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Social predictors of psychotic experiences in adolescence

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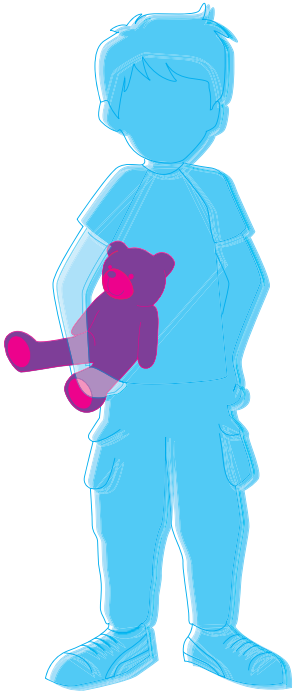
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General introduction

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 (Majjer, 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; Majjer, Begemann, Palmén, 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 (Majjer 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 assess 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, Brelsinger, 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, Galla, 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).

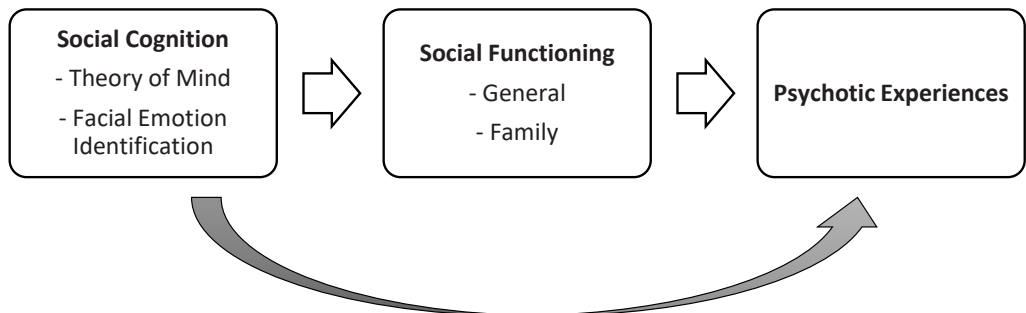


Figure 1. Potential mediation model: social cognition (predictor), social functioning (mediator) and psychotic experiences (outcome) in adolescence.

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, Borrás, 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 (Évans 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.

