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Social predictors of psychotic experiences in adolescence

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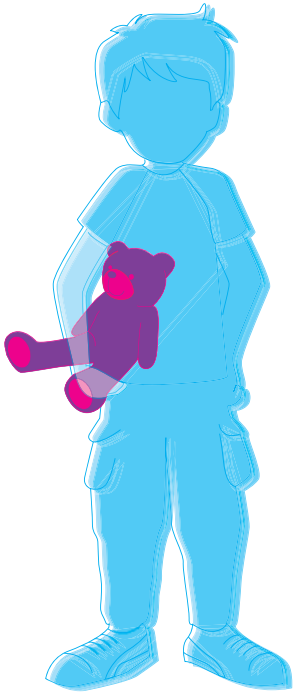
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General Discussion

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; Majjer, 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; Majjer, 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 (Majjer, 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 DISCOVER 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 MIORR 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

Subtiële 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 psychotische 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 onderscheidt 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 inhoudt dat de items van de AVHRS-Q sterk samenhangen en hetzelfde begrip blijken te meten. De ernstscores van de AVHRS-Q hadden een sterke 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 redentatie 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 aantoonde 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 samenhangen 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.

