Growing up with autism spectrum disorders: outcome in adolescence and adulthood

Barneveld, P.S.

CHAPTER 6

Summary and discussion

Summary and integration of main results

Social cognition entails a vast set of abilities that allow people to live in large, complex social groups. Core deficits in people with ASD are difficulties in adapting their behaviour to the social environment which hampers or restrics the possibilities to communicate adequately and to have reciprocal relationships. The problems with adaptation to the social environment in people with ASD have a serious impact on functioning in their daily life. Since ASD are severe and lifelong conditions it is particularly relevant to examine how children and adolescents with ASD develop troughout their life and to investigate which factors constitute an advantageous or an unfavourable contribution to their development.

Social outcome: Quality of Life in ASD

Findings of this thesis provided more insight into the consequences of difficulties of adapting behaviour to the social environment in ASD, by revealing that young adults diagnosed with ASD in childhood are at specific risk of poor QoL. Several studies have shown that QoL is threatened in individuals with psychopathology in general (e.g., Bastiaansen et al., 2004), but the follow-up study of chapter 2 revealed that ASD have a more profound unfavourable effect on QoL in young adulthood than ADHD, DISR, and AFF disorders. In comparison to adults diagnosed in childhood with these disorders, relatively many adults with ASD were single and only some of them were cohabiting or married. Most of the adults with ASD lived with their parents, relatively few lived with a partner or family and many of them were institutionalized. The highest educational level of the adults with ASD was significantly lower than in the other patient groups, relatively few had paid employment, and relatively many were

social security recipients. When the adults with ASD (had) used medication, relatively many were on anti-psychotics.

Although these objective judgements of life conditions are important in evaluating QoL in ASD, the patient's own, subjective, appraisal of satisfaction with life is also essential to their well being. Outcomes of the study of subjective QoL indicated that adults with ASD were less content about their work or education, partner relationships, and future perspectives, but more satisfied about their physical condition than adults with other psychiatric disorders diagnosed in childhood. The outcome of subjective QoL is the resultant of the judgements of the hopes and expectations of a person versus present experience, influenced by the subject's personal frame of reference. One might argue that patients with developmental psychiatric disorders in general might have lowered their own standards to what would be desirable levels as a consequence of adaptation to life conditions, and specifically ASD patients might have personal frames of references that run counter to generally accepted standards (e.g., less need for social interactions and therefore more satisfaction on these matters). Nevertheless, adults with ASD appeared to be less satisfied on several QoL domains than the adults with the other psychiatric disorders, so, it is concluded that they experience relatively more distress in their life.

When examining the influence of level of education on QoL in patients without mental retardation (IQ exceeding 70), no differences in subjective outcomes were found between lower and higher educated patients with ASD, unexpectedly indicating that subjective QoL is not primarily determined by criteria related to educational level. However, findings demonstrated that lower educated adults with ASD showed poorer objective QoL concerning living arrangements and work than those with higher educational qualifications, indicating that educational levels are significant in societal outcome in ASD. Therefore, it was interesting to examine whether or not the differences in outcomes of the psychiatric disorders still exist when only higher educated adults with ASD were compared to higher educated adults with the other psychiatric disorders. Results show that both objective and subjective QoL remained to be more unfavourable in adults with ASD compared to other disorders. This indicates that, even if they appeared to be successful during education and have the same employment, higher education level is not a protective factor to QoL in ASD.

Cognitive dysfunction in relation to age in ASD

The second aim of this dissertation was investigating factors contributing to presumed progressive developmental problems when children and adolescents with ASD grow up. When we examined the impact of age on cognitive functioning of 6-to-15-year-old children and adolescents, the results clearly demonstrated lower global intelligence levels in children aged eight years and older compared to younger children with ASD (chapter 3). Although the results have to be interpreted with caution because only cross-sectional data could be analyzed, the findings suggest a progressive impairment of cognitive functioning in children with ASD. The differences in global intelligence level were mostly due to the performances on the subtests of the Freedom from Distractibility factor, indicating that older children (of eight years and older) had more difficulties to sustain their attention, were more distractible, or had more graph motor difficulties when compared to younger (6-and-7-year-old) children. The apparent decline in intelligence might be associated with a possible absence of the typically expected growth spurt in executive functioning, which runs parallel to the maturation of the frontal lobe, as seen in typically developing children (Anderson, 2002). The development of EF might especially be affected in ASD by abnormal growth processes, explained by the observation of the relatively late and prolonged period of maturation of the putative underlying cortical areas (Courchesne & Pierce, 2005). The suggested impairment of intellectual functioning over age and the specific performance on FFD might be mediated by the impaired development of EF. Furthermore, since EF, such as attentional control and response inhibition, are required when performing tasks of the FFD factor, the impairment of EF presumably contributes to a less harmonious distribution of factor profiles in older children when compared to younger ones.

When profiles of peaks and troughs of intellectual skills in children with ASD were examined at the subtest level, an effect of age was also found with respect to the relatively poor performance on the subtest Comprehension when compared to other VC subtests, suggesting that specifically the impairments in verbal comprehension and social reasoning abilities are more profound in older children when compared to younger (6-and-7-year-old) children with ASD. Since the ability of social reasoning is believed to be mediated by the frontal regions (Walker & Bollini, 2002), the specific age-effect of performance on Comprehension possibly suggests executive dysfunction in older

children with ASD. Typically developing children show increased reasoning and problem-solving abilities and the capacity to think in multiple dimensions develops at approximately seven years of age (Anderson, 2001). These EF's are required for social reasoning as measured by the subtest Comprehension, and inefficient acquisition of these skills in children with ASD might result in deviations from expected patterns of development. In contrast to the characteristic verbal comprehension and social reasoning problems in patients with ASD, the typical superior or relatively preserved abstract visuo-spatial abilities in children with ASD as reflected in the peak of performance on Block Design (e.g., Asarnow et al., 1987; Happé, 1994; Siegel et al., 1996; Shah & Frith, 1993) were also found in the present study. However, no effect of age was found with respect to abstract visuo-spatial abilities.

Schizophrenia spectrum pathology in ASD

The third aim of this thesis was to unravel the relation between autism spectrum and schizophrenia spectrum traits in adolescents diagnosed with ASD in childhood. The outcome revealed that adolescents with ASD scored higher on all symptom dimensions of the schizophrenia phenotype than typically developing adolescents (chapter 4). Besides high levels of negative symptoms, adolescents with ASD also displayed high levels of positive symptoms and disorganised symptoms. Our finding that an overlap between autistic traits and schizotypal symptoms was found is equivalent to the vision of Bleuler (1911) and supports the idea of correspondence between both spectrum disorders (Hurst et al., 2007; Konstantareas & Hewitt, 2001; Sheitman et al., 2004).

The present findings suggest that behavioural overlap is not limited to negative schizotypal symptoms but extend to disorganised and positive symptoms as well. These results were consistent with other studies by Dykens et al. (1991) and Rumsey et al. (1986) who reported shared symptoms in ASD and schizophrenia, like poverty of speech. Considering positive symptoms, Blackshaw et al. (2001) and Craig et al. (2004) indicated some degree of paranoid ideation in adults who were diagnosed with Asperger syndrome. In addition, Solomon et al. (2008) and Van der Gaag et al. (2001) described illogical thinking and loose associations in children with ASD.

It may be emphasised that the associations between autistic and schizotypal symptomatology in the present study were almost exclusively accounted for by two traits of the autistic symptoms, i.e., attention switching problems and communication difficulties. High levels of communication problems were associated with more negative and disorganised symptoms of the schizotypal dimensions. The autistic feature attention switching stands out prominently, as it appeared to be related to all three dimensions of schizotypy. This suggests that inattentional behaviour might be an underlying manifestation of a broad range of schizotypal behaviours. Therefore, further investigation was needed to identify underlying neurocognitive mechanisms that contribute to SSD in ASD.

Neurocognitive markers underlying vulnerability to SSD in ASD

The fourth aim of this dissertation was to examine whether deficits in cognitive control contribute to SSD symptomatology in ASD, and to identify specific neurocognitive vulnerability markers indicating a risk of SSD in adolescents diagnosed with ASD in early childhood. The outcome revealed high levels of schizotypal symptomatology and a substantial level of impaired neurocognitive control in adolescents with ASD, i.e., problems with inhibiting prepotent responses, mental flexibility, visuo-motor control with high EF demands, and difficulties in controlling interference (chapter 5). However, only impaired response inhibition in ASD was associated with schizotypal symptoms, whereas no significant associations between measures of other cognitive control and ASD symptomatology were found. This result was further specified when, after controlling for schizotypal symptoms, response inhibition no longer discriminated between groups, reveiling that impaired response inhibition in ASD was mainly associated with the presence of schizotypal symptoms and can not be explained by autism symptoms. We therefore conclude that impaired response inhibition might be a marker of vulnerability to SSD symptoms developing in ASD.

The presence of schizotypal symptoms co-occurring with ASD symptoms emphasises the relevance of examining comorbidity in assessment of ASD. This underscores that inconsistencies in the literature concerning inhibition in ASD may be the resultant of high numbers of comorbidity factors (Kenworthy et al., 2008). Meta-analytic studies on inhibition functions report that inhibition of prepotent responses is specifically impaired in ASD (e.g., Hill 2004), as we also found in our study. Moreover, our findings suggest that specifically response inhibition above other impairments in EF in ASD is associated with high risk of developing SSD symptoms. Others have found that in-

hibition problems are related to degree of schizotypal traits in other disorders, concluding an association of inhibition problems with increased vulnerability to SSD pathology as well (Van Rijn, Aleman, De Sonneville, & Swaab, 2009).

Regarding the relation between specific EF deficits and various separate dimensions of schizotypy, deficiencies in inhibiting responses were associated with disorganised behaviour and positive symptoms. These findings are supported by the results of the meta-analysis by Dibben et al. (2009), in which the failure to inhibit responses was associated with disorganised symptoms. However, where Dibben's results were found in adults with schizophrenia, our findings indicate that impaired response inhibition is also related to schizotypal symptomatology within an ASD sample in adolescence.

General discussion, implications for the future and clinical implications

In order to gain a better understanding of how children with ASD develop throughout their life and to get more insight into the consequences of difficulties in adaptation to the social environment as characteristically is seen in ASD, long-term outcome in childhood ASD was evaluated by studying quality of life in young adulthood, compared to other childhood developmental disorders (chapter 2). Although several studies suggested that developmental psychopathology is generally associated with poor outcome, this study revealed that the QoL of young adults diagnosed with ASD in childhood is specifically more compromised than QoL in adults diagnosed with other child psychiatric disorders. Even when highly educated adults with ASD were compared to highly educated adults diagnosed with ADHD, disruptive behaviour, or affective disorders, adults with ASD and high educational qualifications were at specific risk of poor QoL.

This was the first study examining the long-term impact (follow-up period of almost 14 years) of ASD for QoL in adults, using no less than three age-matched comparison groups of patients presenting with the other major childhood psychiatric disorders. This approach enabled to examine the specific impact of ASD on QoL, which is not possible when including only typically developing individuals as controls as is usually done in QoL studies. An important strength of the study was the exclusion of mutual comorbidity of the three psychiatric control groups, leaving pure comparison groups. More research is required to enhance our understanding of relations between QoL and other factors besides characteristics of the diagnosis itself, like the impact of symptom severity, social skills or social network factors. This study provides a first step in demonstrating poor QoL in ASD, but the next step should be to further investigate the factors that lead to this outcome.

From a clinical point of view these findings are highly relevant. Parents of children with ASD need accurate information about the prognosis of their child's identified impairments (Kisler & McConachie, 2010). We can now provide a better indication of the consequences of ASD for their daily life functioning that may become more prominent when these children grow older and are faced with increasing demands for personal independence. Receiving accurate perceptions of their child's prognosis has numerous advantages (Goin-Kochel, Peters, Treadwell-Deering, 2008), including setting reasonable expectations in terms of relationships and achievements for their child and more realistic goals for interventions and therapies. For children with ASD, functioning in daily life requires support beyond what is normally needed by others at a similar age and stage of life. This underscores the relevance of further development of specific treatment to improve social skills or adjust the child's environment in order to increase their quality of life and subjective satisfaction of their life conditions. Such treatment and support may include a variety of forms such as guidance, or specially designed environmental or social arrangements. Providing these forms of support has been a major function of education, health, and human service programmes. In this process, the concept of QoL has become increasingly central in developing programmatic policies and practices as well as in evaluating the impact that programmes have on the lifestyles of their users (Schalock, 2004).

The focus of the study described in chapter 3 was on intelligence profiles in 6-to-15-year-old children and adolescents diagnosed with ASD, with particular interest in the role of age. Results of the cross-sectional study showed that it is relevant to take age into account when evaluating the developmental impact of cognitive impairments on intelligence in children with ASD, since the impact of these developmental disorders might be different at different ages. Longitudinal studies are desirable to examine whether or not children with ASD actually have progressive impairments during development, as suggested by our study. For clinicians and parents, this means that re-evaluation of cognitive function during development is recommended.

The results of the study, described in chapter 4, drew attention to this risk of SSD symptomatology in ASD. Although other studies provide empirical support for co-occurring diagnostic criteria between both spectrum disorders, the present findings add to the literature that behavioural overlap is not limited to negative schizotypal symptoms, but extends to disorganised and positive symptoms as well. Although speculative, the current findings may have clinical implications. As high levels of schizotypy appear to reflect a higher risk of developing schizophrenia (Mata et al., 2000; Miller et al., 2002; Vollema et al., 2002), finding high levels of positive symptoms and disorganised behaviour in ASD may implicate an increased risk of schizophrenia spectrum pathology later in life. Implications about the prognostic value of specific childhood symptoms in ASD to the risk of adult schizophrenia should be further explored in a longitudinal design.

The here presented findings are in line with the on-going discussion on the possible relation between ASD and SSD. Classification systems (like the DSM-IV) suggest no direct relation to the underlying aetiology of the disorders. It is, however, very plausible that psychiatric disorders show different clinical presentations at different ages as manifestations of the same underlying disorder, resulting in “cross over” of classification in some cases. The idea of age-specific manifestations of psychopathological symptomatology needs to be given more emphasis to solve on-going questions on co-morbid developing psychiatric disorders and symptoms over time and their possible relation to the aetiology (Hollis, 2001). In addition to using a dichotomous categorical classification system in which an individual does or does not possess a characteristic pattern of symptoms, the use of a dimensional symptom system in which an individual can be characterized by a level on a continuum of a specific characteristic could be helpful in subtyping the ASD spectrum disorders. The degree to which a child or adolescent with ASD shows elevated levels of autistic characteristics and elevated levels of schizotypal characteristics, (such as a large degree of instability of functioning, affect dysregulation and high levels of anxiety), can assist in recognising developmental risk.

Finally, the dynamics of underlying cognitive development of SSD symptomatology in ASD were investigated. Impaired response inhibition appeared to be strongly associated with positive and disorganised schizotypal symptoms, which clearly suggests that impaired response inhibition is a vulnerability marker for the development of SSD pathology within ASD already during adolescence. We recommend a follow-up study in order to examine whether these response inhibition problems in ASD are predictive for full-threshold psychotic illness. Future studies should incorporate a developmental context, since the manifestations of SSD symptomatology in ASD at different ages may be dependent on developmental milestones of response inhibition.

These results indicate that clinicians should be aware of inhibition problems in adolescents with ASD because this may be associated to the risk of serious schizophrenia pathology later in life. The inhibition problems are possibly related to the difficulties in regulating thoughts and feelings in these adolescents.

Limitations

In order to appraise the findings of this thesis one should take the following general limitations into account. Since the sample selection covers a long time span (between 1984 and 2004) and standardized diagnostic parent interview procedures were developed during this period (e.g. the Autism Diagnostic Interview (ADI), these interviews were not used as a validation criterion for the ASD diagnosis in the first en second study. However, in the last two follow-up studies the ASD diagnoses at childhood were validated by the Dutch translation of the ADI in adolescence. In addition, the exclusion of mentally retarded ASD patients in the first study and the inclusion of high-functioning ASD populations in the last three studies limit the representativeness of the sample and, as such, preclude generalisability to the whole autistic spectrum. Moreover, the information obtained from questionnaires in the first, third and fourth study was affected by the limitations inherent in self-report. This specifically applies to ASD adolescents and adults, who may have difficulties judging their own behavior.

Concluding remarks

Given the four research questions of this dissertation, we can conclude the following:

Growing up, children with ASD are at specific risk of poor quality of life in adulthood when compared to other children with psychiatric disorders. Secondly, the performance of children and adolescents with ASD on specific domains of intellectual functioning is different at different ages, indicating a possible progressive impact of the developmental disorders. Therefore, re-evaluation of cognitive function during development of children and adolescents with ASD is recommended. Thirdly, children with ASD who are at risk of SSD symptomatology, may show negative schizotypal symptoms, but also disorganized and positive symptoms in addition to ASD symptomatology. These symptoms of schizotypy appear to be associated with neurocognitive inhibition problems in childhood. Parents, teachers and clinicians should be aware of inhibition problems in children and adolescents with ASD because they may be an indicator of high risk to serious schizophrenia spectrum pathology later in life.

References

Anderson, P. (2002). Assessment and development of executive function (EF) during childhood. *Child Neuropsychology, 8*, 2, 71-82.

Anderson, V., Northam, E., Hendy, J., & Wrennall, J. (2001). *Developmental neuropsychology, a clinical approach.* Hove: Psychology Press Ltd.

Asarnow, R.F., Tanguay, P.E., Bott, L., Freeman, B.J. (1987). Patterns of intellectual functioning in non-retarded autistic and schizophrenic children. *Journal of Child Psychology and Psychiatry, 28,* 2, 273-280.

Bastiaansen, D., Koot, H.M., Ferdinand, R.F., Verhulst, F.C. (2004). Quality of life in children with psychiatric disorders: self, parent, and clinican report. *Journal of American Academy Child Adolescent Psychiatry, 43*, 221-30.

Blackshaw, A.J., Kinderman, P., Hare, D.J., Hatton, C. (2001). Theory of mind, causal attribution and paranoia in asperger syndrome. *Autism 5* (2) 147-163.

Bleuler, E., 1911. *Dementia Praecox oder Gruppe der Schizophrenien,* in: Van Aschaffenburg, G. (Ed.), Handbuch der Psychiatrie. Duticke, Leipzig.

Courchesne, E. & Pierce, K. (2005). Brain overgrowth in autism during a critical time in development: implications for frontal pyramidal neuron and interneuron development and connectivity. *International Journal of Developmental Neuroscience, 23,* 153-170.

Craig, J.S., Hatton, G., Craig, F.B., Bentall, R.P. (2004). Persecutory beliefs, attributions and theory of mind: comparison of patients with paranoid delusions, asperger's syndrome and healthy controls. *Schizophrenia Research, 69* (1) 29-33.

Dibben, C.R.M., Rice, C., Laws, K., & McKenna, P.J. (2009). Is executive impairment associated with schizophrenic syndromes? A meta-analysis. *Psychological Medicine, 39,* 3, 381-392.

Dykens, E., Volkmar, F., Glick, M. (1991). Thought disorder in high-functioning autistic adults. *Journal of Autism and Developmental Disorders, 21* (3) 291-301.

Goin-Kochel, R.P., Peters, S.U., Treadwell-Deering, D. (2008). Parental reports on the prevalence of co-occurring intellectual disability among children with autism spectrum disorders. *Research in Autism Spectrum Disorders, 2* (3) 546-556.

Happé, F. G. (1994). Wechsler IQ profile and theory of mind in autism: a research note. *Journal of Child Psychology and Psychiatry, 35*, 1461-1471.

Hill, E.L. (2004). Executive dysfunction in autism. *Trends in Cognitive Sciences, 8,* 1, 26-32.

Hollis, C. (2001). *Diagnosis and differential diagnosis.* In: Remschmidt, H. (Ed). Schizophrenia in children and adolescents. Cambridge: University Press.

Hurst, R.M., Nelson-Gray, R.O., Mitchell, J.T., Kwapil, T.R. (2007). The relationship of Asperger's characteristics and schizotypal personality traits in a non-clinical adult sample. *Journal of Autism and Developmental Disorders, 37* (9) 1711-1720.

Kenworthy, L., Yerys, B.E., Anthony, L.G., & Wallace, G.L. (2008). Understanding executive control in autism spectrum disorders in the lab and in the real world. *Neuropsychology Review, 18*, 4, 320-338.

Kim-Cohen, J., Caspi, A., Moffitt, T.E., Harrington, H., Milne, B.J., Poulton, R. (2003). Prior juvenile diagnoses in adults with mental disorder: developmental follow-up of a prospective-longitudinal cohort. *Archives of General Psychiatry, 60*, 709-717.

Kisler, J., & McConachie, H. (2010). Parental reaction to disability. *Paediatrics and Child Health, 20* (7) 309-314.

Konstantareas, M.M., Hewitt, T. (2001). Autistic disorder and schizophrenia: Diagnostic overlaps. *Journal of Autism and Developmental Disorders, 31* (1) 19-28.

Mata, I., Sham, P.C., Gilvarry, C.M., Jones, P.B., Lewis, S.W., Murray, R.M. (2000). Childhood schizotypy and positive symptoms in schizophrenic patients predict schizotypy in relatives. *Schizophrenia Research, 44* (2) 129-136.

Miller, P., Byrne, M., Hodges, A., Lawrie, S.M., Owens, D.G., Johnstone, E.C. (2002). Schizotypal components in people at high risk of developing schizophrenia: Early findings from the Edinburgh high-risk study. *British Journal of Psychiatry, 180,* 179-184.

Rumsey, J.M., Andreasen, N.C., Rapoport, J.L., (1986). Thought, language, communication, and affective flattening in autistic adults. *Archives of General Psychiatry, 43* (8) 771-777.

Schalock, R.L. (2004). The concept of quality of life: what we know and do not know. *Journal of Intellectual Disability Research, 48* (3) 203-216.

Shah, A., Frith, U. (1993). Why do autistic individuals show superior performance on the block design task? *Journal of Child Psychology and Psychiatry, 34,* 8, 1351-1364.

Siegel, D. J., Minshew, N. J., & Goldstein, G. (1996). Wechsler IQ profiles in diagnosis of high-functioning autism. *Journal of Autism and Developmental Disorders, 26,* 389-406.

Sheitman, B.B., Bodfish, J.W., Carmel, H. (2004). Are the negative symptoms of schizophrenia consistent with an autistic spectrum illness? *Schizophrenia Research, 69* (1) 119-120.

Solomon, M., Ozonoff, S., Carter, C., Caplan, R. (2008). Formal thought disorder and the autism spectrum: Relationship with symptoms, executive control, and anxiety. *Journal of Autism and Developmental Disorders, 38,* 1474-1484

Van der Gaag, R.J., Caplan, R., Van Engeland, H., Loman, F., Buitelaar, J.K. (2005). A controlled study of formal thought disorder in children with autism and multiple complex developmental disorders. *Journal of Child Adolescent Psychopharmacology, 15* (3) 465-476.

Van Rijn, S., Aleman, A., De Sonneville, L., & Swaab, H. (2009). Cognitive mechanisms underlying disorganization of thought in a genetic syndrome (47,XXY). *Schizophrenia Research, 112,* 91-98.

Vollema, M.G., Sitskoorn, M.M., Appels, M.C., Kahn, R.S. (2002). Does the schizotypal personality questionnaire reflect the biological-genetic vulnerability to schizophrenia? *Schizophrenia Research, 54* (1-2) 39-45.

Walker, E., & Bollini, A.M. (2002). Pubertal neurodevelopment and the emergence of psychotic symptoms. *Schizophrenia Research, 54* (1) 17-23