosis is complex, and the evidence regarding the question whether social functioning predicts the onset of a first psychotic episode is not always consistent (Brandizzi et al., 2015). Although social functioning was shown to predict transition to psychosis in individual studies, a recent meta-analysis of 42 studies (Schultze-Lutter et al., 2015), led to the conclusion that a social impairment does not significantly increase transition rates to a first psychotic episode in UHR samples, over and above the significant contribution of positive and cognitive basic symptoms. In addition, a substantial number of individuals in UHR samples demonstrate social impairments that persist over time without transitioning to psychosis, while other individuals in UHR samples who do not have a social impairment do transition to psychosis (Brandizzi et al., 2015; Yung, Nelson, Thompson, & Wood, 2010). It is plausible that inter-individual differences underlie the inconsistency found in the UHR state regarding the role of social functioning.

Studies using experience sampling methodology (ESM) have shown that different aspects of social functioning and social context can have a varying (and sometimes contradicting) impact on the expression of psychotic symptoms in psychotic disorders (Delespaul, deVries, & van Os, 2002; Verdoux, Husky, Tournier, Sorbara, & Swendsen, 2003). One of the first ESM studies (Delespaul et al., 2002) demonstrated that in patients with a psychotic disorder, social withdrawal and inactivity may actually be beneficial for decreasing the intensity of hallucinations, whereas social engagement can raise this hallucinatory intensity. In contrast, a different study (Myin-Germeys, Nicolson, & Delespaul, 2001) in patients with a psychotic disorder demonstrated that the presence of family members or friends is protective for delusional experiences, whereas social withdrawal made these more likely to occur. These studies highlight that social functioning is a dynamic and multifaceted concept, and that the direction of the association between psychotic symptoms and social functioning in psychotic disorders may be person-specific.

Novel statistical techniques allow us to better incorporate this large between-individual heterogeneity. Existing ESM studies often use multilevel analysis, which incorporate inter-individual differences but still average individual regression terms for all participants. In order to estimate bidirectional associations separately for each individual and thus to investigate the question whether this directionality can indeed differ within individuals, a within-subject time-series approach is more suitable. In such an approach, all variables can be modeled as both predictors and outcomes for each person individually (Brandt & Williams, 2007). The question of how social functioning is associated with psychotic experiences in the UHR phase could benefit from such an approach, as it could reveal unique insights regarding the UHR stage and might have important implications for clinical interventions.

Although previous ESM studies have examined psychotic symptoms such as hallucinations (Delespaul et al., 2002) or delusions (Myin-Germeys et al., 2001) in patients with psychotic disorders, the current study will assess mild psychotic experiences, specifically paranoia. Given that paranoia is a common psychotic experience present before the first psychotic episode (An et al., 2010; Cannon et al., 2008) and frequently reported on a daily basis in UHR patients (Yung et al., 2003), it is a suitable measure for the daily assessment of psychotic experiences in this sample. Therefore, the current study examined the association between social functioning and psychotic experiences in depth in a sample of four individuals over a period of 90 days, exploring for each individual separately the directionality, temporal dynamics and statistically causal effects of this association. Given the previously ambiguous results with regards to the role of social functioning in the UHR phase (Schultze-Lutter et al., 2015), the current study was explorative and we had no explicit hypothesis regarding the type and direction of the association amongst individuals.

5.2 Materials and Methods

Design

For the current study, the association between social functioning and paranoia was examined in four individuals at ultra-high risk (UHR) for psychosis, as assessed with the CAARMS (Comprehensive Assessment of At-Risk Mental States; Yung et al., 2005). UHR status was confirmed if one of three criteria were met: (i) a genetic risk, (ii) brief limited intermittent psychotic symptoms (BLIPS) or (iii) attenuated positive symptoms (APS), and in the presence of a significant social impairment as assessed with the Social and Occupational Functioning Scale (SOFAS; Goldman, Skodol, & Lave, 1992). Participants were the first four participants to enter the UHR subgroup of the Mapping Individual Routes of Risk and Resilience (MIRORR) study, a 90-day diary study of mental symptoms, stress and experiences in individuals at risk for psychosis. For more information about the MIRORR study, inclusion/exclusion criteria and recruitment procedures, see the study protocol (Booij et al., 2018). To give a short summary, participants were recruited at mental health care facilities in the Netherlands, where they received treatment for a non-psychotic psychiatric disorder. Participants received a package with information on the study, screening questionnaires, and an informed consent form. After providing informed consent, participants were assessed with the mini-SCAN (Nienhuis, Van De Willige, Rijnders, De Jonge, & Wiersma, 2010), and received information on the daily diary procedure. All participants received a personal report of their diary results and a financial compensation. The study was approved by the Medical Ethical Committee of the University Medical Center Groningen (ABR no. NL52974.042.15).

Diary Assessment Application

Participants completed the diary assessment application online on their phone for 90 days. The application generated a text message containing a link to the online diary questionnaires every evening (see study protocol; Booij et al., 2018). One assessment per day was chosen in order to capture the average experiences over one day, without sampling too often. Participants had a time window of 1.5 hours to fill out the diary. It took on average 7 minutes to complete the diary assessment.

Measures

Baseline Assessment. The Comprehensive Assessment of At-Risk Mental States (CAARMS; Yung et al., 2005) and the Social and Occupational Functioning Scale (SOFAS; Goldman et al., 1992) was used to determine the presence of an UHR state. The mini-SCAN (Nienhuis et al., 2010) was used to assess and confirm the presence of a DSM-IV axis-I psychiatric disorder. The Community Assessment of Psychic Experiences (CAPE; Konings, Bak, Hanssen, Van Os, & Krabbendam, 2006) was utilized to assess the frequency and distress of positive psychotic experiences.

ESM Items. Paranoia was assessed in ways similar to previous ESM studies (Myin-Germeys, Delespaul, & van Os, 2005; Oorschot, Kwapil, Delespaul, & Myin-Germeys, 2009; Wigman et al., 2013) on a VAS-scale (from 'not at all' 0 to 'very' 100). The items were "I felt suspicious today" and "Today I had the feeling that others did not like me". Social functioning was assessed as the quantity of social contacts on a given day, on a 7-point Likert scale ("How much was I alone today" from 1 'not at all' to 7 'all day') and as the quality of social contacts on a given day, on a VAS scale ("Did you feel supported today?" from 0 'not at all' to 100 'very').

Statistical Analysis

Vector autoregressive (VAR) modeling was used to analyze the multiple time series of each individual in this study. VAR modeling allows to model a set of regression equations for two or more variables, in this case consisting of social functioning (1. time spent alone and 2. perceived social support) and paranoid psychotic experiences (1. feeling of being suspicious and 2. feeling of being disliked by others). All four variables in this model could be both determinant and outcome, allowing the temporal order of effects to be tested, including bidirectional associations and feedback loops. Each variable was regressed on its own lagged value (e.g. t-1) and the lagged values of the other variables. The number of lags in this model was a priori set to one, equivalent to a period of one day. The lagged effect is indicative of a delayed effect of the past day's social functioning on current psychotic experiences over time (and vice versa for the opposite effect). The Likert scale of the item 'Time spent alone' was re-scaled to a 0-100 VAS scale to accommodate the scaling differences between items. Autoregressive Moving Average (ARMA) models were run to confirm that the separate items of social functioning and paranoia measure different aspects of the concepts under study, and were not highly correlated over time. In order to estimate the VAR coefficients, a maximum likelihood estimation with a degrees of freedom adjustment was used, which is recommended for small samples (Lütkepohl, 2005). VAR model assumptions, such as normality, stationarity and no residual autocorrelation (Lütkepohl, 2005), were assessed with diagnostic checks, and if assumptions were not met, they were addressed using methods suggested by Stavrakakis et al., (2015).

Contemporaneous correlations (i.e. associations at the same assessment point) between variables were computed from the residuals in the final model to assess the association between social functioning and psychotic experiences. Granger causality Wald tests (Granger, 1969) were used to test the significance of the directionality of the influence between two time series. It takes into account the joint effect of previous lags of the predictor variable (e.g. social functioning) on the outcome variable (e.g. paranoia), whilst controlling for previous lags of the outcome variable.

Cumulative Orthogonalized Impulse Response analysis (COIRF) was computed to calculate the dynamic effect of social functioning on psychotic experiences, and vice versa (Brandt & Williams, 2007; Rosmalen, Wenting, Roest, De Jonge, & Bos, 2012). Impulse response functions (IRFs) demonstrate the dynamic effect of changes in each of the variables over time, by visualizing the impact of an isolated shock in one variable (e.g. a shock of 1SD in social functioning) to the other variable (e.g. paranoia) over time. IRFs incorporate all estimated parameters of the VAR analysis, including lags and feedback loops. Orthogonalized IRFs (OIRFs) account for both contemporaneous and lagged effects, and assume a pre-defined order of the contemporaneous associations between variables. We tested both orderings of relations and reported the order most in line with the Ganger causality tests (order 1: social functioning $\rightarrow$psychotic experiences, order 2: psychotic experiences $\rightarrow$ social functioning). Cumulative OIRFs (COIRFs) demonstrate the cumulated impulse of a shock in one variable on another variable over a certain period, in our case three days. The duration of three days was chosen as it was deemed long enough to reflect maintenance of effects, without compromising on reliability of results (the longer the period, the less reliable the effects (Brandt & Williams, 2007)). For the dynamic effects, we assumed a two-tailed alpha level of 0.10 to determine statistical significance (in line with Stavrakakis et al., 2015). For each individual, effect sizes were standardized. Analyses were computed in STATA 15 using the suite of VAR commands (StataCorp, 2017).

5.3 Results Descriptives

Participants in the current sample were two males and two females, ranging between 20 and 31 years of age. Clinical background information for the four participants can be found in Table 1. In Table 2 and Figure 1 descriptive statistics for each participant can be found. There were no clear trends (increasing or decreasing) in social functioning or paranoia for the participants over the study period.

Table 1. *Clinical Background Information for Participants 1 to 4*

	Participant 1	**Participant 2**	**Participant 3**	**Participant 4**
Number of Daily Assessments (max. 90)	87	81	85	82
Diagnoses (mini-SCAN)	depressive disorder	recurrent depressive disorder	depressive episode	depressive disorder and obsessive compulsive disorder
CAPE score (frequency of psychotic experiences – weighted mean item score)	1,20 (average)	1,05 (low)	1,85 (high)	1,30 (average)
Fulfillment of CAARMS criteria	genetic risk + attenuated psychotic symptoms	attenuated psychotic symptoms	genetic risk	attenuated psychotic symptoms
Transition to a psychotic disorder after 1 year	no	no	no	no

Note.
CAPE, Community Assessment of Psychic Experiences; CAARMS, Comprehensive Assessment of At Risk Mental States.

Table 2. *Descriptive Statistics for all Variables for Participants 1 to 4*

Participant	**Suspiciousness**		**Others dislike me**		**Time spent alone**		**Experienced social support**	
	Mean (SD)	**Range**	**Mean (SD)**	**Range**	**Mean (SD)**	**Range**	**Mean (SD)**	**Range**
1	17.71 (5.64)	8.27 – 42.81	15.09 (4.74)	0.72 – 32.01	7.25 (12.97)	0 – 50	55.98 (15.09)	14.71 – 83.45
2	55.20 (26.36)	.36 – 95.28	50.67 (29.45)	0 – 100	51.69 (31.53)	0 – 100	33.56 (30.31)	0 – 88.05
3	45.90 (17.19)	6.69 – 77.24	54.49 (19.34)	0 – 82.89	43.78 (13.95)	0 – 66.67	50.17 (19.28)	17.46 – 99.76
4	59.70 (15.74)	.96 – 86.51	50.06 (13.84)	16.33 – 76.57	28.13 (23.95)	0 – 100	47.90 (19.97)	.06 – 79.78

Note.
All variables were assessed on a VAS-scale (0-100); SD, Standard Deviation.

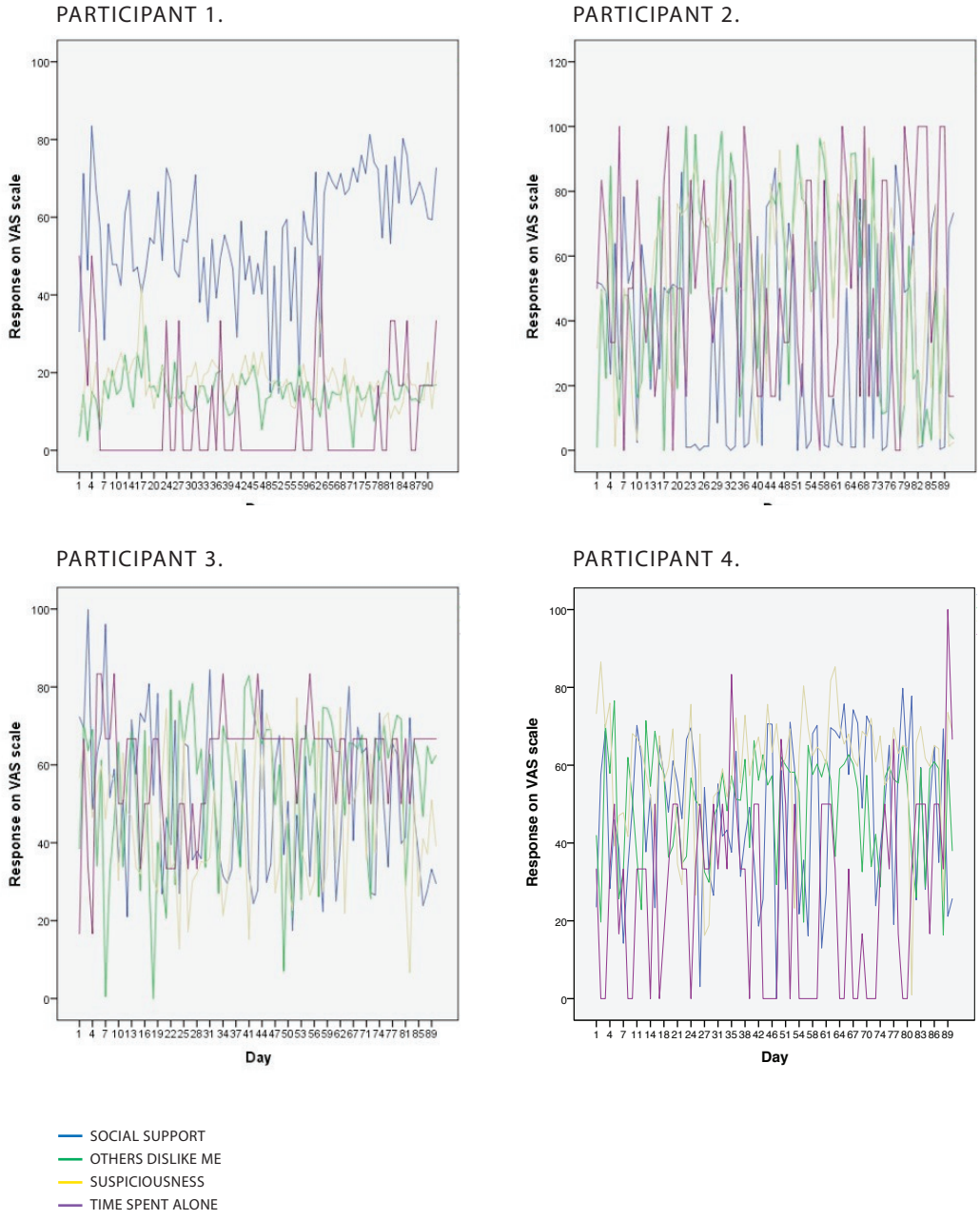


Figure 1. *Line plots for each participant depicting variations in daily responses to each item over a period of 90 days*

Contemporaneous Associations between Social Functioning and Paranoia

In Table 3, contemporaneous associations (within the same day) between social functioning and paranoia are displayed. For participant 1, there was a significant negative correlation between suspiciousness and experienced social support and time spent alone. Also, there was a significant positive correlation between the feeling of being disliked and the time spent alone. For participant 2, there were no contemporaneous correlations and the variable 'experienced social support' was not tested, as it did not meet the VAR assumption of normally distributed residuals. For participant 3, there was a positive correlation at trend level between suspiciousness and time spent alone. For participant 4, there were no contemporaneous correlations between social functioning and paranoia.

Table 3. *Contemporaneous Correlations between Social Functioning (Time Spent Alone and Experienced Social Support) and Paranoia (Suspiciousness and Others Dislike Me)*

Participant	Suspiciousness		Others dislike me	
	Time spent alone	Experienced Social support	Time spent alone	Experienced social support
1	0.53#	-0.43*	0.73**	0.06
2	-0.09	-	-0.10	-
3	0.20#	0.08	0.01	-0.01
4	-0.10	-0.01	0.12	-0.33

Note.
*#p<0.10 (trend-level), *p<0.05, **p<0.01.*

Direction of the Association (Granger Causality)

To test whether changes in social functioning preceded changes in paranoia over a period of one day, or the other way around, Granger causality tests were performed (see Table 4). For participant 1, an increase in suspiciousness (t-1) predicted a decrease in experienced social support (t). For participant 2, the relation between social functioning and paranoia was bi-directional, as an increase in time spent alone (t-1) predicted an increase in the feeling of being disliked by others (t), whereas an increase in the feeling of being disliked (t-1) predicted a decrease in time spent alone(t). For participant 3, an increase in the feeling of being disliked (t-1) predicted less time spent alone (t). For participant 4, an increase in feelings of suspiciousness (t-1) predicted less time spent alone (t), in addition to an increase in experienced social support (t).

Dynamic effects give the opportunity to assess whether the previously found (isolated) associations in the Granger causality tests are maintained over three days' time. Findings are presented in Table 5. To give an example, for participant 1 a 1 SD increase in suspiciousness led

to an (non-significant) increase in time spent alone of 0.20 SD, and a (significant) decrease in experienced social support of 0.41 SD. Overall, there was no lasting effect of social functioning (time spend alone or experienced social support) on paranoia (suspiciousness or others dislike me) in the COIRFs for the four participants. For participants 1 and 4, the effects found in the granger causality test of paranoia (suspiciousness) on social functioning (time spend alone and experienced social support) were maintained in the COIRFs.

Table 4. *Granger Causality Tests for both Directions of the Association between Social Functioning and Paranoia from One Day to the Next Day*

Participant	1. Causality test = Social functioning → Paranoia	X2	df	Estimate	2. Causality test = Paranoia → Social functioning	X2	df	Estimate
1	-	-	-	-	More suspiciousness → Less experienced social support	6.50**	1	-10.57
2	More time spent alone → More feeling that others dislike me	3.25#	1	.12†	More feeling that others dislike me → Less time spent alone	3.30#	1	-.16†
3	-	-	-	-	More feeling that others dislike me → Less time spent alone	2.88#	1	-.10†
4	-	-	-	-	More suspiciousness→ Less time spent alone More suspiciousness→ More experienced social support	4.01* 9.65**	1 1	-14.37 18.63

Note.
*#p<0.10 (trend-level), *p<0.05, **p<0.01, † Log-transformed; df, degrees of freedom. Dynamic effects (COIRFs) over a period of three days.*

Table 5. *Orthogonalized Cumulative Impulse Response Functions over a Period of Three Days for the Four Participants*

Impulse	**Suspiciousness**		**Others dislike me**		**Time spent alone**		**Experienced social support**	
Response	**Time spent alone**	**Experienced Social Support**	**Time spent alone**	**Experienced Social Support**	**Suspiciousness**	**Others dislike me**	**Suspiciousness**	**Others dislike me**
Participant 1	0.20	**-0.41**	-0.07	**-0.29**	-0.19	-0.12	-0.12	-0.14
Participant 2	-0.13		-0.11		0.02	0.09		
Participant 3	0.26	0.07	-0.29	0.05	0.03	-0.14	0.07	-0.16
Participant 4	**-0.53**	**0.49**	-0.03	0.08	0.08	-0.15	0.03	0.00

Note.
Bold effect sizes indicate significance at p-level <0.10. Results are presented assuming order 2 of contemporaneous associations: within-day changes in paranoia precede changes in social functioning.

5.4 Discussion

The main aim of this study was to explore if the nature of the association in social functioning and paranoia differs between individuals at UHR for psychosis. The findings confirm the association between social functioning and paranoia manifests itself in different ways for four individuals in the UHR phase for psychosis. Given that it is often indicated that social impairments are present long before the first psychotic episode (Addington et al., 2008; Ballon et al., 2007) and are often associated with a transition to the first psychotic episode (Cannon et al., 2008; Nelson et al., 2013; Velthorst et al., 2009; Yung et al., 2008), one may have expected that previous day changes in social functioning would lead to current day changes in paranoia. This was found only for one participant, namely that increases in time spent alone resulted in increases in the feeling that others disliked this person. At the same time this effect was bidirectional, as the presence of increased feelings of others disliking this person also resulted in a decrease in time spent alone. This individual seems sensitive to social isolation, but also seems to protect themselves by utilizing their social network and seeking out social contact, as to prevent a further increase in paranoia. These associations were no longer present in the COIRF analysis, where the net effect after three days was assessed. Thus, although the literature often states that impaired social functioning represents a 'risk factor' for psychosis (Cannon et al., 2008; Nelson et al., 2013), the current study demonstrates that social functioning may also represent a 'protective factor' in daily life during the UHR phase.

It was examined whether previous day changes in paranoia would lead to current changes in social functioning. This was found for all four individuals. One may expect that increases in paranoia would lead to decreases in social functioning, as it is known that paranoia can cause a person to experience social threat and therefore withdraw themselves (Green & Phillips, 2004). However, only one participant in this study demonstrated that an increase in previous day suspiciousness led to a decrease in experienced social support on the current day, an effect that was maintained over a period of three days. On the contrary, for three participants, previous day increases in paranoia led to current increases in social functioning. This effect was also maintained for one individual over a period of three days, demonstrative of a potentially profound and lasting effect. These findings suggest that for three participants, social interactions may serve as a coping factor. The literature on UHR for psychosis is often focused on the social 'impairment'(Addington et al., 2008; Cannon et al., 2008; Velthorst et al., 2009), but the current study highlights the potential for the social network to also represent a source for boosting and maintaining mental health in the UHR for psychosis phase.

Current treatments for UHR psychosis are effective in treating positive symptoms, but social functioning often remains impaired regardless of treatment (Brandizzi et al., 2015; Van Der Gaag et al., 2012). It therefore appears there is room for improvement in the treatment of a social impairment in the UHR phase for psychosis. A next step would be to investigate whether the found individual patterns are associated with transition to psychosis or an increase in psychotic symptoms. A further step could be to examine the feasibility of using diary assessments in clinical

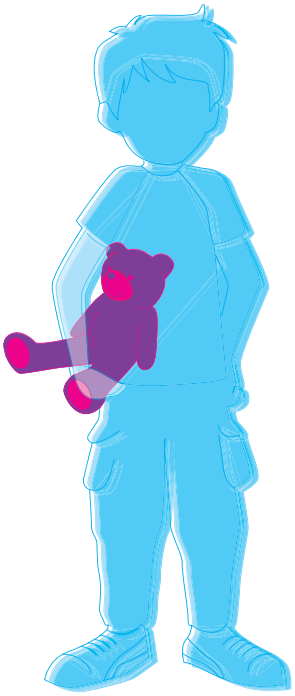
practice, as this may provide unique insights into individual patterns of psychotic symptoms and social functioning that may not be obvious when using standard assessments. By using diary techniques, it may be hypothetically possible to develop individualized interventions, targeting one aspect (e.g. social contact) to potentially achieve the expected change in another aspect (e.g. paranoia). Such techniques are only just beginning to be explored in clinical practice, and more research is needed to verify the effectiveness of individualized intervention techniques in clinical practice.

To the best of our knowledge, the current study is the first to approach the association between social functioning and paranoia during the UHR phase for psychosis using an idiographic time-series analysis. The time-series design allowed us to examine the association at the individual level and to make inferences about the directionality, temporal dynamics and statistically causal effects of the examined association. Although the design of repeated assessments over a period of 90 days is time-consuming and demanding for the participant, compliance was high and participants were highly motivated to take part in the study. Our study also has some limitations. First, not all aspects of social functioning (e.g. occupational functioning) or psychotic experiences (e.g. delusions) were addressed. Second, due to the design of one-measurement-a-day and the choice for lags of one day (granger causality tests) and three days (dynamic effect sizes), it is possible that we missed variations if these occurred in different time intervals. Third, we did not examine whether the found associations were important for prognosis or transition to psychosis.

To conclude, using an idiographic analytic method it was found that the association between social functioning and paranoia differs amongst four UHR individuals. The current study shows that besides social functioning representing a risk factor in the UHR for psychosis phase, it may also be viewed as a 'protective factor' for psychotic experiences in the daily life of UHR individuals. These findings underline the importance of the social network as a resource for managing psychopathology and the potential it has in helping individuals with distressing experiences. We believe that social functioning deserves more attention as a potential coping mechanism in the UHR phase for psychosis and that this should be explored further in intervention studies for UHR psychosis.

Religiosity in Young Adolescents with Auditory Vocal Hallucinations

CHAPTER 6



Steenhuis, L.A., Bartels-Velthuis, A.A., Jenner, J.A., Aleman, A., Bruggeman, R., Nauta, M.H. & Pijnenborg, G.H.M. (2016)

Religiosity in young adolescents with auditory vocal hallucinations

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Abstract

Aim

The current exploratory study examined the associations between auditory vocal hallucinations (AVH) and delusions and religiosity in young adolescents.

Methods

337 children from a population-based case-control study with and without AVH, were assessed after five years at age 12 and 13, on the presence and appraisal of AVH, delusions and religiosity. AVH status (persistent, remittent, incident or control) was examined in relationship to religiosity.

Results

Results demonstrated a non-linear association between AVH and religiosity. Moderately religious adolescents were more likely to report AVH than non-religious adolescents (O.R. = 2.6). Prospectively, moderately religious adolescents were more likely to have recently developed AVH than non-religious adolescents (O.R. = 3.6) and strongly religious adolescents (O.R. = 7.9). Of the adolescents reporting voices in this sample (16.3%), more than half reported positive voices. Religious beliefs were often described as supportive, useful or neutral (82%), regardless of the level of religiosity, for both adolescents with and without AVH. Co-occurrence of AVH and delusions, and severity of AVH were not related to religiosity.

Conclusions

The present findings suggest there may be a non-linear association between religiosity and hearing voices in young adolescents. A speculative explanation may be that religious practices were adopted in response to AVH as a method of coping.

6.1 Introduction

Auditory vocal hallucinations (AVH) occur relatively frequent in the general population in children, adolescents and adults, yet commonly disappear over time (Altman et al., 1997; van Os et al., 2009; Bartels-Velthuis et al., 2011). Studies using large pediatric samples in England (5-15 year olds, Egdell and Kolvin, 1972; 11 year olds, McGee, Williams, Poulton, 2000) and the Netherlands (7-8 year olds, Bartels-Velthuis et al., 2010) have found prevalence rates of AVH in children and adolescents varying from 8 to 9% (for a review see: Jardri et al., 2014). In a proportion of these adolescents AVH were persistent two years later (27% in Dutch 15-16 year olds; De Loore et al., 2011) and five years later (23.5% in Dutch 12-13 year olds; Bartels-Velthuis et al., 2011). The course of AVH over time depends on various individual and environmental factors (van Os et al., 2009). One of these factors might be religiosity, since several studies have demonstrated that religiosity is associated with a higher prevalence of psychotic experiences (Mohr et al., 2006), both in adults in the general population (Aird et al., 2010) and in adult patient samples (Getz et al., 2001; Suhail & Ghauri, 2010). Explanations for this association have ranged from using religion as a coping strategy (Mohr et al., 2006), through the notion that religion may promote distorted perceptions and distrust of others (Aird et al., 2010), to the idea that a connection with an omnipotent force (God) yields a conviction of 'super human' abilities (Suhail & Ghauri, 2010). The consensus in these notions is that religion may have both a positive and negative effect on mental health and well-being in adults (Koenig, 2009; Pargament et al., 1998).

Little is known about the association between AVH, delusions and religiosity during adolescence. There are studies that have examined the relationship between religiosity and other mental health aspects in adolescent samples, such as depressive episodes, anxiety, suicidal ideation, behavioral problems, and substance abuse (12-21 year olds, Dew et al., 2008). Reviews conclude that religion mostly has a positive relationship with mental health in children/adolescents (Dew et al., 2008; 10-20 year olds, Wong et al., 2010), yet some studies report a negative relationship (20 year olds, Exline et al., 2000) or none at all (e.g. Evans et al., 1996; for a review see: Dew et al., 2008). One study reported a curvilinear relationship between religiosity and emotional problems (11-19 year olds, Meltzer et al., 2011). Adolescents with weakly held religious beliefs were more likely to have emotional problems in relation to adolescents with no or strongly held beliefs. Overall, there is some evidence for a relationship between religiosity and mental health during adolescence, yet the direction is still equivocal.

Several studies examined the association between religiosity and psychotic experiences in adult samples. Religious adults from the general population who experience and appraise their AVH within the context of their religion, tend to experience them more positively and less stressful compared to non-religious psychotic patients and non-religious healthy controls (Davies, Griffin, & Vice, 2001). In clinical samples, patients can report both positive (as a resource for coping) and negative (as an aggravation of psychopathology) influences of religion (Cottam et al., 2011; Koenig, 2009). The valence of religious influences on psychopathology has been related to outcomes (e.g.

Shah et al., 2011). For patients, negative religious coping in response to life stressors (indicative of a 'spiritual struggle') has been found to be related to increased suicidal ideation, depression and anxiety, whilst positive religious coping was related to decreased depression and anxiety (Rosmarin et al., 2013). Similarly, Mohr and colleagues (Mohr et al., 2011) reported that 83 percent of patients with psychosis found religion helpful, which was predictive of decreased negative symptoms and improved quality of life. Notably, the aforementioned studies were conducted in both Western (Britain, Davies et al., 2001; Switserland, Mohr et al., 2006) and non-Western (India, Shah et al., 2011) countries.

Factors that have been identified as important for the course of AVH during childhood, are (amongst others) the co-occurrence of AVH with delusions (Smeets et al., 2012) and the persistence of voices over time (Bartels-Velthuis et al., 2011). AVH severity is positively associated with delusions (Bartels-Velthuis, van de Willige, Jenner, Wiersma, et al., 2012), and compared to experiencing hallucinations or delusions in isolation, a combination of these experiences is more persistent and associated with more help seeking (Smeets et al., 2012). Moreover, persistent and incident AVH during childhood in itself are also associated with more problem behaviour and worse school performance (Bartels-Velthuis et al., 2011). It is both interesting and important to explore how religiosity is related to the course of AVH and the co-occurrence with delusions. If religion is indeed a source of comfort and hope for individuals who are faced with psychotic symptoms (Koenig, 2009; Rosmarin et al., 2013) and improves quality of life (Shah et al., 2011), adolescents reporting AVH might be more likely to report religious activity, as a method of coping. However, if religiosity is experienced negatively as a 'spiritual struggle', it could also aggravate psychopathology and instead be related to severity of AVH in adolescents.

Here, in a 5-year follow-up study of the case-control sample of 7- and 8-year-old children with and without AVH (Bartels-Velthuis et al. 2010), religiosity is examined in relation to the (i) frequency, (ii) course, (iii) co-occurrence with delusions, (iv) positivity, (v) usefulness, and (vi) severity of AVH. Given that previous studies have used heterogeneous methods of conceptualising religiosity (Dew et al., 2008) and the literature indicates that a) religiosity is best captured as a multidimensional concept (Meltzer et al., 2011), and b) different degrees of religiosity have different effects on, for example, the degree of delusional ideation (Getz et al., 2001), the current study will conceptualize religiosity in both a continuous (more or less religious) and categorical (non-, moderate or strongly religious) manner. In line with these recommendations, religiosity will be assessed in terms of multiple facets (religious beliefs, activities and upbringing), whilst tapping into the conceptualisations of previous studies (Meltzer et al., 2011). Given that previous studies have yielded mixed findings and that this study is, to the best of our knowledge, the first to examine these relationships in a young sample of non-clinical adolescents, our analyses are exploratory.

6.2 Methods

Subjects

The current study included 337 young adolescents, derived from a case-control sample of children with and without AVH (n=694; 50% with AVH) from a general population study on auditory hallucinations (Bartels-Velthuis et al., 2010). The original sample was composed five years earlier, from a survey on AVH in 3870 7- and 8-year-old children attending primary school in the province of Groningen, the Netherlands. Participants were thus assessed twice, at baseline (T0: age 7-8) and at 5- year follow-up (T1: age 12-13). Data from both time points were used.

T1 represented 56% (n=337) of the T0 sample with parental consent to follow-up (n=605). Participation at T1 was not associated with baseline AVH or control status. The mean age of the participants was 13.1 years (SD=0.5) and 46.7% of the participants were male. At T1, 55 adolescents reported AVH (16.3%), see also table 1.

Procedures

Approval for the current study was obtained from the Medical Ethics Committee of the University of Medical Center Groningen. Parents who gave informed consent for being approached for their child's participation in the follow-up study were sent a notification letter via mail. In case of non-response, parents were reminded with a second letter, and if necessary they were later contacted by telephone.

Seven interviewers conducted the interviews at the adolescents home, in the absence of parents. The interviewers all followed a comprehensive training and booster sessions were arranged to prevent interviewer 'drift' (for more details see Bartels-Velthuis et al., 2011). To prevent bias, the interviewers were blind to adolescents' AVH status at baseline. Before the interviews took place, written informed consent was obtained by both the adolescents and one of their parents. In case parents or adolescents had questions as a result of the interviewing procedure, they could contact the research team.

Measures

Auditory Vocal Hallucinations. Consistent with studies investigating AVH (e.g. De Loore et al., 2011; Fujita et al., 2015), all adolescents were asked about the presence of AVH in the past five years: 'In the past five years, have you heard one or more voices that only you and no one else could hear?'. Those scoring positive on AVH in this period were interviewed with the Auditory Vocal Hallucination Rating Scale (AVHRS; Jenner and van de Willige, 2002; Bartels-Velthuis et al., 2012a), a structured interview to assess the characteristics and severity of AVH, in terms of frequency, duration, loudness, negative content, distress, anxiety, control, and interference with thinking and daily life. Scores range from 0 (not applicable) to 4 (most applicable). The AVHRS was developed in Dutch language for adult patients and in a later study (Bartels-Velthuis et al., 2010) the language was adapted for children/adolescents. The AVHRS has good inter-rater reliability,

internal consistency and discriminative validity (Bartels-Velthuis, van de Willige, Jenner, & Wiersma, 2012). All AVH variables were constructed in agreement with previous research (Bartels-Velthuis et al., 2010). A dichotomous variable was constructed indicating whether the child reported AVH (1) or not (0) at the T0 and T1 assessments. The AVHRS items were recoded into 0 (none or mild consequences) and 1 (considerable to severe consequences), after which a severity index (ranging from 0 to 12) was composed. The adolescents were divided into two groups: 'severe AVH' (adolescents who scored in the highest quartile of the severity index; 5 or more) and 'mild AVH' (the remainder of adolescents, score of 4 or less).

Delusions. Delusional ideation was assessed with three items enquiring about 'mind reading', 'paranoid ideas' and 'receiving media messages', originating from the Diagnostic Interview Schedule for Children (DISC-C; Costello, Edelbrock, & Costello, 1985) for the DSM-III (American Psychiatric Association, 1980). These items were previously used by Bartels-Velthuis et al., 2011, De Loore et al., 2011 and in the Dunedin study by Poulton et al., 2000, developed to investigate delusions in non-clinical samples of children and adolescents. The items were validated by numerous groups (e.g. Kelleher et al., 2011; Polanczyk et al., 2010) and found to have good predictive validity for a diagnosis of schizophrenia during adulthood (Poulton et al., 2000). All items were originally in English and directly translated to Dutch for the current study. Delusions were scored as 0 (no), 1 (yes, likely) and 2 (yes, definitely), and were assessed over the lifetime. A dichotomous variable was constructed indicating presence of at least one definite delusion (hereon referred to as: 'delusions' or DEL).

Positive and Useful Voices. Positive and useful voices were assessed with two items from the Positive and Useful Voices Inquiry (PUVI; Jenner et al., 2008). This is a 53-item self-report questionnaire assessing prevalence, course, characteristics and attribution of positive and useful voices, administered at T1. The PUVI was designed in Dutch language for child and adolescent samples. It has two subscales assessing (i) positivity (twelve items) and (ii) usefulness of these voices (nine items), which have a good internal consistency (Cronbach's alpha 0.93 for positive voices and 0.89 for useful voices (Jenner et al., 2008). For the purpose of this study the two prevalence questions of both subscales of the PUVI were used: 1) 'have you ever heard positive voices'(positivity subscale) and 2) 'have you ever experienced your voices as useful' (usefulness subscale). Questions regarding the course, characteristics and attribution of voices were only asked to adolescents giving a positive response to the two prevalence questions and not included in the analyses. Positive voices were scored as 0 (no, I have never experienced voices as positive) or 1 (yes, I have experienced voices as positive). Useful voices were scored as 0 (no, I have never experienced voices as useful) or 1 (yes, I have experienced voices as useful).

Religiosity. Religiosity was assessed with the five questions from the Dutch Spirituality and Religiosity Questionnaire (Jenner, 2006). This Dutch questionnaire was developed for the current study for application in child and adolescent samples. It is developed in line with suggestions from the literature (Dew et al., 2008; Getz et al., 2001) and is consistent with a previous measure

(Meltzer et al., 2011). The first four questions, scored with 0 (no) or 1 (yes), were as follows: (1) 'Do you believe in God or a supernatural spiritual force?', (2) 'Do you consider yourself religiously or spiritually active, for example by praying, visiting meetings or rituals?', (3) 'Were you raised with religion?' and (4) 'Are you currently a member of a religious or spiritual community?'. In this sample, a Cronbach's alpha calculation on these four items was 0.87. The last question (5) 'How do you experience your belief?' was only answered in case of a positive answer to the first question and has the following response categories: (a) 'supportive/helpful', (b) 'oppressive/negative', (c) 'alternating between positive and negative' or (d) 'neither'.

Data Analysis

Analyses were performed using SPSS for Windows, version 20.0. A variable 'AVH status' was constructed for the course of AVH from T0 to T1, based on the screening at both time points (analogue to previous analysis; Bartels-Velthuis, van de Willige, Jenner, Wiersma, et al., 2012), yielding four groups: (i) adolescents with AVH at T0 and T1 (the persistent group) (ii) adolescents with AVH at T0 but not at T1 (the remitted group), (iii) adolescents without AVH at T0 but with AVH at T1 (the incident group), and (iv) adolescents without AVH both at T0 and T1 (the referent group).

In line with previous research on this sample (Bartels-Velthuis, van de Willige, Jenner, Wiersma, et al., 2012) an ordinal variable 'AVH + DEL' was constructed at T1, dividing the adolescents into four groups: (i) adolescents with AVH only, (ii) adolescents with DEL only, (iii) adolescents with both AVH and DEL, and (iv) adolescents without AVH and DEL.

A sum score of religiosity was computed, by adding up the positive responses to questions 1 - 4. In line with Meltzer et al. (2011) a categorical religiosity variable with three groups was computed to specify the level of religiosity (non-, moderately - and strongly religious). We constructed this variable basis of questions 1 - 4, whereas question 5 was examined qualitatively. The religiosity categories consisted of 'strongly religious adolescents' (responded 'yes' to all four questions), 'moderately religious adolescents' (responded 'yes' to at least one question and to at most three questions) and 'non-religious adolescents' (responded 'no' to all four questions).

Pearson's chi-square tests were used to examine associations between religiosity (non-, moderately - and strongly religious) and respectively AVH and/or delusions, the presence of positive and useful voices, AVH severity and AVH status. A non-parametric Mann-Whitney U test was also computed to compare religiosity sum scores between adolescents with and without AVH. Cramer's V was computed for significant chi-square associations as a measure of effect size. Significant chi-square associations were followed by logistic regression analyses, in order to calculate odds ratio's and confidence intervals (CIs). Significance tests were two-tailed with alpha set at 0.05.

6.3 Results

Descriptives

The mean time gap between T0 and T1 was 5.1 years (SD = 0.4). It has been previously examined whether there was any significant or suggestive differential attrition according to demographics at baseline or psychiatric service use in this follow-up sample (Bartels-Velthuis et al., 2011), finding no evidence for this. Religiosity scores (T1) were missing for two adolescents, yielding a total of 335 religiosity scores. Of the 335 adolescents, 146 (43.6%) were not religious, 110 (32.8%) moderately religious, and 79 (23.6%) strongly religious (table 1).

Religiosity and AVH (T1)

AVH were reported by 55 adolescents (16.3%). The mean religiosity sum score for adolescents with AVH was higher (mean = 1.69, SD = 1.51) than the mean religiosity sum score for adolescents without AVH (mean = 1.49, SD = 1.68), yet this was not significant as evidenced by a non-parametric Mann-Whitney U test. The association between religiosity groups (non-, moderately or strongly religious) and AVH was significant ($X^2(2) = 8.55$, $p<0.01$), with a small to moderate effect size(φ .16, $p<0.01$). Specifically, moderately religious adolescents had significant higher odds of reporting AVH, compared to non-religious adolescents (O.R. = 2.6, 95% C.I. = 1.34 - 5.20) (table 2).

Religiosity and AVH Status (T0-T1)

Forty adolescents reported persistent AVH (11.9 %), 130 remission of AVH (38.5%), 15 incidence of AVH (4.5%) and 152 no AVH (45.1%) over five years' time as measured from T0 to T1 (Bartels-Velthuis et al., 2011). There was a significant association between the religiosity groups (T1) and AVH status (T0-T1) (X 2(6) = 13.11, $p<0.04$), with a moderate effect size (φ .14, $p<0.04$). Specifically, moderately religious adolescents (compared to strongly religious adolescents) had 7.9 higher odds (95% C.I. = 1.00 - 64.31) of belonging to the incident group rather than to the referent group. In addition, moderately religious adolescents (compared to non-religious adolescents) had 3.6 higher odds (95% C.I. = 1.05 – 12.05) of belonging to the incident group, rather than to the referent group.

Table 1. *Associations of Religiosity with AVH, Delusions, the Combination of AVH and Delusions, AVH course, and Positive Voices (n = 335)*

		Not Religious	Moderately Religious	Strongly Religious	Total	X^2	df
AVH	Yes	16 (11.0%)	27 (24.5%)	12 (15.2%)	55	8.55*	2
	No	130 (89.0%)	83 (75.5%)	67 (84.8%)	280		
	Total	146 (100.0%)	110 (100.0%)	79 (100.0%)	335		
AVH Severity	Mild	11 (68.8%)	17 (63.0%)	8 (66.7%)	36	8.72	4
	Severe	5 (31.3%)	10 (37.0%)	4 (33.3%)	19		
	Total	16 (100.0%)	27 (100.0%)	12 (100.0%)	55		
DEL	Yes	36 (24.7%)	40 (36.3%)	25 (31.6%)	101	8.72	4
	No	110 (75.3%)	70 (63.6%)	54 (68.4%)	234		
	Total	146 (100.0%)	110 (100.0%)	79 (100.0%)	335		
AVH + DEL	AVH & DEL	11 (7.5%)	18 (16.4%)	8 (10.1%)	37	8.72	4
	AVH	5 (3.4%)	9 (8.2%)	4 (5.1%)	18		
	DEL	25 (17.1%)	22 (20.0%)	17 (21.5%)	64		
	None	105 (71.9%)	61 (55.5%)	50 (63.3%	216		
	Total	146 (100.0%)	110 (100.0%)	79 (100.0%)	335		

		Not Religious	Moderately Religious	Strongly Religious	Total	X^2	df
AVH course	Incident	4 (2.7%)	10 (9.1%)	1 (1.3%)	15	13.11*	6
	Persistent	12 (8.2%)	17 (15.5%)	11 (13.9%)	40		
	Remitted	63 (43.2%)	36 (32.7%)	30 (38.0%)	129		
	Referent	67 (45.9%)	47 (42.7%)	37 (46.8%)	151		
	Total	146 (100.0%)	110 (100.0%)	79 (100.0%)	335		
Positive voices	Yes	9 (56.3%)	15 (55.6%)	8 (66.7%)	32	0.46	2
	No	7 (43.8%)	12 (44.4%)	4 (33.3%)	23		
	Total	16 (100.0%)	27 (100.0%)	12 (100.0%)	55		
Useful voices	Yes	2 (22.2%)	9 (60%)	4 (50%)	15	2.10	2
	No	7 (77.8%)	6 (40%)	4 (50%)	17		
	Total	9 (100%)	15 (100%)	8 (100%)	32		

Note.
**p<0.05, **p<0.01, ***p<0.001.*
AVH, Auditory Vocal Hallucinations; DEL, delusion.

Table 2. *Binomial and Multinomial Regression Analysis to Examine the Odds Ratios Between the Religiosity Groups and AVH and AVH Course (n=335)*

		Non-religious	Moderately religious	Strongly religious
		OR (95% CI)	**OR (95% CI)**	**OR (95% CI)**
AVH[a]	Yes	†	2.64 (1.34 – 5.20)**	1.46 (0.65 – 3.25)
		0.69 (0.31 – 1.54)	1.82 (0.86 – 3.85)	†
AVH course[b]	Incident	†	4.38 (1.28 – 14.96)*	0.525 (0.06 – 4.90)
		1.91 (0.20 – 17.79)	8.33 (1.01 – 68.87)*	†
	Persistent	†	2.48 (1.07 – 5.77)*	1.93 (0.76 – 4.87)
		0.52 (0.21 – 1.31)	1.29 (0.52 – 3.17)	†
	Referrent	†	1.23 (0.71 – 2.14)	1.16 (0.64 – 2.01)
		0.86 (0.48 – 1.56)	1.06 (0.55 – 2.02)	†

Note.
**p<0.05, **p<0.01, ***p<0.001*
a: AVH (no): reference category, b: AVH course (Remitted): reference category, †: religiosity group reference category.
AVH, Auditory Vocal Hallucinations.

Religiosity and Delusions, and the Co-occurrence of AVH and Delusions (T1)

Hundred and one adolescents reported at least one definite delusion (30.1%). There were no significant differences in delusions between the religiosity groups ($X^2(4) = 8.72$, $p = 0.12$). A combined occurrence of AVH and delusions was reported by 37 adolescents (11%) in the total sample. There was no significant association between religiosity and combined AVH and DEL ($X^2(4) = 8.72$, $p = 0.10$).

Religiosity and Positivity, Usefulness and Severity of Voices, and Appraisal of Religious Beliefs (T1)

The majority (n = 32; 58.2%) of the adolescents with AVH reported to have experienced positive voices at least once. There was no significant association between the religiosity groups and positive voices ($X^2(2) = 0.46$, $p = 0.10$). Of the adolescents who reported positive voices, 48.6% found these useful. Usefulness of voices was not significantly associated to religiosity ($X^2(2) = 2.10$, $p = 0.24$.). There was no significant association between religiosity groups and severity of voices ($X^2(4) = 8.72$, $p = 0.92$).

Appraisal of religious beliefs (the Dutch Spirituality and Religiosity Questionnaire, question 5) was reported by 151 adolescents. Of these adolescents, 72 indicated they experienced their religious beliefs in a supportive and helpful manner (47%), 53 reported them to be neither positive or negative (35%), 25 found them alternating between positive and negative (17%), and only one found them oppressive and negative. Of the adolescents who responded to this item and also reported AVH (31; 20.5%), 17 experienced their beliefs in a supportive and helpful manner (54.8%), 8 reported them to be neither positive of negative (25.8%), 5 found them alternating between positive and negative (16.1%) and only one adolescent reported them to be oppressive and negative. Appraisal of religious beliefs was not significantly associated to the reporting of AVH ($X^2(3) = 5.25$, $p = 0.36$).

Qualitative Exploration of the Moderately Religious Group

Given that adolescents with AVH (present and incident) were significantly more likely to be belong to the moderately religious group rather than to the other groups, we aimed to qualitatively examine the nature of religiosity in this group. The pattern of responding to the religiosity questions was examined for the moderately religious adolescents with AVH. Our findings demonstrated that of those who believed in a god or a spiritual force and/or practised religion (n=22; 81%), only a minority (n=7; 32%) was also raised with religion. Thus more than half of the moderately religious voice-hearers who believed in a god/spiritual force and/or practised religion, were not raised with religion, nor were they part of a spiritual community (n = 15; 55.6%). Of the adolescents who were raised with religion and/or were part of a spiritual community (n = 12; 44%), 50% did not believe (n=6). A minority of the sub-sample (n = 6; 22%) was raised with religion but did not believe in god/spiritual force themselves.

6.4 Discussion

The current study investigated the association between AVH, delusions, and religiosity in a five-year follow-up of a population based case-control sample of children with and without AVH (Bartels-Velthuis et al., 2010). Our findings demonstrated that the relationship between AVH and religiosity that has been reported in adults (Aird et al., 2010; Getz et al., 2001; Mohr et al., 2006; Suhail & Ghauri, 2010), is also found in young adolescents in the general population. However, we found no evidence for a linear association, but indications for a non-linear association. Specifically, moderately religious adolescents were more likely to report AVH than non-religious adolescents, but there were no differences between strongly religious adolescents and respectively non- or moderately religious adolescents. Prospectively, moderately religious adolescents were more likely to have recently developed voices than non-religious adolescents and strongly-religious adolescents but there were no differences between strongly- and non- religious adolescents. Interestingly, the majority of moderately religious adolescents with AVH believed and/or practised some sort of religion or spirituality, yet were not raised with religion nor belonged to a religious community. Many adolescents with AVH in this sample had positive voices, unrelated to level of religiosity. Religious beliefs were most often described as supportive and useful, for both adolescents with and without AVH, again unrelated to level of religiosity. In this study, adolescents with concurrent AVH and delusions or severe AVH were not more or less likely to be religious.

In this sample, moderately religious adolescents had a higher likelihood of reporting AVH, both cross-sectionally and over five years' time, in comparison to non- and strongly religious adolescents. This is suggestive of a non-linear relationship between religiosity and AVH in young adolescents. A relationship of this kind has been found previously, i.e. between religiosity and emotional problems in British youth (Meltzer et al., 2011). Being moderately religious was associated with a greater chance of having emotional or anxious complaints, compared to non-religious or strongly religious youth. Meltzer and colleagues noted that moderately religious adolescents may be at a higher risk of psychopathology because they are at odds with their environment and their parents, rendering them more likely to experience a range of emotions, stemming from feelings of guilt, ambivalence and hostility. In line with this were the findings of Kim-Spoon and colleagues (2012). They found that adolescents with a lower level of religiosity than their parents had an increased risk to develop internalizing and externalizing problems than adolescents whose religiousness matched that of their parents. Adolescents who reported a higher level of religiousness than their parents did not have this risk.

However, the reasoning provided by Meltzer and colleagues (2011) and Kim-Spoon and colleagues (2012) is not fully supported by our findings. The majority of the moderately religious adolescents with AVH in our sample, believed in a god or spiritual force and/or practised some form of religion or spirituality, yet were not raised with religion by their parents nor belonged to a religious community. This makes it unlikely that moderately religious adolescents in our

study had a lower level of religiousness than their parents. Moreover, given that in other studies a discrepancy between religiousness of the parent and child signified a source of conflict (Kim-Spoon et al., 2012; Meltzer et al., 2011), one may expect the religiousness to be experienced negatively. On the contrary, many adolescents in the current sample reported supportive and helpful religious beliefs and experienced their voices positively and useful, regardless of the level of religiosity or reporting of AVH.

Religion often functions as a coping strategy (Koenig, 2009), is associated with a higher quality of life (Shah et al., 2011), and a better prognosis (Rosmarin et al., 2013). Moderately religious adolescents with AVH may have adopted religious practices and/or beliefs as a method of coping, appraisal or support for their recently developed experiences. In the current study, religiosity was measured at follow-up, whilst the status of AVH captures the development of AVH from baseline to 5-year follow-up. Therefore it is possible that religiosity may be consequential of the recently developed AVH. This indicates that moderately religious adolescents may have been non-religious at baseline and adopted coping methods in the form of spiritual beliefs and practices over time. The notion that the majority reported either solely having a belief and/or praying, yet did not belong to a community or were raised that way, is supportive of this idea. Given that strongly religious adolescents were less likely to report AVH compared to moderately religious adolescents, their strong religiosity may have served as a protective factor over time. This assumption is in line with studies showing a positive impact of religion in adolescents (Davis, Kerr, & Kurpius, 2003; Pearce, Little, & Perez, 2003; Ritt-Olson et al., 2004) on substance abuse, anxiety, and depressive symptoms.

An alternative explanation may be that adolescents who report an anomalous experience are simply more likely to report believing in (or potentially seeing) a spiritual force and thus acquire the label of moderate religiosity. This indicates that the 'label' of moderate religiosity and AVH may coincide, yet not be resultant of one another. Strong religiosity would still serve a protective factor and is therefore not related to AVH. Even though we regard this explanation less likely, it should be kept in mind when interpreting our findings.

In the current sample of adolescents, religious convictions were not related to the experience of delusions, to AVH severity, or to the combination of AVH and delusions. However, religiosity has been associated with more delusions (Suhail & Ghauri, 2010) in adult clinical samples. Perhaps the association between religiosity and delusions and AVH severity is only evident in patients with current psychosis, and is not present in the context of AVH in adolescents in the general population.

This study has several limitations. First, only a relatively small number of adolescents (n=55) reported AVH, and an even smaller amount reported hearing positive voices (n=32). This may have reduced statistical power of the analyses, limiting robust inferences. Second, religiosity was measured cross-sectionally at follow-up, hampering solid conclusions about a possible

causal relationship. A third limitation is that we did not explicitly measure whether religiosity was used as a coping mechanism. Based on the literature, we merely speculate that the moderately religious adolescents might have used their religious beliefs as a way of coping with AVH. Fourth, as delusions can consist of themes other than mind reading, paranoid ideas or receiving media messages (e.g. delusions of grandiosity), the full scope of delusional ideation may not have been covered in this study. Fifth, the inclusion of our sample was limited to one geographical area, namely Groningen. The adolescents from the rural province of Groningen may differ from adolescents living in more urbanised areas in the prevalence of psychotic experiences, and also in level and form of religiosity (van Os et al., 2001). Groningen is known as the least religious province in the Netherlands, and those who are religious regard themselves mostly as Protestant-Calvinist (Pellenbarg & Van Steen, 2015). Other areas of the Netherlands (e.g. Limburg or Brabant) are more religious and consist largely of Roman-Catholics. Therefore this study needs replication in urbanised and religiously more diverse areas, with religiosity measurements at two time points.

More generally, it should be noted that AVH in itself are also a phenomenon related to other non-psychotic psychopathology (Askenazy et al., 2007), or not to psychopathology at all (Jardri et al., 2014). The occurrence of AVH is considered to be of non-pathological nature providing it occurs within an appropriate cultural context (American Psychological Association, 2013). An indirect indication that AVH reported in this sample are not of psychotic nature lies in the fact that religiosity is not related to the co-occurrence of AVH and delusions; a potential indicator of more severe underlying psychopathology (Smeets et al., 2012).

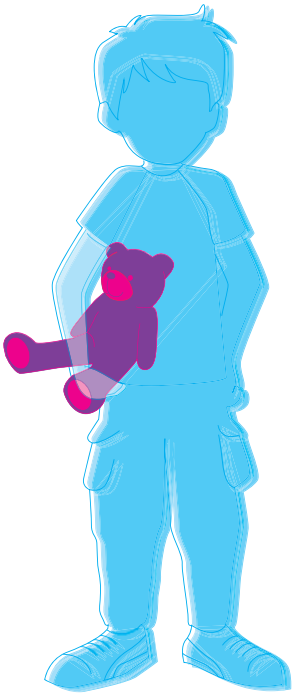
Last, little is known about cultural influences on the reporting and development of AVH during childhood and adolescence, for both clinical and non-clinical samples (Larøi et al., 2014). The literature implies that there is a lower reporting of AVH in non-western cultures, as it is less culturally accepted to do so and is often seen as an indicator of psychopathology (Al-Issa, 1995). In addition, non-western cultures often (though not always) experience AVH as more positive and less distressing in comparison to western cultures (Larøi et al., 2014). Although many adolescents in this study reported positive voices, a substantial amount reported AVH as neutral; a finding which may be altered in a different (non-western) cultural context. Future research should aim to replicate this study in a non-western context as to examine to what extent these findings are culture-dependent.

In conclusion, although religiosity and psychotic experiences have frequently been examined in adults in the general population (Mohr et al., 2006) and in adult patient samples (Suhail & Ghauri, 2010), to the best of our knowledge, such an examination in young adolescents is novel. The current study provides evidence that moderately religious adolescents are more likely to report current and incident AVH, compared to non- or strongly religious adolescents. Based on our data we argue that religiosity may be utilized positively and as a method of appraisal and coping in response to the AVH. If this is the case, these findings may have important implications for clinical practice. Although the current sample consists of non-clinical adolescents

and the majority of their reported AVH may be transitory over time, some adolescents with more persistent AVH may in a later stage be referred to clinical services. In that case, clinicians need to be aware of potential religious beliefs and practices as factors that may relate to coping with AVH. Finding the most appropriate and sensitive manner of adopting these factors into treatment in a way that also fits with the mental health service, is both challenging and crucial.

General Discussion

CHAPTER 7



7.1 Summary and Integration of Findings

Psychotic experiences are prevalent in the general population, not only in adulthood but also in childhood and adolescence (Bartels-Velthuis et al., 2016; Kelleher et al., 2012; Maijer, et al., 2017). Psychotic experiences have the ability to predict psychotic disorders in young adulthood (Fisher et al., 2013; Kaymaz et al., 2012), rendering it essential to understand what predicts the presence, frequency and course of psychotic experiences in childhood and adolescence. As impairments in social cognition and social functioning are prevalent in psychotic disorders, and are often present before the first psychotic episode (Cornblatt et al., 2012; Lavoie et al., 2013; Lee et al., 2015), deficits in social cognition and social functioning may represent a "trait vulnerability" for psychosis (Lavoie et al., 2013; Lee et al., 2015). If an impairment in social cognition is present already in childhood or adolescence, this may cause problems in social functioning in adolescence as a result. Both impaired social cognition and social functioning (and their inter-relations), may render the adolescent more vulnerable for psychosis in young adulthood. By studying whether social predictors of psychotic experiences can be detected in adolescence, it is possible to take a first step to determine when this trait vulnerability can be intervened upon and ultimately, to prevent the first psychotic episode. In this thesis, social predictors such as social cognition, social functioning and religiosity were examined in relation to psychotic experiences in adolescence.

A series of five studies were conducted. First, the Auditory Vocal Hallucination Rating Scale-Questionnaire (AVHRS-Q) was validated in two clinical samples of patients with AVH. Subsequently, the predictive role of social cognition (specifically theory of mind (ToM) and facial emotion identification) was examined in association with the reporting of psychotic experiences in adolescence, in two longitudinal studies. In addition, it was explored whether social functioning mediates the association between social cognition and psychotic experiences. Besides examining social predictors of psychotic experiences in large cohort studies, it was also addressed how the association between social functioning and psychotic experiences manifests itself in four individuals at ultra-high risk (UHR) for psychosis from an idiographic perspective on a day to day basis. Last, the role of religiosity was examined in a case-control sample of young adolescents with and without AVH. In the current chapter, the main findings are summarized and integrated. Strengths and critical points of the chapters are brought forward, and the clinical relevance of the main findings is discussed. Finally, future perspectives and concluding remarks regarding the research in this thesis are presented.

How Can One Reliably Measure Auditory Vocal Hallucinations Through Self-Report?

One of the aims of this thesis was to validate a self-report version of the Auditory Vocal Hallucination Rating Scale (AVHRS; Bartels-Velthuis, van de Willige, Jenner, & Wiersma, 2012; Jenner & van de Willige, 2002). The AVHRS is a semi-structured interview to assess the presence, characteristics and severity of AVH. It has been validated previously in a child and adult sample demonstrating good psychometric abilities (Bartels-Velthuis, van de Willige, Jenner, & Wiersma, 2012). Given that self-report measures are likely more cost-effective, time-efficient, do not require training of interviewers and can be delivered online, the Auditory Vocal Hallucination Rating Scale Questionnaire (AVHRS-Q) was developed.

In Chapter 2, the AVHRS-Q was evaluated in two clinical samples. In the first sample, 32 psychiatric patients with AVH were assessed with both the AVHRS and AVHRS-Q, and the internal reliability and convergent validity was studied. In the second sample, 82 psychiatric patients with AVH completed the AVHRS-Q and measures of psychological distress (the Outcome Questionnaire, OQ-45; Lambert et al., 1996 and the Symptom Checklist, SCL-90; Derogatis et al., 1976) and quality of life (the Manchester Short Assessment of Quality of Life, MANSA; Priebe, Huxley, Knight, & Evans, 1999), as part of ROM assessments and their data was retrospectively examined to determine divergent validity. The findings showed that the AVHRS-Q had a good internal consistency. The AVHRS-Q had a high convergent validity with the AVHRS, as evidenced by high correlations between the overall severity score and the separate items of both measures. The AVHRS-Q had only moderate correlations with the measures of psychological distress and quality of life, indicative of good divergent validity. Overall, the AVHRS-Q is a valid and reliable instrument that can readily be used to assess characteristics and severity of AVH in a quick (about six minutes) manner in individuals with AVH. The AVHRS-Q can be used both for research purposes and in clinical contexts.

It is important to note that the AVHRS-Q was not validated in an adolescent sample. The AVHRS-Q was used in the second (online) follow-up assessment of a case-control study on AVH in adolescence (Bartels-Velthuis, et al., 2011; Bartels-Velthuis et al., 2016; Bartels-Velthuis et al., 2010). However, given that only 15 of 293 adolescents reported AVH at age 18-19 years during this second follow-up, this data was not sufficient for a validation study. Instead, data was used from two patient samples with AVH, one recruited for the purpose of the validation study, and another retrospectively retrieved from the Routine Outcome Monitoring (ROM) database of the University Medical Center Groningen (UMCG). Given that the AVHRS-Q was based on and converges with the AVHRS (interview), which was validated in a child and adolescent sample, it is likely that the self-report version has the same good psychometric properties in adolescent samples. However, future research should replicate the validation study of chapter 2 in an adolescent sample with AVH, to confirm that our assumptions are correct.

Is Social Cognition Predictive of Psychotic Experiences in Adolescence and is this Mediated by Social Functioning?

The psychosis literature consistently demonstrates that social cognition may represent an underlying trait vulnerability for the development of psychosis (Lavoie et al., 2013; Lee et al., 2015). Evidence in support of this association can be found in studies which demonstrate that social cognition is impaired in first episode psychosis (Thompson et al., 2012), the UHR phase of psychosis (Lee et al., 2015; Van Donkersgoed et al., 2015), and in siblings of individuals diagnosed with psychosis (Bora & Pantelis, 2013). This inspired the aim of the current thesis, namely to investigate whether social cognitive abilities at preadolescence can predict psychotic experiences in adolescence, with the aim of potentially informing pre-emptive interventions as to prevent the development of a first psychotic episode. This question was addressed in chapters 3 and 4, by examining two different components of social cognition in relation to psychotic experiences.

Specifically, in chapter 3 it was examined whether ToM ability (at age 12-13 years) can predict psychotic experiences six years later (age 18-19 years) in a sample of 157 adolescents partaking in the second follow-up of a case-control study on AVH. Subsequently in chapter 4, it was examined whether facial emotion identification (age 11 years) can predict psychotic experiences five years later (age 16 years) in a sample of 2059 adolescents taking part in an epidemiological cohort study. These chapters also explore whether social functioning (general functioning and within the family environment) mediates the relationship between social cognition and psychotic experiences.

In this thesis, evidence for the trait vulnerability of impaired social cognition for psychotic experiences in adolescence was not found. Specifically, neither ToM ability at age 12-13 years (chapter 3) nor facial emotion identification at age 11 years (chapter 4) was associated with psychotic experiences at age 18-19 and age 16 respectively. In both chapters, it was argued that these findings could be explained by the characteristics of our community samples. Perhaps social cognitive abilities in our samples were too high (or too well developed) to detect a trait vulnerability for psychosis. It is possible that only when social cognitive abilities are below a certain threshold, they will represent a risk factor for future psychotic experiences. By conducting a post-hoc examination of the lowest scorers on social cognition in both cohorts (the 10% lowest scorers on ToM in chapter 3, and the 5% lowest scorers on facial emotion identification in chapter 4) it was speculated that this subgroup may represent a more vulnerable 'at risk' group of adolescents and thus were more representative of individuals with actual trait impairments in social cognition. However, even adolescents with the lowest social cognition scores in both samples did not demonstrate increased psychotic experiences over a six (chapter 3) and five (chapter 4) year follow-up period.

It is possible that our null-findings can be explained by the non-specific and transient nature of psychotic experiences during adolescence. To specify, the rationale behind studying psychotic experiences as an outcome measure, was that psychotic experiences are a precursor to (and thus a proxy for) psychotic disorders in adulthood (Fisher et al., 2013; Kaymaz et al., 2012), and when they persist they will progress into clinical symptoms and eventually a first psychotic episode (clinical staging model; McGorry et al., 2010). Therefore, risk factors present at clinical stages (e.g. social cognition impairments in first episode psychosis; Thompson et al., 2012) may already be present at (non-clinical) prodromal stages. However, a recent study of Mollon and colleagues (2018) found that increasing cognitive impairments between the ages of 8 and 20 years were only evident for individuals with psychotic disorders, with only weak evidence for individuals with psychotic experiences. This might be because most psychotic experiences are transient and possibly not an indicator of risk in itself (van Os et al., 2009). Indeed, a longitudinal cohort study in the general population with a follow-up period of 11 years found that although 50% reported AVH at age 7-8 years (case-control study on AVH), only 6% still reported AVH at age 18-19 years (Bartels-Velthuis, et al., 2011; Bartels-Velthuis et al., 2016; Bartels-Velthuis et al., 2010). Similarly, in a large population based sample of young adults, it was found that of those

who reported psychotic experiences at age 12 years, 79% of these had remitted at age 18 years. Therefore, predicting psychotic experiences early in life, may not necessarily be indicative of a psychotic disorder (or other mental health problems) in the future, which may also explain why an association between a psychotic experiences and lowered social cognitive ability in adolescence was not found. This will be further addressed in the 'Strengths and Critical Points' section in the current chapter.

Another explanation for the findings in chapters 3 and 4 is that the social cognitive impairment that is evident throughout multiple phases of early and chronic psychosis, is actually a state impairment. The four primary criteria for a trait vulnerability are that the impairment (1) is present in individuals with the disorder (a psychotic disorder in this case), (2) does not only occur during clinical episodes, (3) is observed in unaffected family members, and (4) is heritable (Green et al., 2015). There are relatively strong empirically supported indications that social cognition may indeed signify a trait vulnerability for psychosis, as (1) social cognition is indeed impaired in psychotic disorders (Mehta et al., 2013), (2), social cognition remains impaired during remission of psychosis (Herold et al., 2002; Inoue et al., 2006), (3) social cognition is also impaired in unaffected siblings (Bora & Pantelis, 2013) and (4) may be heritable (Leppänen et al., 2008). However, there is also evidence for the contrary: not all studies confirm that social cognitive deficits are present in earlier phases of illness. Some studies in UHR samples did not find an impairment in facial emotion identification (Pinkham, Penn, Perkins, Graham, & Siegel, 2007), or ToM ability specifically (Couture, Penn, Addington, Woods, & Perkins, 2008). In addition, there is some suggestion that social cognitive deficits are poorer in acute episodes than in phases of remission (Addington & Addington, 1998; Kee et al., 2003; Pinkham et al., 2007). Moreover, several studies did not find a (longitudinal) association between social cognition and psychotic experiences in childhood and adolescence (Bartels-Velthuis, et al., 2011; Sullivan et al., 2013; Thompson et al., 2011). In sum, the evidence is not conclusive that social cognition is a trait deficit in psychotic disorders. Therefore, poorer social cognition seems to be a vulnerability for clinical psychosis, but the evidence is still inconsistent whether social cognition in childhood and adolescence is predictive of psychotic experiences in adolescent general population samples.

As there was no association between social cognition and social functioning in chapter 3 nor in chapter 4, there was also no indication that (general or family) functioning mediated this (non-evident) association in adolescence. To specify, in chapter 3 it was formally tested whether ToM was associated with psychotic experiences, and whether this was mediated by social functioning. In Chapter 4 the mediating role of social functioning between facial emotion identification and psychotic experiences was only explored if a significant association between facial emotion identification and psychotic experience was found. In the psychosis literature, it is often suggested (and confirmed) that poor functioning may be a result of poor social cognition in individuals diagnosed with a psychotic disorder (Couture et al., 2006). However, there is some evidence that in healthy adult samples (Pijnenborg et al., 2009) there may not be an association between social cognition and social functioning. Therefore, perhaps only at levels of chronic

impairment in social cognition, this ability may have an impact on social functioning. As such, social functioning may indeed mediate the association between social cognition and psychotic symptomatology in psychotic disorders, but this association is not consistent (or perhaps not even present) in adolescent community samples.

Is the Family Environment Predictive of Psychotic Experiences in Adolescence?

The family environment has received much attention in the psychosis literature. The evidence shows that the family environment is an important risk factor for the prognosis of psychosis and future relapse in psychotic disorders (Butzlaff & Hooley, 1998; Goldstein, 1985; Hooley, 2007; Wahlberg et al., 2004; Weintraub et al., 2017). For these reasons, family interventions addressing expressed emotion, family communication, and parenting styles, have been developed with the aim of improving prognosis of psychosis (Haddock & Spaulding, 2011). These interventions generally focus on improving the interpersonal environment, by providing problem formulations, psychoeducation, problem-solving strategies and goal setting, with the overall aim of improving social functioning of all family members. These interventions show good results on relapse rates, hospital admissions and compliance to medication (Pfammatter, Junghan, & Brenner, 2006).

In the current thesis, it was examined whether family factors can predict psychotic experiences in adolescence, before the presence of a psychotic disorder. This is an interesting question, because the majority of studies examine the family environment in clinical samples with psychotic disorders (e.g. Hooley, 2007). However, it is also possible that the family environment is associated with the development of psychotic experiences (not only the maintenance and prognosis of a psychotic disorder). In chapter 4, it was examined whether family functioning at age 11 years (parenting styles, overall family functioning and parental stress) was predictive of psychotic experiences at age 16 in a large epidemiological cohort sample of 2059 adolescents. Our findings show that increased overprotective parenting at preadolescence was associated with a higher frequency of psychotic experiences in adolescence, even after adjustment for preadolescent mental health. There was no indication that parenting stress, family functioning, and rejective and warm parenting were associated with psychotic experiences, indicating that perhaps these factors may not pose a vulnerability for psychotic experiences.

It is important to be cautious when interpreting these findings, as there are several possible explanations; there could be a causal relation (in any direction) or there could be another variable explaining the relationship. The first causal explanation could be that overprotective parenting indeed serves as a risk factor for psychotic experiences. When parents overly protect their child, the child may be less able to form its own ways of coping with stressors in daily life, or forming its own ideas about other people and situations. Children therefore may continue to believe that novel situations are beyond their coping skills, and thus rely on withdrawal strategies, avoidance and dependence on parents (Kiel & Maack, 2012). When the child becomes an adolescent and is expected to be more autonomous, they may be less resilient to negative and stressful occurrences, rendering them more vulnerable to develop psychotic experiences. Overprotective parenting as measured by the EMBU (Markus et al., 2003), seems to resemble the

concept of emotional over involvement in the expressed emotion literature in some way (Hooley, 2007). It is thought that emotional over-involvement is predictive of relapse because the relative (most often the parent) overly protects, intrudes, and takes over the individuals' autonomy. In turn, this severely obstructs the individual's own decision-making, self-worth, and opportunities for recovery (Goldstein, 1985; Hooley, 2007). Overprotective parenting in childhood may overlap with emotional over-involvement, as both concepts reflect intrusive/protective behaviors by a relative, which is often out of proportion or exaggerated relative to the situation. It is important to note, that overprotective parenting is associated with a range of other negative outcomes in adolescence as well, such as substance abuse (Creemers et al., 2011; Visser et al., 2013), anxiety (Van Oort et al., 2011), and internalizing and externalizing problems (Kiel & Maack, 2012; Sentse et al., 2010). Therefore, although no cause-effect conclusions can be drawn, it is important to further explore these associations and to understand whether overprotective parenting indeed serves as a risk factor for psychotic experiences in adolescence. If confirmed, it may be especially important to offer family interventions with a focus on psychoeducation, to provide information regarding the role of overprotective parenting in the development of psychotic symptomatology.

Another causal explanation for these findings may be that overprotective parenting is a natural reaction of the parent towards a child who is vulnerable for developing mental health problems. This may indicate that overprotective parenting is warranted, and parents are trying to support their child and make the life of the child predictable and easier to cope with in light of their awareness of the vulnerability. As an alternative explanation, it is also possible that perhaps a shared underlying vulnerability (e.g. low IQ) resulted in both overprotective parenting in the parent and psychotic experiences in the child. Last, a measure of psychotic experiences at age 11 years was not assessed in the TRAILS cohort and therefore the found association was corrected for overall problem behavior at age 11 instead. Perhaps psychotic experiences at age 11 were the driving factor for the parent's overprotecting behavior, a finding that may have gone undetected by examining overall problem behavior at age 11. As such, more research is needed to identify the mechanism that is driving the association between overprotective parenting and psychotic experiences in adolescence.

A last and unexpected finding in chapter 4, was that rejective parenting, parenting stress, lower family functioning and a lack of warm parenting were not significantly associated with psychotic experiences during adolescence. A first explanation may be that rejective parenting is more relevant for the development of other types of psychopathology, such as aggressive problems (Sijtsema et al., 2014), whereas overprotective parenting is specifically relevant for more psychotic or internalizing problems (Van Oort et al., 2011). A second explanation could be that compensating factors (such as strong peer bonds) can decrease the predictive ability of negative parenting styles (such as harsh and dominant parenting) on psychopathology in adolescence (Lansford et al., 2003). Given that overprotective parenting increases the risk of peer victimization and reduces opportunities for making friendships (Olweus, 1993; Smith & Myron-Wilson, 1998), this compensatory effect may not have been present for overprotected children specifically.

Future research is needed to examine whether the association between overprotective parenting and psychotic experiences could be mediated partially by the lack of good-quality peer bonds.

What is the Association between Social Functioning and Psychotic Experiences in Daily Life in the Ultra-High Risk of Psychosis Phase?

The literature indicates that social functioning is often impaired in individuals with a psychotic disorder (Addington et al., 2008; Couture et al., 2006) and that this impairment is evident in earlier phases of psychosis as well, such as the UHR phase (Ballon et al., 2007). The social impairment has often been suggested to be a risk factor for the first transition to a psychotic episode (e.g. Cannon et al., 2008), yet the evidence for this claim is not always consistent (Brandizzi et al., 2015; Schultze-Lutter et al., 2015). One explanation is that inter-individual differences in the association between social functioning and changes in psychotic symptoms underlie the variation in findings. For example, it is possible that for some individuals, changes in social functioning precede changes in psychotic symptoms (therefore leading to the first transition; e.g. Velthorst et al., 2009) and for others it may only be that changes in psychotic symptoms precede changes in social functioning, such as social withdrawal (e.g. Salokangas et al., 2014). So far, examining social functioning in the UHR for psychosis phase has often been done adopting a between-subjects perspective, therefore overlooking potential inter-individual differences that might be important for outcome or treatment. This has motivated the aim of chapter 5, namely to investigate the role of social functioning in the UHR phase over period of 90 days, from an idiographic, within-subjects perspective, in a series of four individuals at UHR for psychosis.

The sample investigated in the study in chapter 5, was small and heterogeneous. The four individuals consisted of two males and two females, ranging between 20 and 31 years of age. They were all in treatment at a mental health facility for a depressive disorder and simultaneously fulfilled criteria for being at UHR for psychosis. By conducting a time-series analysis (T=90) for each individual separately, it was found that the association between social functioning and paranoia manifested itself differently between participants. The most consistent finding was that for all four participants, increases in paranoia on one day were followed by increases in social functioning on the next day. One explanation may be that individuals actually seek support as a reaction to the feelings of paranoia, and that seeking social support and the presence of others may represent a coping mechanism for psychotic experiences in daily life. Interestingly, one individual demonstrated that decreases in social functioning were followed by increases in paranoia, yet this effect was not maintained over time. As such, social functioning may not only represent a 'risk factor' for psychosis in UHR individuals, but it may also represent a manner of coping with psychotic experiences in daily life.

The results of this study imply that social functioning could be further explored as a coping mechanism in the UHR phase for psychosis. These findings are important, as other research demonstrates that by the time the first psychotic episode has occurred, individuals report low social support, loneliness and the absence of a confidant (Sündermann, Onwumere, Kane, Morgan, & Kuipers, 2014). In turn, loneliness has shown to increase anxiety (Heinrich & Gullone, 2006) and

anxiety increases symptoms of paranoia (Freeman & Garety, 2003). Given that the social network may still be actively used as a source of coping in the UHR phase, it is important to intervene and maintain the social network before the first psychotic episode, as to prevent worsening of symptomatology. Currently, treatment of individuals at UHR for psychosis consists of cognitive behavioral therapy with a focus on reducing psychotic symptoms (Van Der Gaag et al., 2012). Although symptoms improve with treatment, the social impairment persists and worsens over time (Brandizzi et al., 2015). Based on the findings in chapter 5, it may be possible that some individuals at UHR for psychosis could benefit from treatments that focus more on utilizing the social network and re-integrating into the social community (similar to treatments in chronic psychosis: Dixon et al., 2010). However, given that only four individuals at UHR for psychosis were examined, it is not feasible to generalize these treatment recommendations to all individuals at UHR for psychosis. Instead, the current research may spark the interest of researchers and clinicians to shift the focus of social functioning as a risk factor, to social functioning as a source for intervention opportunities in the UHR phase for psychosis.

Is Religiosity Associated with Psychotic Experiences (specifically Auditory Vocal Hallucinations) in Adolescence?

Religiosity may be seen as a 'social' phenomenon, which is emotionally and connectively shared amongst others with the same religious beliefs (Beckford, 2004). In the context of social functioning, religion can be viewed as a social construct through which we identify ourselves and connect with others and a 'supernatural' creator or God (Beckford, 2004). Religiosity is associated with a higher prevalence of psychotic experiences (Mohr et al., 2006), both in adults in the general population (Aird et al., 2010) and in clinical samples (Getz et al., 2001; Suhail & Ghauri, 2010). The general consensus in studies utilizing clinical samples, is that religiosity can have both a positive and a negative influence on psychopathology in adults (Koenig, 2009; Pargament et al., 1998). This is because for some patients religion can provide a source of meaning and a way of coping with symptoms (Mohr et al., 2006), whereas for others it may promote distorted perceptions and distrust of others (Aird et al., 2010). In this thesis, it was of interest to explore the association between AVH, delusions, and religiosity in a follow-up study (over five years) of a case-control sample of 337 youth with and without AVH.

The findings in chapter 6 demonstrated that moderately religious adolescents were more likely to report, and to have recently developed, AVH, compared to both non- and strongly religious adolescents. Non-religious adolescents did not differ from strongly religious adolescents in terms of prevalence or development of AVH. The findings were in line with earlier studies (Meltzer et al., 2011) where it was speculated that moderately religious youth may be more at odds with their environment and their parents (who may be more religious than them), resulting in mental distress and psychopathology. Nonetheless, the adolescents in the current study reported mostly positive voices, and reported helpful and supportive religious beliefs. In addition, the majority of the moderately religious adolescents with AVH, believed in a god or spiritual force and/or practiced some form of religion or spirituality, yet were not raised with religion by their parents nor belonged

to a religious community. Placing the findings in the context of the literature, it is speculated that moderately religious adolescents with AVH may have adopted religious practices and/or beliefs as a method of coping, appraisal or support for their recently developed experiences. Placing their experiences in a religious context, whilst identifying themselves with religious others or a God, may also provide a sense of social support. Previous research in clinical samples supports this idea, as patients with psychosis often place their experiences in a religious context, alongside biological explanations, and find comfort in this (Marriott, Thompson, Cockshutt, & Rowse, 2018). It has been found that religion can provide comfort, hope and meaning in individuals who are distressed (Koenig et al., 2009), and eventually even improve prognosis (Rosmarin et al., 2013). Although the majority of AVH may be transient in this sample of 12-13 year old adolescents, some of them may present themselves at services in the future if their AVH persists over time. In that case, clinicians need to be aware of religious beliefs and practices as factors that may represent coping methods with AVH, and to integrate this into treatment in an appropriate and sensitive manner.

Religiosity may provide a source of coping, not only in patients with chronic psychosis, but also in children with milder (subclinical) symptoms, such as AVH. However, future studies should attempt to replicate these findings by measuring religiosity at multiple time-points (in the current thesis religiosity was assessed cross-sectionally) and religiosity questionnaires should include specific questions about religious coping. It is therefore not possible to draw solid conclusions on causal relationships and it can only be speculated that religious beliefs served as a way of coping with AVH.

7.2 Strengths and Critical Points

There are a number of significant strengths to this thesis. First, the research in this thesis has taken a clinical staging approach (McGorry et al., 2010), by examining children and adolescents at different ages (age 11, 12-13, 16, and 18-19 years) and stages of the prodromal period (a general population sample, a case-control cohort and an UHR sample). This allows for conclusions to be drawn from samples with different ages and at different stages along the clinical staging model, providing more evidence that social cognition and psychotic experiences are not consistently associated in adolescence. Second, two domains of social cognition have been examined, namely ToM ability (Chapter 3) and facial emotion identification (chapter 4). Examining multiple components of social cognition, whilst not finding an association with psychotic experiences, again emphasizes that the association between social cognition and psychotic experiences is at least not consistently present in adolescence. Third, the hypotheses in this thesis were often studied using longitudinal data, assessing a span of six years (chapter 3), five years (chapter 4) and daily over a period of 90 days (chapter 5). There was relatively little attrition in chapter 4 and 5, which is a strength of the data presented in this thesis. Fourth, psychotic experiences were assessed in numerous ways, such as AVH (chapter 2 and 6), psychotic experiences in general (chapter 3 and 4), more specific types of psychotic experiences (e.g. delusions, paranoia) (chapter

4 and 5) and the course of psychotic experiences (chapter 6). Fifth, the focus of this thesis was not only on the predictive ability of social factors on psychotic experiences using a between-subjects perspective, but also using a within- subjects perspective (chapter 5). This has provided this thesis with a unique perspective on the association between social functioning and psychotic experiences, when examined from an idiographic perspective in daily life. Sixth, this thesis did not only examine general social functioning (chapter 3), but also family functioning (chapter 4), and social support and presence of others (chapter 5).

A number of critical points are crucial to bring forward. The first is the focus on psychotic experiences in adolescence. Psychotic experiences have been shown to be associated with concurrent impaired social functioning and mental distress (Kelleher et al., 2015) and an increased risk of psychotic disorders in adulthood (Dominguez et al., 2011; Fisher et al., 2013) and are therefore important to examine in adolescence. However, psychotic experiences are also often transient and benign in adolescence (Bartels-Velthuis, et al., 2011; Bartels-Velthuis et al., 2016; Bartels-Velthuis et al., 2010), and some have implied that psychotic experiences may even be part of typical brain development (e.g. immaturity of certain brain regions in adolescence may result in temporary vulnerability for experiencing AVH; Maijer, et al., 2017a; van Os et al., 2009). Therefore, when predicting the frequency of psychotic experiences, it is possible that a year later these psychotic experiences will have disappeared given their transient nature. Moreover, psychotic experiences have shown to raise the risk of psychotic disorders in the future, but also of a range of other psychiatric diagnoses (Barragan, Laurens, Navarro, & Obiols, 2011; Welham et al., 2009; Werbeloff et al., 2012; Wigman et al., 2012; Yung et al., 2008). Psychotic experiences may therefore represent a trans-diagnostic (non-specific) risk factor for general mental health problems. For example, a large study using multiple independent samples demonstrated that the majority of community-based adolescents who reported psychotic experiences met criteria for at least one (non-psychotic) DSM-IV Axis-1 psychiatric disorder (Kelleher et al., 2012). In addition, in a clinical sample of children with AVH, only 11% met criteria for a psychotic disorder whereas the remainder of children met criteria for a range of other psychiatric disorders, such as an anxiety disorder or ADHD (Maijer, et al., 2017). If the examined social risk factors (such as ToM ability) are specific trait vulnerabilities for psychotic disorders only, a trans-diagnostic outcome variable (i.e. a psychotic experience) may not be specific enough to detect a trait vulnerability for psychosis in childhood and adolescence. Instead, it may be more fruitful to examine whether psychotic experiences have improved predictive ability for psychotic disorders when combined with the presence of other social risk factors, such as for example, the presence of AVH in combination with a deficit in ToM and a social impairment.

An important issue is whether it is desirable, ethical and feasible to screen for social risk factors and psychotic experiences from childhood and/or preadolescence. The key argument that is brought forward in this thesis and in prediction research as a whole, is that we want to screen, prevent and intervene in psychotic disorders as soon as possible. Although early intervention for individuals at risk for psychosis provides an opportunity to prevent the development of a

first psychotic disorder (Paolo Fusar-Poli et al., 2012), it also delivers a label of risk with possibly stigmatizing effects (Carpenter, 2009; Corcoran, Malaspina, & Hercher, 2005; Yang et al., 2013). It is therefore important that early screening and consequential 'risk' labeling is only being carried out based on sufficient evidence that it prevents the development of a psychotic disorder. Currently, the earliest occasion to screen for psychotic disorders in the Netherlands is from the age of 14 years and onwards, based on of having sought clinical help for (non-psychotic) mental health problems and in the presence of either a genetic risk for psychosis or psychotic symptomatology (thus meeting UHR for psychosis criteria). Evidence from meta-analyses demonstrate that prevention treatments in the UHR for psychosis phase yield a reduction in 12-month transition rates by 54 to 56%, which is substantial (Schmidt et al., 2015; Van Der Gaag et al., 2013). Although there may be negative side-effects of receiving the UHR label (Carpenter, 2009; Corcoran et al., 2005; Yang et al., 2013), there is sufficient evidence that screening for UHR criteria in young help-seeking samples is effective and feasible. Based on findings in this thesis and earlier studies using the same samples (Bartels-Velthuis, et al., 2011; Bartels-Velthuis et al., 2016; Bartels-Velthuis et al., 2010), there is not enough evidence to recommend screening for social risk factors or psychotic experiences in children and adolescents in the general population. Given the lack of associations between social risk factors and psychotic experiences in this thesis, and the possibly transient and benign nature of psychotic experiences in adolescence, screening in the general population would currently lead to too many false-positives.

Social cognition was assessed at a single time point in adolescence, with a specific aspect (either ToM ability or facial emotion identification) assessed separately in each study. However, evidence shows that social cognition is still developing throughout adolescence (Taylor, Barker, Heavey, & McHale, 2015), rendering it possible that individuals who may have scored low at age 12 - 13 years (chapter 3) or at age 11 (chapter 4) have 'caught up' to competent social cognitive abilities at a later point in adolescence. Indeed, previous studies have shown that adolescents between the ages of 12 and 15 years scored significantly lower on measures of ToM and facial emotion identification, in comparison to young adults between the ages of 18 and 22 years old (Vetter, Altgassen, Phillips, Mahy, & Kliegel, 2013). This indicates that both ToM ability and facial emotion identification ability are not fully developed nor stable throughout adolescence (between ages of 12 to 22 years) and it is possible that low performance at preadolescence will not necessarily predict the level of social cognitive abilities at young adulthood. Perhaps longitudinal trajectories of social cognitive development (e.g. declining or persistently low abilities) are important to determine the development of a psychotic disorder at young adulthood, rather than static moments in time. There is already some evidence that declining (rather than persistently low) trajectories of social skills in childhood are predictive of adolescent psychotic experiences (Hameed et al., 2018). How these findings relate to trajectories of social cognition throughout adolescence, and the subsequent development of a psychotic episode, has not yet been examined. A second perspective to take into account, is that different aspects of social cognition may remain stable throughout adolescence, whereas others may continue to develop. For instance, the development of facial emotion identification in static stimuli has

been shown to be reasonably stable from age 17 onwards, whereas the development of facial emotion identification in dynamic stimuli continues to develop from ages 18 and 20 years (Taylor et al., 2015). Moreover, it has been shown that specific aspects of ToM ability may deteriorate at differing points throughout the development of psychosis. For example, a review by Healy and colleagues (2016) found that second-order ToM ability was more consistently impaired than first-order ToM ability in first episode psychosis. In order to get a true grasp on the presence of a trait vulnerability in social cognition throughout adolescence, it may be necessary to assess different (aspects of) social cognition and at multiple times throughout adolescence.

All studies used observational designs where X and Y were measured at two (or more using experience sampling methodology) different time points and a speculative conclusion was drawn about the potential causal influence that X has on Y. However, by relying on observational designs, causality between X and Y can never be truly tested. In order to assess causality, three conditions must be met: (a) there is a significant association between X and Y, (b) X should occur before Y in time, and (c) there are no other confounding factors which could explain the association between X and Y (the effect must occur in isolation) (Kline, 2011). Longitudinal studies may fulfill criteria a and b, but not criterion c. For example in chapter 4 a significant effect of overprotective parenting on psychotic experiences was found, but as stated previously, this can also be caused by a third variable. In addition, the found association was corrected for mental health problems at baseline, but as psychotic experiences at baseline could not be specifically controlled for, it is still possible that the association was driven by psychotic experiences from the start. Although chapter 6 studied potential causal effects of social functioning and psychotic experiences in the UHR phase, true causality was not actually assessed. Granger causality tests can only assess whether X precedes Y, or whether Y precedes X, but it cannot rule out that the effect was caused by a third variable. Given that diary studies take place in natural contexts without control of the researcher, it is impossible to ensure that the examined association occurs in isolation. However, it is important to note that the testing of condition a (a significant association between X and Y) and b (X should occur before Y in time) is an important first step, because if condition a and condition b are not met, it is unlikely for condition c (the effect must occur in isolation) to be met either. For condition c to be tested, and causality to be established, an experimental design must be used. In this design, the potential cause is manipulated (in our case, for example social cognition), and to examine whether it affects Y (psychotic experiences) in the absence of the influence of other variables. Future research is needed to examine whether it is possible to address this association in a lab setting and, subsequently, to compare these lab findings with how the associations are expressed in real life (which may differ from the lab context). One option for future research would be to use virtual reality to train adolescents in social cognitive abilities (e.g. an emotion identification training; manipulation of X), to determine their social functioning in a virtual reality environment (assessment of M) and subsequently, to assess their level of experienced paranoia in a virtual reality task (assessment of Y), as compared to adolescents who did not receive the manipulation. The current virtual reality programs, such as DISCOVR and VR-CGT (see also: http://www.vrmentalhealth.nl), would allow for such experimental designs to be explored.

Variables were often assessed as aggregations of multiple components. For example, social functioning in chapter 3 consists of (amongst others) functioning at school, at home, with parents, and with friends, whilst psychotic experiences in chapter 4 consist of (amongst others) seeing or hearing things, feeling paranoid, and experiencing delusions. Although it is a valid approach to examine whether one construct is associated with another, subtle variations in associations may only be found when examining specific components of larger multifaceted constructs. In chapter 5, a daily diary assessment was used to assess psychotic experiences and social functioning on a daily basis. Specific components were selected to conduct analyses with, specifically paranoia (the psychotic experience) and social support and social presence (social functioning). By examining specific parts of a larger construct it was possible to detect unique associations that may have gone unnoticed when examining the entire construct, namely that social support or being in the presence of others, may serve as a coping mechanism for paranoid experiences. On the other hand, it is also possible that by examining specific items such as paranoia or social support, the original idea of examining the association between psychotic experiences and social functioning is bypassed. Perhaps social functioning only serves as a risk factor when examining all components and interactions simultaneously (school, community, parents, friends, chores), rather than when focusing solely on the lack of social support. This should be kept in mind when interpreting the findings.

7.3 Clinical Relevance

The rationale behind predicting psychotic disorders using social predictors in childhood and adolescence is to identify individuals vulnerable to psychotic disorders at an earlier stage and to intervene promptly. As a society, we want to be able to foresee negative outcomes, in order to potentially prevent them. However, the current state of scientific evidence does not allow us as a society to do this accurately. Looking at the bigger picture of evidence, there are many variables to take into account when examining how psychotic disorders develop over time. In a very brief summary, it usually involves a combination of genes (a combination of at least 108 genes; Ripke et al., 2014) and the environment (to name a few: cannabis, trauma, urbanicity, migration, social isolation; van Os, Kenis, & Rutten, 2010). However, at the same time, not all individuals who have had a traumatic experience develop psychosis, and not all who have a genetic risk for psychosis end up developing a psychotic disorder. Therefore, it is increasingly complex and difficult to predict the diagnosis of a psychotic disorder. Even in the UHR phase, the transition rate within three years is only 33 percent (Paolo Fusar-Poli et al., 2012), and just one third of pre-clinical psychosis is reportedly preceded by psychotic experiences in adolescence (Dominguez, Wichers, Lieb, Wittchen, & Van Os, 2011). Therefore, in light of the studies conducted in this thesis and the evidence outlined in the literature, it is too premature to address the clinical relevance of predicting psychotic experiences using social predictors in childhood and adolescence.

Integrating the findings from chapters 2 to 6, there are a number of clinical recommendations that can be brought forward. Firstly, it is not recommended to provide social cognitive interventions for adolescents in the general population in the context of preventing psychotic experiences.

Currently, it is only recommended to deliver social cognitive interventions at more clinical stages in psychosis for help-seeking individuals, with moderate to large effects on the social impairment (Kurtz, Gagen, Rocha, Machado, & Penn, 2016). Second, current treatments for individuals in the UHR phase focus on reducing psychotic symptoms, whilst the social impairment is not explicitly treated nor relieved (Van Der Gaag et al., 2012). Based on the findings presented in this thesis, it is recommended that the social network is further explored as a potential coping or protective mechanism in UHR treatments. Third, religiosity may provide a source of comfort and coping for adolescents reporting AVH in the general population. If adolescents seek help for their AVH, it may be beneficial for them to receive the option of obtaining therapy that incorporates religiosity or spirituality in some form. Fourth, the AVHRS-Q shows good psychometric properties in this thesis and can therefore be administered in clinical practice to individuals reporting AVH.

The use of diary methods has potential for clinical practice. Diary methods may give unique insights into individual targets for intervening and in treatment progress. By examining the same concept or associations within one person on a day-to day-basis, this might reveal novel perspectives that are not explicitly reflected on by the patient or the therapist. Anecdotally, it should be emphasized that for the four UHR participants taking part in the MIRORR study (chapter 4), the day- to-day diary assessments were a novel and interesting experience for them. Two of the participants recognized the patterns and associations identified in the diary assessments, whilst the remaining two did not. Although it may give clinicians new insights into the functioning and symptomatology of their clients, it can also give clients themselves a new insight (and possibly empowerment) into their symptoms and the associations between these symptoms. In order to relieve the social impairment in the UHR phase, it might be important to tailor treatments to the individual and offer personalized intervention packages. The use of diary methods might be one of the ways to do this. However, there are some flaws to these methods that one needs to keep in mind. Dynamic time-series models assume that symptoms fluctuate over time and do not take into account clinical cut-offs (Bringmann & Eronen, 2018; Bringmann, Ferrer, Hamaker, Borsboom, & Tuerlinckx, 2018). This could be problematic as, for example, persistent high levels of paranoia might be relevant for treatment outcome, yet cannot be modeled using these methods due to the lack of fluctuations. In addition, fluctuations in relatively 'normal' paranoia is given just as much importance, as fluctuations in clinical levels of paranoia, although the latter is likely much more clinically relevant. Last, it is still unclear if an individual approach would yield better outcomes than current treatments targeting generic or common underlying factors for all individuals. As of yet, more research needs to be conducted before diary methods can be implemented routinely in clinical practice, including replication studies and prognostic validity studies.

7.4 Future Perspectives and Concluding Remarks

Throughout this chapter a number of ideas have been brought forward with regard to how the findings presented in this thesis can be interpreted and explained, and in what way they may be

limited. Taken all together, there are a number of recommendations for future research based on each chapter.

It is important to further examine the association between overprotective parenting and psychotic experiences in adolescence. This association can be explained in many ways (e.g. a third unassessed variable), yet in light of the notion that overprotective parenting has been found to be predictive of other psychological symptoms during adolescence as well (Creemers et al., 2011; Sentse et al., 2010; Van Oort et al., 2011; Visser et al., 2013), it is worth examining whether overprotective parenting could indeed pose a risk factor for psychotic experiences in adolescence. First, it is important to replicate this finding in samples where psychotic experiences were assessed at multiple time points, to control for the presence of psychotic experiences at baseline. Second, a shared underlying vulnerability for both the parent and the child could be taken into account by addressing and controlling for this variable (e.g. IQ, schizotypy, or autism). Third, one of the explanations brought forward in chapter 4, is that children who are overly protected also find it more difficult to form effective relationships with others in adolescence. This is important as peers have a strong influence of psychological wellbeing (Ueno, 2005), health (Låftman & Östberg, 2006) and academic performance (Vaquera & Kao, 2008) in adolescence. Future studies could examine whether peer victimization mediates (and therefore explains) the association between overprotective parenting and psychotic experiences in adolescence, or whether positive peer relationships protect adolescents from developing psychotic experiences in adolescence in the presence of overprotective parenting. Fourth, it is interesting to examine the association over a longer period, in order to assess the persistence of psychotic experiences with a possible transition into psychotic disorders in young adulthood.

Psychotic experiences were examined at one time point in adolescence (with the exception of chapter 6). Given that psychotic experiences may be transient and/or benign (Bartels-Velthuis et al., 2016; van Os et al., 2009), future research may benefit from examining outcomes that have an increased specificity for predicting psychotic disorders. To get a better grasp on the potential causal role of social cognition on psychotic disorders, one could assess the persistence of psychotic experiences (Yung & Lin, 2016), the presence of definite psychotic symptoms (Mollon et al., 2018), or the co-occurrence of psychotic experiences with other risk factors, such as trauma or cannabis use (Morgan et al., 2014) in adolescence. Examining outcomes with an increased specificity for the development of a future psychotic disorder may yield more power to detect a vulnerability in childhood or adolescence.

As outlined previously, social cognitive development is ongoing throughout adolescence (Taylor et al., 2015; Vetter et al., 2013). For future research, it is highly recommended that social cognition is assessed at multiple time points throughout childhood and adolescence, and to examine how its development is associated with future psychotic symptomatology. It may be that developmental trajectories in social cognition contribute to the development of a psychotic

disorder, rather than the presence of impaired social cognitive abilities at any fixed point in time. Using latent growth curve modeling (Jung & Wickrama, 2008), it should be possible to distinguish groups of adolescents with (for example) persistently low, high, increasing, decreasing, or even fluctuating trajectories of social cognition during adolescence, and to examine which group may be more vulnerable to the development of psychosis. Moreover, it might also be interesting to administer social cognitive assessments that are more ecologically valid. Virtual reality environments can offer assessment models that have the ability to combine the experimental control of laboratory settings, with emotionally engaging contexts to enhance similarity to real life social interactions and affective experiences (Parsons, 2015). Last, it may be more relevant to administer a battery of different types of social cognition assessments (e.g. static and dynamic facial emotion identification and, first- and second-order cognitive and affective ToM), rather than focusing on one type of social cognition in one study.

Current interventions for individuals in the UHR phase focus on reducing psychotic symptoms, whilst these interventions are often not effective in relieving social impairment (Van Der Gaag et al., 2012). This is surprising as the presence of a social impairment is currently one of the key criteria for being considered at UHR for psychosis, an impairment that often persists throughout the UHR phase (Yung, et al., 2005). Future research could focus on examining interventions for UHR individuals that combine both the CBT techniques for reducing positive symptoms (van der Gaag et al., 2012), in addition to reintegrating individuals into the social community and strengthening their social network. By focusing on preventing an increase in psychotic symptoms and a decrease in social functioning, interventions delivered during the UHR phase may potentially become more effective in preventing a transition to a first psychotic episode.

Given the present awareness that most young individuals who present themselves at services have a mixture of non-specific psychopathology at adolescence (symptoms of depression, anxiety, psychosis and mania; Costello et al., 1996; Fusar-Poli et al., 2014; Laceulle, Vollebergh, & Ormel, 2015), an important question may be whether it is fruitful to focus on 'preventing' one type of disorder in young adulthood. Perhaps a shift towards a more general staging model of psychopathology (Fusar-Poli et al., 2014) is more effective, whilst focusing on preventing general mental distress. With this perspective in mind, it may be more relevant to focus on predicting which adolescents will become mentally distressed, become socially isolated, drop out of school and are not able to obtain employment. Similarly, once young adolescents show the first signs of dropping out of the social community, the focus could be on social recovery, remaining in school or obtaining new employment. When young adolescents retain their social value in the community and serve a productive function or role in society, the mental distress they are facing may also gradually become less or more bearable.

To conclude, identifying social risk factors for psychotic experiences in adolescence may hold promise for furthering our understanding of the development of psychosis. Nevertheless,

the studies outlined in this thesis did not find evidence for a trait vulnerability in social cognition in relation to psychotic experiences in adolescence. However, it was demonstrated that religious activity and seeking out the presence of others (social support), could signify ways of coping with psychotic experiences, which might be explored further in treatment settings. Future research may aim to replicate the current studies by incorporating the dynamic development of social cognition throughout adolescence and to make use of more ecologically valid assessments of social cognition. In addition, incorporating the transition to a first psychotic episode as an outcome measure could reveal more directly whether social cognitive abilities in childhood are predictive of psychotic disorders in adulthood.

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Samenvatting

Psychotische Ervaringen

Subtiele vormen van psychotische symptomen, zogenaamde psychotische ervaringen, komen in de algemene bevolking veel vaker voor dan psychotische symptomen en psychotische stoornissen. Psychotische symptomen bestaan onder andere uit positieve en negatieve symptomen. Onder positieve symptomen worden hallucinaties en wanen verstaan. Een hallucinatie is een zintuigelijke waarneming in de afwezigheid van een externe prikkel, en een waan is een sterke en emotioneel geladen overtuiging die niet overeenkomt met de overtuigingen van anderen. Negatieve symptomen worden omschreven als een verandering in de motivatie en het vermogen om dagelijkse taken uit te voeren. Psychotische ervaringen zijn inhoudelijk vergelijkbaar met psychotische symptomen, maar ze zijn meestal minder frequent, minder ernstig, en minder verontrustend dan psychotische symptomen en voldoen daardoor niet aan klinische criteria. Een voorbeeld van een psychotische ervaring zou kunnen zijn, dat iemand ten onrechte denkt dat haar huisgenoten haar niet mogen en dat ze achter haar rug om de huisbaas willen omkopen, zodat ze het huis uit moet. Een psychotische ervaring onderscheidt zich van een psychotisch symptoom zodra deze persoon zich toch ergens beseft dat dit niet de werkelijkheid is, en deze gedachte ook weer losgelaten kan worden. Bij een psychotisch symptoom zou deze gedachte een zeer verontrustende overtuiging kunnen worden die niet meer uit zichzelf weggaat.

De prevalentie van alle psychotische stoornissen wordt geschat op 3%, terwijl de prevalentie van psychotische ervaringen in de algemene bevolking wordt geschat op ongeveer 7%. De prevalentie gedurende de kindertijd en de adolescentie is vaak hoger: voor kinderen tussen 9 en 12 jaar rond de 17%, afnemend tot 7,5% bij adolescenten tussen 13 en 18 jaar. Psychische stoornissen, zoals een stoornis in het gebruik van middelen, stemmingsstoornissen en psychotische stoornissen uiten zich meestal in de jonge volwassenheid. Eerder onderzoek toont een verhoogd risico op psychotische stoornissen in de volwassenheid aan wanneer er sprake is van psychotische ervaringen in de kindertijd en adolescentie. Naast het risico op psychotische stoornissen worden psychotische ervaringen ook in verband gebracht met een verminderd sociaal functioneren en psychische problemen tijdens de adolescentie. Het is daarom van belang om het optreden, de ontwikkeling en persistentie van psychotische ervaringen tijdens de kindertijd en adolescentie te onderzoeken. In dit proefschrift worden psychotische ervaringen onderzocht aan de hand van sociale voorspellers.

Klinisch Stageringsmodel

Een nuttig kader voor onderzoek en interventie in de ontwikkeling van ernstige psychische aandoeningen is het klinisch stageringsmodel van McGorry et al. (2010). In het huidige proefschrift wordt dit model gebruikt als kader voor het onderzoeken van de invloed van sociale voorspellers op psychotische ervaringen in de adolescentie. Het klinisch stageringsmodel maakt het mogelijk om milde psychotische ervaringen in vroege stadia te onderscheiden van psychotische symptomen in latere stadia die duiden op de ontwikkeling en uiteindelijk de chroniciteit van psychotische stoornissen. Het huidige proefschrift richt zich op het vroegste stadium (de vertaling vanuit het

Engels: het 'prodromale' stadium). Dit vroege stadium omvat twee groepen: 1) jongeren met milde psychotische ervaringen in de algemene bevolking, en 2) jongeren die een ultrahoog risico (UHR) hebben voor psychose (de fase voorafgaand aan een psychotische episode, gekenmerkt door een toename van psychotische ervaringen en sociale terugtrekking).

Sociale Voorspellers

Bij psychotische stoornissen komen beperkingen in het sociaal functioneren veel voor. Deze beperkingen worden niet alleen beschouwd als een gevolg van psychotische symptomen, maar ook als een risicofactor voor het ontstaan van een psychose. Al voor de eerste psychotische episode kunnen mensen tekenen vertonen van sociale terugtrekking. Bij psychotische stoornissen wordt verminderde sociale cognitie verondersteld als één van de oorzaken voor de beperkingen in sociaal functioneren. Sociale cognitie kan worden omschreven als de psychologische processen die betrokken zijn bij het waarnemen, coderen, opslaan, ophalen en reguleren van sociale informatie over onszelf en anderen. Wanneer iemand moeite heeft om een emotie bij iemand anders te herkennen, of moeite heeft om de intenties achter iemands handelen te begrijpen, zal deze persoon naar verwachting ook meer problemen hebben in de omgang met anderen en het functioneren in de samenleving in zijn geheel. Dit sociaal cognitieve tekort wordt gezien als kwetsbaarheidskenmerk omdat het al aanwezig zou zijn vóór de eerste psychotisch episode. De verwachting is dat wanneer een verminderd vermogen in sociale cognitie zich in de kindertijd of adolescentie uit, dit problemen kan veroorzaken in het sociaal functioneren (bijv. met ouders, of op school) als gevolg hiervan. Zodoende zal de beperking in sociale cognitie samen met het verminderd sociaal functioneren, de adolescent op zijn of haar beurt kwetsbaarder maken voor een psychose in de jongvolwassenheid.

Het is belangrijk om te onderzoeken of sociale voorspellers van psychotische ervaringen al in de adolescentie kunnen worden opgespoord, om deze zo vroeg mogelijk te behandelen. In dit proefschrift zijn sociale cognitie en sociaal functioneren onderzocht als sociale voorspellers (en 'kwetsbaarheidskenmerken') van psychotische ervaringen. Naast deze sociale factoren is religiositeit als een sociaal construct onderzocht in relatie tot het vóórkomen en beloop van auditieve vocale hallucinaties (AVH) in de adolescentie. Tot slot is in dit proefschrift een nieuwe zelfrapportage vragenlijst voor AVH gevalideerd.

Hoe Kunnen we Auditieve Vocale Hallucinaties Betrouwbaar Meten door Middel van Zelfrapportage?

Een van de doelstellingen van dit proefschrift was het valideren van een zelfrapportage versie van de Auditory Vocal Hallucination Rating Scale (AVHRS). De AVHRS is een semigestructureerd interview om de aanwezigheid, kenmerken en ernst van AVH te beoordelen. AVH worden gedefinieerd als het horen praten, fluisteren, schreeuwen, zingen of mompelen, zonder externe stimulus. De AVHRS is gevalideerd in een steekproef van kinderen en volwassenen en toonde goede psychometrische vaardigheden. Aangezien zelfrapportage vragenlijsten naar verwachting minder geld kosten en daarnaast online ingevuld kunnen worden, is een zelfrapportage versie van de AVHRS, de Auditory Vocal Hallucination Rating Scale Questionnaire (AVHRS-Q), ontwikkeld.

In hoofdstuk 2 is aan de hand van twee patiënten groepen onderzocht in hoeverre de losse items van de AVHRS-Q hetzelfde begrip meten (interne consistentie), in hoeverre de AVHRS-Q samenhangt met het oorspronkelijke interview instrument (convergente validiteit), en in hoeverre de AVHRS-Q zich onderscheid van andere bestaande begrippen (divergerende validiteit). In de eerste steekproef zijn 32 psychiatrische patiënten met AVH beoordeeld door middel van de AVHRS en de AVHRS-Q. In de tweede steekproef hebben 82 psychiatrische patiënten met AVH de AVHRS-Q, en vragenlijsten over psychologisch leed en kwaliteit van leven ingevuld. De AVHRS-Q toonde een goede interne consistentie, wat inhoud dat de items van de AVHRS-Q sterk samenhangen en hetzelfde begrip blijken te meten. De ernstscores van de AVHRS-Q hadden een sterkte samenhang met de ernstscores van de AVHRS, wat kenmerkend is voor een goede convergente validiteit. De resultaten geven aan dat de AVHRS-Q ongeveer hetzelfde meet als de interview variant (de AVHRS). Daarnaast hadden de ernstscores van AVHRS-Q een matige samenhang met een maat van psychologisch leed en kwaliteit van leven, wat getuigt van goede divergente validiteit. Dit houdt in dat de AVHRS-Q een specifieke maat van AVH is en niet van psychologisch leed of kwaliteit van leven in het algemeen. De AVHRS-Q kan derhalve zowel klinisch als voor onderzoek worden toegepast om AVH snel en betrouwbaar te beoordelen.

Is Sociale Cognitie Voorspellend voor Psychotische Ervaringen in de Adolescentie en wordt Dit Verklaard door Sociaal Functioneren?

In de psychoseliteratuur wordt sociale cognitie veelal aangewezen als onderliggende kwetsbaarheid voor de ontwikkeling van psychose. Daarnaast wordt verminderde sociale cognitie vaak gezien als een van de oorzaken voor de beperkingen in sociaal functioneren die bij psychotische stoornissen voorkomt. Deze redenatie motiveerde het doel van het huidige proefschrift, namelijk om te onderzoeken of sociale cognitieve vaardigheden in de kindertijd (of preadolescentie) psychotische ervaringen later in de adolescentie kunnen voorspellen en of sociaal functioneren deze samenhang kan verklaren. Deze vraag komt aan de orde in hoofdstuk 3 en 4, door twee verschillende componenten van sociale cognitie (theory of mind en emotieherkenning) te onderzoeken in relatie tot de ontwikkeling van psychotische ervaringen.

Theory of mind (ToM) wordt gedefinieerd als het vermogen om de mentale gesteldheden van anderen te begrijpen of om conclusies te trekken over de bedoelingen of emoties van iemand anders. Het doel van hoofdstuk 3 is om bij adolescenten te onderzoeken of ToM vaardigheden bij kinderen de aanwezigheid van psychotische ervaringen kunnen voorspellen over een periode van zes jaar en of sociaal functioneren de relatie tussen ToM en psychotische ervaringen verklaart. Om te onderzoeken of ToM een specifieke voorspeller is voor psychose, zijn ook symptomen van depressie en angst onderzocht. Bij 157 jongeren van 18-19 jaar werden psychotische ervaringen, depressieve en angst symptomen, en sociaal functioneren uitgevraagd. Zes jaar eerder op de leeftijd van 12-13 jaar, deden deze jongeren mee aan een ToM-taak. De bevindingen gaven aan dat ToM vaardigheden op leeftijd 12-13 jaar niet voorspellend waren voor psychotische ervaringen na zes jaar (18-19 jaar) en dat deze relatie dus niet werd verklaard door sociaal functioneren. ToM hing ook niet samen met psychopathologie in het algemeen (depressieve en angstsymptomen). Onze bevindingen geven mogelijk aan dat ToM niet samenhangt met psychotische ervaringen. in adolescenten in de algemene bevolking.

Emotieherkenning verwijst naar het vermogen om emotionele uitingen (zoals woede, walging, angst, verdriet, verrassing en blijdschap) nauwkeurig te kunnen bepalen aan de hand van iemands gelaatsuitdrukking. Het doel van hoofdstuk 4 is om te onderzoeken of emotieherkenning en het functioneren binnen het gezin in de preadolescentie (leeftijd 11 jaar) psychotische ervaringen vijf jaar later voorspellen in de adolescentie (leeftijd 16 jaar). Bij functioneren binnen het gezin kan men denken aan hoe het gezin omgaat met conflicten, welke opvoedstijl (bijv. warm of afwijzend) wordt gehanteerd, of hoeveel stress de ouders ervaren van het opvoeden. Gegevens voor deze studie werden verkregen uit het epidemiologische cohort TRAILS (TRacking Adolescents' Individual Lives' Survey). Op de leeftijd van 11 jaar werden bij 2059 preadolescenten een emotieherkenningstaak en drie vragenlijsten (over (gezin) functioneren, opvoedingsstijlen en opvoedingsstress) afgenomen. Op de leeftijd van 16 jaar kregen ze een vragenlijst over psychotische ervaringen. Hoewel onderzoek aantoont dat klinische symptomen in vroege en chronische psychose samenhangen met een verminderd vermogen in emotieherkenning, was dit verband niet aanwezig in het huidige cohort van adolescenten. Dat houdt in dat de emotieherkenningstaak op de leeftijd van 11 jaar geen verband toonde met het rapporteren van psychotische ervaringen op 16-jarige leeftijd. De resultaten toonden wel dat beschermende opvoedingsstijlen van ouders een verband had met meer psychotische ervaringen bij adolescenten, mogelijk als gevolg van een kwetsbaarheid voor psychose, een natuurlijke reactie op een kwetsbaar kind door de ouder, of een gedeelde kwetsbaarheid bij zowel ouders als adolescenten. Andere factoren binnen het gezin (opvoedingsstress, gezins functioneren, en afwijzende en warme opvoedingsstijlen) tijdens de preadolescentie hingen niet samen met psychotische ervaringen in de adolescentie. Meer onderzoek is nodig om de rol van beschermende opvoedingsstijlen op psychotische ervaringen tijdens de adolescentie verder te verduidelijken.

Wat is De Samenhang tussen Sociaal Functioneren en Psychotische Ervaringen in het Dagelijks Leven van Mensen met een Ultrahoog Risico voor Psychose?

Uit de literatuur blijkt dat het sociaal functioneren vaak slechter is bij mensen met een psychotische stoornis en dat deze beperking zich ook al eerder kan voordoen, zoals in de UHR-fase. Deze sociale beperking is vaak geïdentificeerd als risicofactor voor de eerste overgang naar een psychotische episode maar het bewijs hiervoor is niet altijd eenduidig. Het bewijs voor dit verband wordt voornamelijk gebaseerd op groepsgemiddelden, waarin verschillen tussen mensen binnen deze groepen over het hoofd worden gezien. Een verklaring voor de variatie in bevindingen is dat er verschillen tussen mensen zijn in de samenhang tussen sociaal functioneren en psychotische symptomen, die uiteindelijk van belang kunnen zijn voor de uitkomst of behandeling van psychose. Om deze mogelijke verklaring te toetsen is de rol van sociaal functioneren in de UHR fase vanuit een gedetailleerd individueel perspectief onderzocht in hoofdstuk 5. Dit houdt in dat er voor elke deelnemer apart werd onderzocht hoe sociaal functioneren en psychotische ervaringen samenhingen en elkaar beïnvloeden van dag tot dag. Vier personen met UHR voor psychose voltooiden een dagboekstudie gedurende 90 dagen. Ze werden gevraagd naar sociaal functioneren ('tijd alleen doorgebracht' en 'ervaren sociale steun') en paranoïde ervaringen ('achterdochtig' en 'het gevoel dat anderen mij niet mogen'). De bevindingen tonen aan dat

er aanzienlijke verschillen waren in de associatie tussen sociaal functioneren en paranoia voor de vier individuen. De meest consistente bevinding was dat de toename van paranoia op een bepaalde dag resulteerde in een toename van het sociaal functioneren op de volgende dag. Over het algemeen lieten de resultaten zien dat sociaal functioneren niet alleen als risicofactor beschouwd kan worden, maar ook als een mechanisme voor het omgaan met psychotische ervaringen in het dagelijks leven.

Houdt Religiositeit Verband met Auditieve Vocale Hallucinaties in de Adolescentie?
Religiositeit kan worden gezien als een 'sociaal' construct waardoor we ons identificeren en verbinden met anderen die dezelfde religieuze overtuigingen hebben en een 'bovennatuurlijke' schepper of God. Religiositeit wordt geassocieerd met meer psychotische ervaringen, zowel bij volwassenen in de algemene bevolking als bij patiënten met een psychotische stoornis. De overeenstemming is dat religiositeit zowel een positieve als een negatieve invloed kan hebben op psychopathologie bij volwassenen. Dit komt omdat religie voor sommige patiënten een bron van betekenis en een manier van omgaan met symptomen kan zijn, terwijl het voor anderen hallucinaties en wantrouwen jegens anderen kan bevorderen. In hoofdstuk 6 is gekeken naar het verband tussen AVH, wanen en religiositeit in een vervolgonderzoek van een steekproef van 337 jongeren met en zonder AVH.

337 kinderen van 12- en 13-jarige leeftijd met en zonder AVH, werden beoordeeld op de aanwezigheid en het beloop (in de afgelopen vijf jaar) van AVH, wanen en religiositeit. Het beloop van AVH (aanhoudend, voorbijgaand, recent ontwikkeld of afwezig) werd onderzocht in relatie tot religiositeit. De resultaten lieten zien dat religieuze adolescenten vaker AVH rapporteerden dan niet-religieuze adolescenten. Daarnaast was de kans groter dat matig-religieuze adolescenten recentelijk AVH hadden ontwikkeld dan niet- of sterk religieuze adolescenten. Van de jongeren die stemmen rapporteren, meldden meer dan de helft dat de stemmen positief waren. Religieuze overtuigingen werden vaak beschreven als ondersteunend, nuttig of neutraal, ongeacht het niveau van religiositeit, voor zowel jongeren met als zonder AVH. De huidige bevindingen suggereren dat er mogelijk een non-lineair verband is tussen religiositeit en het horen van stemmen bij jonge adolescenten. Een speculatieve verklaring zou kunnen zijn dat religieuze overtuigingen en rituelen werden aangenomen in reactie op de stemmen, als een manier van omgaan met stemmen.

Klinische Relevantie van dit Proefschrift
Het idee achter het voorspellen van psychotische ervaringen met behulp van sociale voorspellers in de kindertijd en adolescentie is om individuen die kwetsbaar zijn voor psychotische stoornissen in een eerder stadium te identificeren en het ontstaan van de eerste psychotische episode te voorkomen. Op basis van de bevindingen uit dit proefschrift is het te voorbarig om de klinische toepassing van het voorspellen van psychotische stoornissen met behulp van sociale voorspellers (zoals sociale cognitie) in de kindertijd en adolescentie te bespreken.

Door de bevindingen uit de verschillende hoofdstukken te integreren kan een aantal klinische aanbevelingen worden gedaan. Ten eerste is het niet aan te raden om sociaal-cognitieve interventies aan te bieden aan adolescenten met psychotische ervaringen uit de algemene bevolking in het kader van het voorkomen van een psychotische stoornis. Op dit moment is het alleen aan te bevelen om sociaal-cognitieve interventies in meer klinische stadia van psychose uit te voeren voor hulpzoekende individuen. Ten tweede richten de huidige behandelingen voor individuen in de UHR-fase zich op het verminderen van psychotische symptomen, terwijl de sociale beperking niet expliciet wordt behandeld of verlicht. Op basis van de bevindingen in dit proefschrift wordt aanbevolen om meer nadruk te leggen op het sociale netwerk als een potentieel beschermend mechanisme voor het omgaan met psychotische symptomen in UHR-behandelingen. Ten derde kan religiositeit een bron van troost en verbondenheid vormen voor adolescenten met AVH in de algemene bevolking. Als adolescenten hulp zoeken voor hun AVH, kan het mogelijk nuttig voor hen zijn om de optie te krijgen om een therapie te krijgen die religiositeit of spiritualiteit in een of andere vorm omvat. Ten vierde, de AVHRS-Q toont goede psychometrische eigenschappen en kan daarom in de klinische praktijk worden voorgelegd aan personen met AVH.

Beperkingen en Suggesties voor Vervolgonderzoek

Psychotische ervaringen hangen samen met een verhoogd risico op psychotische stoornissen gedurende de volwassenheid en zijn daarom belangrijk om te onderzoeken in de adolescentie. In de adolescentie zijn psychotische ervaringen echter ook vaak van voorbijgaande aard en mogelijk onschuldig. Het is dus mogelijk dat de psychotische ervaringen die men voorspelt in het kader van onderzoek, een jaar later weer verdwenen zijn. Bovendien is gebleken dat psychotische ervaringen niet alleen het risico op psychotische stoornissen in de toekomst verhogen, maar ook van een reeks andere psychiatrische stoornissen. Psychotische ervaringen kunnen daarom een trans-diagnostische (niet-specifieke) risicofactor vormen voor algemene psychische problemen. Als de onderzochte sociale risicofactoren (zoals ToM) kwetsbaarheden zijn voor alleen psychotische stoornissen (en niet psychische problemen in het algemeen), dan zijn psychotische ervaringen mogelijk niet specifiek genoeg om een kwetsbaarheid voor psychose in de kindertijd en adolescentie te kunnen detecteren. Om deze reden hadden de onderzoeken in dit proefschrift versterkt kunnen worden door ook rekening te houden met de eerste overgang naar psychose.

In dit proefschrift is sociale cognitie op één moment in de adolescentie beoordeeld, waarbij in twee hoofdstukken twee specifieke aspecten (ToM of emotie herkenning) afzonderlijk zijn beoordeeld. Er zijn echter aanwijzingen dat sociale cognitie zich in de adolescentie nog steeds ontwikkelt, waardoor het mogelijk is dat lage prestaties bij preadolescentie niet noodzakelijkerwijs het niveau van de sociale cognitieve vaardigheden in de jonge volwassenheid voorspellen. Misschien zijn longitudinale trajecten van sociaal-cognitieve ontwikkeling (bijv. afnemende of aanhoudend lage vaardigheden) van belang om de ontwikkeling van een psychotische stoornis bij jongvolwassenheid te bepalen, in plaats van statische momenten in de tijd. Daarnaast is het mogelijk dat verschillende aspecten van sociale cognitie stabiel kunnen blijven gedurende de adolescentie, terwijl andere zich verder kunnen ontwikkelen (bijv. statische

versus dynamische beoordeling van emoties). Om echt grip te krijgen op de aanwezigheid van een kwetsbaarheid in sociale cognitie voor psychose gedurende de adolescentie, kan het nodig zijn om (verschillende aspecten van) sociale cognitie op meerdere momenten gedurende de adolescentie te beoordelen. Daarnaast kan het ook interessant zijn om sociale cognitie taken toe te passen die meer overeenkomen met sociale interacties in de dagelijkse werkelijkheid. Virtual Reality zou een methode kunnen bieden met de mogelijkheid om de experimentele controle van laboratoriumomgevingen te combineren met een emotionele context, om de gelijkenis met echte sociale interacties en affectieve ervaringen te versterken.

In alle studies werd een observationele onderzoeksopzet gebruikt, waarbij X en Y werden gemeten op twee (of meer) verschillende tijdstippen, waarna een speculatieve conclusie getrokken werd over de richting van de relatie tussen X en Y (causaliteit). Echter, door te vertrouwen op observationele onderzoeksopzetten kan causaliteit tussen X en Y nooit echt worden getest. Om de causaliteit te kunnen beoordelen, moet aan drie voorwaarden worden voldaan: (a) er is een significant verband tussen X en Y, (b) X moet vóór Y in de tijd optreden, en (c) er zijn geen andere beïnvloedende factoren die het verband tussen X en Y kunnen verklaren (het effect moet in isolatie optreden). Longitudinale studies kunnen voldoen aan de criteria a en b, maar niet aan criterium c. Het is wel zo dat het testen van conditie a (een significant verband tussen X en Y) en b (X moet voor Y op tijd optreden) een belangrijke eerste stap is, omdat het onwaarschijnlijk is dat ook aan conditie c (het effect moet in isolatie optreden) wordt voldaan als niet aan voorwaarde a en voorwaarde b wordt voldaan. Om voorwaarde c te testen en de causaliteit vast te stellen, moet een experimentele onderzoeksopzet worden gebruikt. Vervolgonderzoek kan zich richten op manipulatie van de potentiële oorzaak (in ons geval bijvoorbeeld sociale cognitie), om vervolgens te kijken of het Y (psychotische ervaringen) beïnvloed heeft bij afwezigheid van de invloed van andere variabelen. Meer onderzoek is nodig om na te gaan of het mogelijk is om deze associatie in een laboratoriumomgeving te onderzoeken, en vervolgens te kijken of deze bevindingen vergelijkbaar zijn met hoe deze verbanden zich uiten in het dagelijks leven.

Conclusie

Hoewel het identificeren van sociale risicofactoren voor psychotische ervaringen tijdens de adolescentie veelbelovend klinkt voor het uitvoeren van preventieve interventies om psychotische stoornissen te voorkomen, kon ons onderzoek geen bewijs leveren dat dit lonend of haalbaar zou zijn. Sociale cognitie in de kindertijd toonde geen voorspellend verband met psychotische ervaringen of sociaal functioneren in de adolescentie. De beschreven resultaten laten wel zien dat zowel religieuze activiteit als de aanwezigheid van sociale steun, manieren zijn om met psychotische ervaringen om te gaan, wat verder zou moeten worden verkend in interventies.

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Publication List

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About the author

Laura Steenhuis was born on the 29th of August 1989 in Arnhem, the Netherlands. In 2008, she finished her pre-university education at Bonn International School in Germany and started studying Psychology at the University of Glasgow in Scotland. During her bachelor studies her interest in research was sparked, and after receiving a summer research grant, she spend the summer of 2011 doing research in the area of psycholinguists. Upon completing her bachelor in 2012, she started the Research Master in Clinical Psychology at the University of Groningen. During this time she worked as a research assistant for the Reflex project (research project on training insight in patients diagnosed with schizophrenia, led by prof. dr. Pijnenborg) and became a statistics tutor for the first year psychology bachelor. After completing her Research Master in 2014, she started working on her PhD project on social factors and psychotic experiences, which she wrote, applied for and was granted together with her supervisors. From July 2018 she worked as a university teacher in the psychology bachelor and master program, and as a researcher on a consortium project about cognitive behavioural therapy for anxiety in youth. From July 2019 onwards she works as a postdoctoral researcher for ACCARE on a project about behavioural interventions in the treatment of children with ADHD.