

The influence of parental and offspring ASD and ADHD symptoms on family functioning

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The influence of parental and offspring ASD and ADHD symptoms on family functioning

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*Voor mijn lieve ouders
en mijn soulmate Sven*

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General introduction,
aims and outline of the thesis

GENERAL INTRODUCTION

This thesis focuses on family functioning in families with offspring with Autism Spectrum Disorder (ASD) (with/ without Attention- Deficit/ Hyperactivity Disorder [ADHD]). Family functioning is an umbrella term for aspects that are proven to be important in dealing with families and defined by internal and external characteristics such as family structure, organization, communication, roles, affective responsiveness and behavioral control to meet the needs of individual family members (Epstein, Bishop & Levin, 1978; Rueschenberg & Buriel, 1989). Importantly, family functioning must be viewed in a family system framework in which individuals of a family cannot be understood in isolation of each other and transactional patterns of the family system are involved in shaping the behavior of family members (see for a review Head & Abbeduto, 2007). This means that child pathology, subthreshold or above threshold symptoms of ASD and ADHD in parents, or the combination between parental and child symptoms may be related to the quality of family functioning. In this thesis we aim to disentangle the possible different effects of child symptoms, parental symptoms and the reciprocal relationships between these factors on family functioning. In the introduction, the influence of child diagnosis and parental symptoms on family functioning are described, illustrated by a case report. Thereafter, the possible influence of the combined effect of parental and child symptoms and spouse symptoms on family functioning are set out, before discussing how this thesis contributes to the research field by overcoming some previous shortcomings in the literature.

"Parenting is the hardest question that is presented to people"
Immanuel Kant (1724-1804)/ German philosopher

Parenting a child with a disorder

ASD is characterized and defined by impairments in social interaction skills and communication, as well as repetitive and restricted behavior and interest (APA, 2000; Fombonne, 2009; Ornstein- Davis & Carter, 2008). ADHD is defined by severe inattention and hyperactivity/ impulsivity problems (APA, 2000; Polanczyk, de Lima, Horta, Biederman, & Rohde, 2007). Previous literature has mainly focused on the biological and genetic origins of ASD and ADHD, but relatively little research has been conducted on the functioning of families in which children with ASD or ADHD grow up, despite the fact that family functioning may have a substantial impact on the child's social and cognitive development and functioning (Reed, Osborne, McHugh & Saunders, 2008; Wachtel & Carter, 2008). Children with developmental psychopathology, such as ASD and ADHD, put a larger strain on parenting skills than typically developing

children do (Harpin, 2005; Herring et al., 2006; Rutgers et al., 2007). Therefore, parenting is not always an easy process and can be referred to as 'the hardest question that is presented to people' (Immanuel Kant [1724-1804]/ German philosopher), especially in families where severe developmental neuropsychological disorders are present, such as ASD and ADHD.

Several studies regarding parenting and the influence of it on child pathology have revealed that parents of children with ASD report lower levels of the more responsive authoritative parenting style (characterized by higher levels of control and high responsiveness of the parents towards the child) than parents in non-clinical groups (Baumrind, 1996; Gau et al., 2010; Rutgers et al., 2007; Woolfson & Grant, 2006). In contrast, parents of children with ADHD have the tendency to use a more authoritarian parenting style (characterized by higher levels of control, but little responsiveness of the parents towards the child) (Alizadeh & Andries, 2002; Bögels, Lehtonen, & Restifo, 2010; Hinshaw, 2002; Johnston & Mash, 2001; Lange, Sheerin, Carr, Dooley, Barton, Marshall, et al., 2005). Families with children with ASD or ADHD are also characterized by higher levels of family conflict (Biederman et al., 1995; Higgins, Bailey, & Pearce, 2005; Kelly, Garnett, Attwood, & Peterson, 2008; Wells et al., 2000), strained parent- child relationships (Harpin, 2005; Kaminsky & Dewey, 2002; Weiss & Hechtman, 2000), and an increased stress level in parents when compared to families with typically developing children (Dunn, Burbine, Bowers, & Tantleff-Dunn, 2001; Estes et al., 2009; Graziano, McNamera, Geffken, & Reid, 2011; Hastings & Johnston, 2001; Hayes & Watson, 2013; Johnston & Reader, 2002; Lange, Sheerin, Carr, Dooley, Barton, Lawlor, et al., 2005; Pimentel, Vieira- Santos, Santos, & Vale, 2011; Schieve, Blumberg, Rice, Visser, & Boyle, 2007; Smith, Oliver, & Innocenti, 2001; Weiss, 2002). It is evident that many studies have indicated that child psychopathology has a negative influence on family functioning, which in turn may have a negative impact on the child's cognitive, emotional and behavioral functioning (Baker & Heller, 1996; Belsky, Woodworth, & Crnic, 1996; Crnic & Greenberg, 1990; Harpin, 2005; Hastings, 2002; IJzendoorn et al., 2007; Phares & Renk, 1998; Reed et al., 2008; Wachtel & Carter, 2008). The influence of child psychopathology on family functioning is also illustrated by the case report of Benjamin and his family. This case report is a detailed description of a family that struggles with the implications of a child with ASD on the family life.

Case report Benjamin

The family of Benjamin consists of two children, a 8-year-old girl named Amy and a 5- year-old boy named Benjamin. The father of this family is 40 years old, works fulltime as an architect and completed university. The mother of this family is 39 years old, works part-time as a caregiver for dementia patients and completed community college. Benjamin receives special education and Amy normal education on grade 6 level.

Both Amy and Benjamin were planned pregnancies. Mother got pregnant from Amy quickly, but the parents tried for two years, before they were pregnant by Benjamin. Both pregnancies were uncomplicated and the children were born after 40 and 41 weeks, respectively. Amy developed well and achieved milestones very quickly. Benjamin on the other hand, started crying a lot just after birth, and it was difficult to comfort him. Both parents found it difficult to get contact with Benjamin when he was upset. Benjamin achieved particular milestones delayed, he did not crawl and it was not before the age of two years that he took his first steps. When Benjamin was 18 months old he was referred for his physical development to a clinic for physiotherapy. Benjamin was also delayed in his language development. For a long time he did not speak at all and when his parents did not understand him, he got upset. Although the parents were very concerned about Benjamin, the problems were not recognized by the environment e.g. grandparents, family and neighbors. Often it was said by others that he was a 'lazy child', but that nothing else was wrong with him.

When Benjamin was three years old his problem behavior increased. Parents increasingly noticed his lack of flexibility; everything had to go in a certain way, he would not go to bed before all his stuffed animals were in a straight line and every night the same bed time story had to be told. The relationship between Amy and Benjamin deteriorated; there were a lot of conflicts between them and the parents could not leave their children alone with one another. By now, the problems were recognized by the teachers in the kindergarten; he bit and hit other children and got easily upset when others did not understand him.

At the age of four, Benjamin began his school career on the same school as Amy. However, almost immediately school reported concerns about Benjamin. The teacher described Benjamin as an 'einzeltgänger', with only brief contact with his peers. Although he tried to make friends, he had difficulties with adjusting his behavior to others and often showed rigid behavior in play situations. He teased other children by taking toys away. He also showed stubborn behavior and some (mild) temper tantrums. Parents were very worried and puzzled with the behavior of Benjamin, but it was not before the age of five that he was referred to Karakter Child and Adolescent Psychiatry with the suspicion of a disorder in the autistic spectrum.

Diagnostic assessment

In the first contact with Benjamin, he looked anxious and shy. When the researcher called his name in the waiting room, he ran towards his mother. He did not shake hands with the researcher and did not want to participate in the assessments without his mother. After a while, the researcher succeeded in being alone with Benjamin in the room. Throughout the assessment, it was difficult to make eye contact with Benjamin; he tended to look around in the room, but never at the face of the researcher. However, there were moments of shared pleasure with the researcher. His mood often

seemed rather flat, it was difficult to challenge Benjamin to a laugh when the researcher intentionally made a joke. Benjamin spoke in proper sentences and a short conversation between the researcher and Benjamin was possible. However, he had difficulties with adjusting his story to the foreknowledge of the researcher. During the assessments, Benjamin told a lot of stories by himself, but it was difficult for the researcher to slow him down on some of his stories. Benjamin was able to answer specific questions, but seemed to have more difficulties with open questions. Sometimes he did not respond at all or just repeated the questions. The assessments revealed that Benjamin's cognitive functioning was overall age-appropriate with weak skills in the area of processing of abstract visual and auditory information (Vocabulary, Block design and Matrix Reasoning). Both the Autism Diagnostic Observation Schedule (semi-structured, observational assessment [ADOS]: Lord, Rutter, DiLavore, & Risi, 2001) and the Autism Diagnostic Interview- Revised (semi-structured, standardized parent interview [ADI-R]: Rutter, Le Couteur, & Lord, 2003) showed scores above threshold. Benjamin was diagnosed with a diagnosis in the autistic spectrum.

Father's perception of family functioning

Father reported concerns about the behavior of his son. Although he described himself as a man that was strict and consistent in his parenting approach, he found it difficult to raise Benjamin. Particular Benjamin's self-determining behavior contributed significantly to daily conflict situations between father and son, and father found it difficult to remain strict and consistent. Father reported that he was frustrated because he tried many different approaches, but none of them had a positive effect on the behavior of Benjamin. In his opinion, his partner offers too little structure and discipline towards Benjamin and Amy. Father reported that Amy also sometimes is disobedient and gets upset easily, but father indicated that Amy listens more to him than Benjamin does. His relationship with Amy is very good and she often talks to his father about her feelings. He also reported that his partner has problems with the organization of the household. Their home is often a mess and mother does not complete everything she starts. Father does not feel supported by mother in raising their children and this puts a large burden on the relationship between him and his partner.

Mother's perception of family functioning

Mother reported a good relationship with her son. She recognized the problems between father and son, but indicated that the relationship with her son is good. However, she reported that the rigidity of Benjamin gives a lot of problems. She finds it hard to handle this behavior, especially because father always has comments about her approach. She recognizes her problem with offering structure and consistent parenting, but in mother's opinion, father punishes the children too much and she blames the large amount of conflicts in the family to the punitive attitude of father.

Mother finds herself being more patient with Benjamin than father is. Mother reported a good relationship with Amy, although she sometimes is disobedient. Mother recognized that she has problems with organizing the household. She explained that father does not understand that Benjamin, Amy and her work is time consuming. Although she enjoys her work, conflict situations are common and give a lot of pressure and stress. She sometimes is overwhelmed by everything and finds it hard to finish her work on time. Mother reported that her relationship with her partner is characterized by a lot of conflicts. She feels she will never be able to meet the expectations of her partner.

Conclusion

This case report illustrates clearly that child psychopathology has a negative effect on family functioning. It seems that father tends to apply an authoritarian parenting style (characterized by a large amount of control, but little responsiveness of the parents towards the child), while mother applies a more permissive parenting style (characterized by little control, but high responsiveness of the parent towards the child). Literature has shown that both parenting styles are an important risk factor for the cognitive and social development of a child (Baumrind, 1991; S. M. Lee, Daniels, & Kissinger, 2006; Rogers, Wiener, Marton, & Tannock, 2009). In addition, Benjamin's ASD symptoms also evoke conflicts between individual family members and both parents' experiences a high level of parenting stress. In accordance with previous literature, parenting a child with ASD puts a large burden on parents and family functioning.

ASD and ADHD

The burden of parenting a child with ASD and the possible negative influence on family functioning may further be enhanced by the fact that ASD and ADHD frequently co-occur within the same child (Rommelse, Franke, Geurts, Hartman, & Buitelaar, 2010; Ronald, Simonoff, Kuntsi, Asherton, & Plomin, 2008; Rowlandson & Smith, 2009) and within the same families (Freitag, 2007; Pamploma et al., 2009). Recent studies using clinical samples and population-based samples revealed that 22-83% of children with ASD have symptoms that satisfy DSM-IV criteria for ADHD (Frazier et al., 2001; Lee & Ousley, 2006; Ronald et al., 2008; Rowlandson & Smith, 2009; Simonoff et al., 2008; Sinzig, Walter, & Doepfner, 2009). Vice versa, 22-65% of children with ADHD have clinical symptoms of ASD (Clark, Feehan, Tinline, & Vostanis, 1999; Ronald et al., 2008; Santosh & Mijovic, 2004). Shared genetic and neurobiological underpinnings may explain why both disorders occur so frequently within the same patient and family. About 50-72% of the contributing genetic factors overlap between ASD and ADHD (Lichtenstein, Carlström, Råstam, Gillberg, & Anckarsäter, 2010; Rommelse et al., 2010) and twin and family studies revealed that ASD and ADHD

share very similar structural and functional brain abnormalities (see for a review Rommelse, Geurts, Franke, Buitelaar, & Hartman, 2011). However, for the last decades, ASD and ADHD have been studied in isolation from each other, based on the rationale that ADHD symptoms in patients with ASD are primarily attributable to the ASD diagnosis which preventing a comorbid diagnosis of ASD and ADHD. In other words, there is a lack of evidence for the combined effects of ASD and ADHD on family functioning.

Influences of parental symptoms on family functioning

Another important issue in examining family functioning in ASD and/ or ADHD families, is that suboptimal family functioning may also arise from parental symptoms. The influence of parental symptoms on family functioning has been reported before in dimensional studies of personality and parenting in which the level of various personality traits of parents may play a significant role in parenting (de Haan, Prinzie & Dekovi, 2009; Prinzie, Stams, Dekovi, Reijntjes, & Belsky, 2009). For example, fathers and mothers with low scores on emotional stability show greater harshness and less sensitivity towards their children (Smith, 2010) and high neuroticism (characteristics of anxiety, moodiness, worry and jealousy) was associated with less parental warmth and less control (Koenig, Barry, & Kochanska, 2010; Prinzie et al., 2009). Based on the extensive evidence that personality and psychopathology are tightly associated with each other (see for a review, Anderson, & Bienvenu, 2011), it could be hypothesized that subthreshold symptoms of ASD or ADHD have a negative influence on family functioning.

Because of the high heritability of ASD and ADHD, children with ASD or ADHD may often have one or two parents that show subthreshold or above subthreshold symptoms of ASD or ADHD. About 1% (Fombonne, 2009) and about 2.5% to 3.4% (Fayyad et al., 2007; Simon, Czobor, Bálint, Mészáros, & Bitter, 2009) of the adults have an actual diagnosis of ASD or ADHD, respectively. For instance, social and communication deficits and preferences for routines are more often found in parents of ASD children than parents of controls (Bishop et al., 2004; Bishop et al., 2008; Gillberg, 1989; Hoekstra, Bartels, Verweij, & Boomsma, 2007; Piven, Palmer, Jacobi, Childress, & Arndt, 1997). In a recent study in young children with autism it was shown that, although Autism Quotient scores of mothers of a child with ASD were similar to that of control mothers, abnormalities in visual scanning were present in the mothers (and to a lesser extent in fathers) and these visual scanning abnormalities correlated with those of their offspring (Groen et al., 2012). Cognitive abnormalities appear also to be present in parents of ASD children, for example regarding weak central coherence (Happé, Briskman, & Frith, 2001) and preference for nonsocial activities and abilities in detail-focused processing (Briskman, Happé, & Frith, 2001). Regarding ADHD-like characteristics, results indicate that parents of children with ADHD are

more likely to have ADHD themselves (Epstein et al., 2000; Macek, Gosar, & Tomori, 2012). Moreover, the literature provides evidence that executive functioning problems are present in children with ADHD and these problems are also more often found in parents of ADHD than parents without ADHD (Jester et al., 2009). For example, parents of children with ADHD show deficits in trail making (the ability to rapidly alternate mental set) and have delayed stop-signal reaction times similar to their children (Nigg, Blaskey, Stawicki, & Sachek, 2004). The findings above support the concept of subthreshold symptoms and associated subtle cognitive abnormalities in parents of children with ASD and/or ADHD.

The study of ASD and ADHD symptoms in parents and the impact thereof on family functioning is a very important area of research, but is also a very sensitive area of research. In the 1940's the cause of autism was attributed to a lack of maternal warmth, which resulted in blaming the parents for their children's autism (Bettelheim, 1967). It is universally accepted that this hypothesis is flawed, but parental ASD and ADHD symptoms and the impact on family functioning for long remained a very sensitive and neglected area of research. Earlier research provides some evidence that parents with high ASD symptoms experience more parenting stress (Berg-Nielsen et al., 2002) and depressive symptoms (Sterling et al., 2008) than parents with few or no symptoms which were associated with more negative parent-child interactions and harsh authoritarian parenting styles (Hastings, 2002; Van IJzendoorn et al., 2007; Wilson et al., 2010). Families with parents with elevated ADHD symptoms appear to be associated with suboptimal family functioning, less optimal parenting style, higher levels of family conflict, less family cohesion and warmth, more criticism (Buschgens et al., submitted; Johnston et al., 2012; Psychogiou, Daley, Thompson, & Sonuga-Barke, 2008; Psychogiou, Daley, Thompson, & Sonuga-Barke, 2007), and more parenting stress (Berg-Nielsen, Vikan, & Dahl, 2002). Above results suggest that high levels of parental ASD or ADHD might interfere with the maintenance of positive family functioning and consequently lead to more child behavioral problems (Baker & Heller, 1996; Belsky et al., 1996; Crnic & Greenberg, 1990; Harpin, 2005; Hastings, 2002; Van IJzendoorn et al., 2007; Phares & Renk, 1998; Reed et al., 2008; Wachtel & Carter, 2008). Therefore, in the present study we examine the influence of parental symptoms on family functioning.

In the case of Benjamin's family...

It seems like father can provide a sufficient rearing environment for both of his children. However, he needs specific guidelines to cope with particular behavior of Benjamin. In contrast, mother's parenting skills raised questions; mother seems less capable of dealing with conflicts and she even avoids conflicts, she has problems with the organization of the household and offering structure and above that, seems mostly overwhelmed by the different situations. Specific questions about the functioning of

mother revealed that she found it difficult to maintain the rules for Benjamin when he had a temper tantrum. She also found it hard to provide Benjamin with the structure he needed. Regarding household chores, she is easily distracted and finds it difficult to keep track of what needs to be done. Mother reported that these problems also exist at her work. In fact, even as child she had problems with her concentration and the organization of her home work. Striking is the fact that mother seems really frustrated about the fact that, although she is mature, she still fails to meet the expectations of others. In consultation with both parents, mother was referred to a clinic for adult psychiatry where after intensive assessment mother received the diagnosis ADHD. This illustrates that suboptimal family functioning can also arise from parental symptoms, and is not only due to child (ASD) psychopathology.

The reciprocal relation between child and parental symptoms in relation to family functioning

Suboptimal family functioning may not only be related to either parental or child symptoms, but also to a combination of parent and child symptoms. This refers to the hypothesis that a low goodness-of-fit between parent and child characteristics may influence family functioning (Chess & Thomas, 1999; Thomas & Chess, 1977). It is likely that a good fit between parental and child characteristics is associated with more optimal family functioning and therefore positively affects the development of a child, whereas a poor fit will result in more suboptimal family functioning and negatively affect the development of a child. It has been hypothesized that a poor-fit may exist when (1) a child has the same symptoms as one of its parents (a homotypic concordant family), or when (2) there are differences in symptoms between parent and child (a heterotypic concordant family), or when (3) a family contains an affected parent and an unaffected child or an unaffected parent and an affected child (a discordant family). Evidence for the discordant hypothesis is reported in two studies that found that parental ADHD symptoms were associated with poorer school performance and prosocial behavior in offspring without ADHD, but not in offspring with ADHD (Biederman et al., 2002; Griggs & Mikami, 2011). Vice versa, behavioral and emotional problems of a child in combination with a parent with low or no symptoms, contributes significantly to parental stress, parents' mental health, family dysfunction and marital problems (Berg- Nielsen et al., 2002; Herring, et al., 2006 ; Piven et al., 1991). Evidence for the homotypic concordant hypothesis has been found before in a study of Tuijl, Branje, Semon Dubas, Vermulst & Van Aken (2005) that reported that adolescents showed less internalizing and externalizing problem behavior when they shared similarities in personality with their parents. Chronis-Tuscano et al. (2008) observed that parental ADHD and child ADHD contributed to the reciprocal negative interactions in families. This was also demonstrated in a study of Roger et al. (2009) where more parental ADHD symptoms

were associated with the use of more controlling strategies regarding children's academic achievement, higher parental stress and more hyperactive and impulsive symptoms in children with ADHD. However, it has also been suggested that mothers with high ADHD symptoms may be more positive and affectionate towards their children with high ADHD symptoms (Psychogiou et al., 2008). To the author's knowledge, the discordant and homotypic concordant hypotheses have never been reported regarding parental and child ASD.

The heterotypic concordance hypothesis regarding parental and child ASD and ADHD symptoms is also a rather unexplored area of parent-child pathology in relation to family functioning. However, it is possible that having a child with ADHD that is talkative, distractible, demanding, and less cooperative (Anastopoulos, Sommer, & Schatz, 2009; Pimentel et al., 2011) may be particularly straining for parents who struggle with rigid and poorer social skills (Ornstein- Davis & Carter, 2008). Vice versa, a child with high ASD symptoms requiring a predictable and organized family functioning may probably be worse off having a parent with high levels of ADHD symptoms, like in Benjamin's situation. The negative effect of the heterotypic concordance has also been demonstrated in studies of depressed mothers and parenting a child with emotional and behavioral disturbances (Civic & Holt, 2000; Harrison & Sofronoff, 2002). Unfortunately, it remains unclear if and how specific combinations of parental and child symptoms contribute to suboptimal family functioning.

The influences of spouse symptoms on family functioning

Family functioning can further be complicated by the fact that spouse symptoms may be related to symptoms of the other spouse. It may be, for example, that adults with ASD traits attract spouses with ADHD traits or vice versa, or adults with ADHD traits attract spouses with similar high ADHD symptoms. This process is called (cross-) assortative mating. Assortative mating is a term used to describe one's tendency to (not randomly) choose a partner that is either similar and dissimilar from oneself in a variety of traits, such as age, education, personality or religion (Vandenberg, 1972). Though studies were unable to find support for assortative mating regarding ASD (Hoekstra et al., 2007) and only found some evidence for ADHD (Boomsma et al., 2010), the possibility of cross-assortative mating for ASD and ADHD has not yet been examined. Such cross- assortative mating has been described for certain other psychiatric disorders, such as affective disorders and conduct problems (Kim-Cohen, Moffitt, Taylor, Pawlby, & Caspi, 2005) and for alcoholism, generalized anxiety disorders, panic disorders and phobias (Maes et al., 1998). However, another possibility is that, for example, depressive symptoms and parenting stress of one spouse may evoke similar symptoms of depression or stress in the other spouse. Previous studies have found that mothers' parenting stress was predictive of fathers'

parenting stress in families with a child with Down syndrome (Roach, Orsmond, & Barratt, 1999) and mothers' parenting stress was associated with fathers' depressive symptoms in families with a child with ASD (Hastings, 2003; Hastings et al., 2005). This relationship between partners' symptoms/ parenting stress is not surprising when considering the fact that spouse symptoms/ parenting stress affect co-parenting and the amount of experienced support by their partner when handling a difficult to rear child (Hastings, 2003). In the case of Benjamin, it is not hard to imagine that father scored high on parenting stress because mother has high levels of ADHD. Father does not feel supported by mother in raising their children and this puts a large burden on his partner and himself.

Scope and outline of this thesis

Since ASD and ADHD are highly heritable disorders and often co-occur in the same patient and/ or family, children with ASD or ADHD may have one or two parents who show subthreshold or above threshold symptoms of ASD or ADHD. These parental ASD and/or ADHD symptoms may affect their functioning, and in this way create a suboptimal family environment for these already vulnerable children (see Figure 1). However, family functioning may also be influenced by child symptoms or the combination between parental and child symptoms. In addition, family functioning can further be complicated by the fact that spouse symptoms may be related to the symptoms of the other spouse and may affect, for example, parenting styles and parenting stress of the spouse. Therefore, our main aim of this thesis is to disentangle the effects of child symptoms, parental symptoms and the reciprocal relationships between these factors on family functioning.

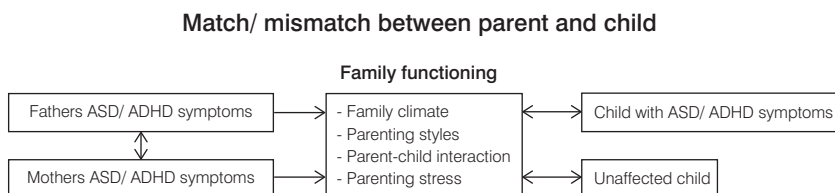


Figure 1 A potential model linking (the combination of) parental symptoms and child diagnosis with family functioning

Methodological shortcomings of previous studies

The main advantages of our thesis compared to previous studies are (a) in contrast to other studies that have been studying ASD and ADHD in isolation with each other, we provide insight in the combined effect of ASD and ADHD on family functioning, (b) most of the previously described studies that focused on family functioning did not include unaffected siblings as a reference group and/or did not take into account parental pathology. With the inclusion of both factors into our research design, we are more able to disentangle the influences of these effects on family functioning, and (c) child pathology, parental symptoms and spouse symptoms are clearly related to each other and in order to grasp the reciprocal dynamic nature of family functioning, it is important to not only focus on the perspective of the parent, but also to that of the child.

BOA and IMAGE-project

Families were recruited from two family genetics projects (*Biological Origins of Autism [BOA]* and *International Multicenter ADHD Genes study [IMAGE]*). The BOA- and IMAGE- project aim to examine the genetic, biochemical and cognitive origins of ASD and ADHD, and study the overlap between ASD and ADHD on these levels. In addition, family functioning of ASD and ADHD families were examined. Families were included in the studies if (a) they had at least one child (between 2 and 20 years old) with a clinical diagnosis of ASD (with/ without ADHD) (BOA) or if they had at least one child (between 5-19 years old) with a clinical ADHD (combined subtype) diagnosis (IMAGE), (b) at least one biological sibling (regardless of possible ASD or ADHD- status) and, (c) at least one biological parent willing to participate. In the current studies only families with two participating biological parents were included. All families had to be of European Caucasian descent. Exclusion criteria for all families were an IQ ≤ 60 , specific learning or language disorders, a diagnosis of epilepsy, a diagnosis of a defined genetic or non-genetic cause of ASD (Rett's syndrome, fragile X syndrome) or ADHD, or a genetic disease such as Down-syndrome. Comorbid DSM-IV disorders were not excluded, with the exception of a diagnosis of autistic disorder in the IMAGE study (other ASD subtypes were allowed).

Chapters

In *chapter 2* (cross-)assortative mating (one tendency to [not randomly] choose a partner that is either similar or dissimilar from oneself in ASD and/ or ADHD symptoms) and parent-of-origin effects (whether parents differ in the relative quantity of risk factors they transmit to the offspring) regarding ASD and ADHD symptoms were examined. In *chapter 3* we examine the influence of ASD and ADHD symptoms on the family climate since the quality of the family climate plays a significant role in child problem behavior. Parenting styles from the perspective of the parents were examined

in *chapter 4*. We explore whether suboptimal parenting styles exist in families with a child with ASD (with/ without ADHD) and to what extent these were related to parent and/ or offspring symptoms. In *chapter 5* we explore the influence of parental ASD and ADHD symptoms in combination with offspring ASD and ADHD symptoms on the parent-child relationship as perceived by the child. In *chapter 6* we explore the role of own and spouse ASD, ADHD and depressive symptoms in parenting stress. In chapter 7 a summary of the results were given and the results will be discussed.

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The co-occurrence
of Autism Spectrum Disorder symptoms
and Attention-Deficit/Hyperactivity Disorder
- in parents of children with ASD or ASD
with ADHD

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ABSTRACT

Background ASD and ADHD share about 50-72% of their genetic factors, which is the most likely explanation for their frequent co-occurrence within the same patient or family. An additional or alternative explanation for the co-occurrence may be (cross-) assortative mating, e.g. the tendency to choose a partner that is similar or dissimilar to oneself. Another issue is that of parent-of-origin effect which refers to the possibility of parents differing in the relative quantity of risk factors they transmit to the offspring. The current study sets out to examine (cross-)assortative mating and (cross-)parent-of-origin effects of ASD and ADHD in parents of children with either ASD or ASD with ADHD diagnosis.

Methods In total, 121 families were recruited in an ongoing autism-ADHD family-genetics project. Participating families consisted of parents and at least one child aged between 2 and 20 years, with either autistic disorder, Asperger disorder or PDD-NOS, and one or more biological siblings. All children and parents were carefully screened for the presence of ASD and ADHD.

Results No correlations were found between maternal and paternal ASD and ADHD symptoms. Parental ASD and ADHD symptoms were predictive for similar symptoms in the offspring, but with maternal hyperactive-impulsive symptoms, but not paternal symptoms, predicting similar symptoms in daughters. ASD pathology in the parents was not predictive for ADHD pathology in the offspring, but mother's ADHD pathology was predictive for offspring ASD pathology even when corrected for maternal ASD pathology.

Conclusions Cross-assortative mating for ASD and ADHD does not form an explanation for the frequent co-occurrence of these disorders within families. Given that parental ADHD is predictive of offspring' ASD but not vice versa, risk factors underlying ASD may overlap to a larger degree with risk factors underlying ADHD than vice versa. However, future research is needed to clarify this issue.

The classical prototypes of autism spectrum disorder (ASD) and attention-deficit/hyperactivity disorder (ADHD) seem to provide outstanding examples of disorders that are so incompatible in their manifestation that they cannot co-occur. Based on their *DSM-IV* diagnostic criteria (APA, 2000), ASD and ADHD indeed have little in common. ASD has a prevalence of around 1% in children and is defined by impaired communication and social interaction skills, as well as repetitive and restricted behavior and interests (APA, 2000; Fombonne, 2009), whereas ADHD has a prevalence of around 5% in children and is defined by severe inattention, hyperactivity and impulsivity (APA, 2000; Polanczyk, de Lima, Horta, Biederman, & Rohde, 2007). The diagnostic guidelines in the *DSM-IV* have so far prevented making a comorbid diagnosis, based on the rationale that ADHD symptoms in patients with ASD are primarily attributable to the ASD diagnosis. As a result, over the past decades, ASD and ADHD have been studied in isolation from each other, each disorder within its research tradition, networks of collaborating experts and theoretical frameworks, without too much cross-fertilization. However, recent studies using clinical samples indicate that 22-83% of children with ASD have symptoms that satisfy *DSM-IV* criteria for ADHD (e.g. Frazier et al., 2001; Lee & Ousley, 2006; Rowlandson & Smith, 2009; Sinzig, Walter, & Doepfner, 2009). Vice versa, 30-65% of children with ADHD have clinically significant symptoms of ASD (Clark, Feehan, Tinline, & Vostanis, 1999; Santosh & Mijovic, 2004). A population-based study used the ADI-R and the ADOS-G to confer an ASD diagnosis, and the Child and Adolescent Psychiatric Assessment (CAPA) structured interview to establish an ADHD diagnosis, and reported that 28.2 % of children with ASD have co-occurring ADHD (Simonoff et al., 2008). A population-based twin study classified suspected children as having ASD using the Diagnostic and Wellbeing Assessment (DAWBA) and classified suspected ADHD by setting a cut-off on the Revised Conners' Parent Rating Scale (CPRS-R). This twin study reported that 41% of children with ASD had co-occurring ADHD, and 22% of children with ADHD had co-occurring ASD (Ronald, Simonoff, Kuntsi, Asherton, & Plomin, 2008). With *DSM-5* on its way (see draft criteria at <http://www.dsm5.org>), wherein the presence of autistic disorder (the proposed new name for ASD) no longer excludes a diagnosis of ADHD, it is likely that this situation will boost research on the shared pathophysiology of ASD and ADHD.

Examination of a shared pathophysiology of ASD and ADHD up to now has already shown that the two disorders share very similar structural and functional brain abnormalities (see for a review Rommelse, Geurts, Franke, Buitelaar, & Hartman, 2011). Furthermore, recent family and twin studies provide support for the hypothesis that ASD and ADHD originate from partly similar familial/genetic factors (Rommelse, Franke, Geurts, Hartman, & Buitelaar, 2010). Both disorders are highly heritable (ASD > 90% and ADHD about 76% (Freitag, 2007; Pamploma et al., 2009) and about 50-72% of the contributing genetic factors overlap between ASD and ADHD. These

shared genetic and neurobiological underpinnings form an explanation why both disorders occur so frequently within the same patient and family.

An intriguing, but virtually uninvestigated, additional explanation for the frequent co-occurrence of ASD and ADHD is that (cross-)assortative mating may occur in the parents of children with these disorders. Assortative mating is a term used to describe one's tendency to (not randomly) choose a partner that is either similar or dissimilar from oneself in a variety of traits, such as age, education, personality or religion (Vandenberg, 1972). It may be, for example, that adults with ASD traits attract spouses with ADHD traits or vice versa. Though studies were unable to find support for assortative mating regarding ASD (Hoekstra, Bartels, Verweij, & Boomsma, 2007) and only found some evidence for ADHD (Boomsma et al., 2010), the possibility of cross-assortative mating for ASD and ADHD has not yet been examined. Such cross-assortative mating has been described for certain other psychiatric disorders, such as affective disorders and conduct problems (Kim-Cohen, Moffitt, Taylor, Pawlby, & Caspi, 2005) and for alcoholism, generalized anxiety disorders, panic disorder and phobias (Maes et al., 1998). If present, cross-assortative mating may result in a 'double-whammy' effect with respect to risk genes segregating to the offspring: two separate sets of risk genes, an ASD and ADHD set, one from each parent, are inherited together, resulting in the co-occurrence of ASD and ADHD in the offspring.

Another issue that deserves further attention in the symptom transmission of ASD and ADHD is whether parents differ in the relative quantity of risk factors they transmit to the offspring. This is also known as parent-of-origin effect. If present, it could imply that the effect of a risk allele depends on whether it originates from the mother or father. Absence of parent-of-origin effect indicates that the risk allele is more or less equally transmitted from mothers and fathers to the offspring. For both ASD and ADHD mixed findings of parent-of-origin effects have been documented. Some studies reported that both disorders were mainly transmitted through the maternal line (Arking et al., 2008; Banerjee et al., 2006; Lauritsen, Pedersen, & Mortensen, 2005), other studies reported the opposite (Anney et al., 2008; Fradin et al., 2010; Goos, Crosbie, Payne, & Schachar, 2009; Hawi et al., 2010) and a few found no evidence for parent-of-origin effects (Goos, Ezzatian, & Schachar, 2007; Kim et al., 2007). To the authors' knowledge, thus far, no studies have focused on the cross-parent-of-origin effects of ASD and ADHD, i.e. whether it matters if fathers or mothers have ADHD symptoms for the children's risk of also developing ASD next to ADHD. This may be influenced by the child's gender as well, as suggested by two previous studies showing that girls may be more susceptible to the inheritance of ADHD through either parent (Hawi et al., 2005) or only the maternal line (Goos, et al., 2007). The parent-of-origin effects may also be influenced by different inheritance patterns of the two symptom domains of ADHD, e.g. inattentive versus hyperactive-impulsive symptoms (Nikolas & Burt, 2010).

It is clear that the relationship of ASD and ADHD pathology between parents deserves further attention, as well as possible parent-of-origin effects in the transmission of ASD and ADHD symptoms to the offspring. Therefore, the current study sets out to examine these issues in 121 families in which at least one child was affected with ASD and at least one additional biological sibling was available for analyses. Self-reported ASD and ADHD symptoms were obtained from the parents and were related to each other and their offspring ASD and ADHD symptoms.

METHODS

Participants

Families were recruited as part of an ongoing family-genetics project (Biological Origins of Autism [BOA]). The BOA project aims to examine the genetic, biochemical and cognitive origins of ASD and, in addition, study the overlap between ASD and ADHD on these levels. Families were included in the current study if at least one child between 2 and 20 years old, with either an autistic disorder, Asperger disorder or PDD-NOS (proband), at least one biological sibling (regardless of possible ASD-status) and at least one biological parent wanting to participate. All families had to be of European Caucasian descent. Exclusion criteria for the probands and siblings were epilepsy, a diagnosis of a defined genetic or non-genetic cause of ASD (Rett's syndrome, fragile X syndrome) or a genetic disease such as Down-syndrome. Comorbid *DSM-IV* disorders were not excluded.

All children were screened with the Social Communication Questionnaire (SCQ) (Rutter et al., 2003) completed by parents and teachers. Even though the SCQ has not been studied and validated as an instrument for teachers, we use also the teachers report as screenings method, to avoid missing any actual case. Families were included if at least one child presented a score above 10 on the parent version (to avoid the exclusion of children with milder ASD symptoms e.g. false negatives) or above 15 on the teacher version of the SCQ. We chose a higher cutoff for the teacher than for the parent reported SCQ because teachers often reported more subtle ASD symptoms that were not confirmed by parents' SCQ reports or the administered Autism Diagnostic Interview Revised (ADI-R) to parents. For all children scoring above the cut-off, a formal diagnosis of ASD was made by a certified clinician using the Autism Diagnostic Interview-revised (ADI-R) (Le Couteur, Lord, & Rutter, 2003). The protocol for screening and measuring ADHD was similar to the protocol used in the International Multicenter ADHD Genetics (IMAGE) study (Brookes et al., 2006). In short, the Conners long version Rating Scales-Revised (CRS-R) (Conners, 1997) completed by parents and teachers was used for screening for ADHD. Participants of 18 years and older filled out the Conners Adult Rating Scales-Self-report: Long

version (CAARS-S:L). A T-score ≥ 63 on one of the ADHD-subscales of the CRS-R (parent or teacher) or CAARS was considered clinical. For all children scoring above cut-off and/or having a previous clinical diagnosis of ADHD, the Parental Account for Childhood Symptoms (PACS) (Taylor, Sandberg, Thorley, & Giles, 1991) was administered by a certified clinician to obtain a diagnosis of ADHD. We were able to enroll 121 families in this study, see Table 1 for the descriptive characteristics. Due to the study-design, all probands had a diagnosis of ASD and there were no children with a pure ADHD diagnosis in this group. In total, 38.8% of the probands with ASD also fulfilled criteria for ADHD. Of the 184 siblings, 15.6% had pure ASD, 9.4% pure ADHD, and 5.4% had ASD and ADHD. Both fathers and mothers scored above population average with respect to self-reported ASD symptoms. The mean scores of ADHD inattentive symptoms of parents were comparable to the norm, however the mean ADHD hyperactive-impulsive symptoms were significantly lower than the mean scores of the general population.

Instruments

Self-reported ASD symptoms of parents and parent-reported ASD symptoms in children were measured using the child and adult version of the Autism Spectrum Quotient (AQ) (Baron-Cohen, Wheelwright, Skinner, Martin, & Clubley, 2001). These questionnaires have been found reliable and valid (Auyeung, Baron-Cohen, Wheelwright, & Allison, 2008; Hoekstra, Bartels, Cath, & Boomsma, 2008) and have the advantage that the parent and child versions are directly comparable. The questionnaires consists of 50 items rated on a 4-point scale. Total scores for children and parents were obtained by summing up all items, resulting in a score between 50 and 200 (Hoekstra, et al., 2008; Hoekstra, et al., 2007). The ASD symptom scores were treated on the same dimension, because the AQ has not been designed to differentiate between ASD symptom classifications. Self-reported ADHD symptoms of parents and adult children (18 years and older) were measured with the CAARS-S:L (Conners, Erhardt, & Sparrow, 1998, 1999). The *DSM-IV* ADHD subscales were used to operationalize inattentive and hyperactive-impulsive symptoms of parents. For children of 18 years and older, the scaled scores were averaged across raters (self-report and parent-report). For offspring below the age of 18 years, parent and teacher reports on the CRS-R (Conners, 1997) were averaged. If no teacher report was present ($N = 23$, 7.5%), only the parent report was used.

Procedure

Families potentially satisfying inclusion criteria registered at an outpatient clinic specialized in ASD and ADHD pathology (Karakter Child and Adolescent Psychiatry University Center) and members of the Dutch Autism Association (NVA) received a brochure containing information regarding the study and were requested to return a

pre-stamped response card. A short telephone screening and, subsequently, screening questionnaires were used to verify if families could participate. Those families were invited to visit the clinic, where a trained researcher conducted the ADI-R and the PACS. Additional data collected included blood samples of all family members and neuropsychological data of the children. The study was approved by the local medical ethics board and parents and children (12 years and older) signed for informed consent.

Data-analyses

Analyses were performed with SPSS 16 (Statistical Package for the Social Science version 16; IBM Corporation Armonk, New York). Less than 5% of child data, < 7% of father data and < 2% of mother data was missing and we used the Expectation Maximization (EM) algorithm (Dempster, Laird, & Rubin, 1977) to impute the missing values. The AQ and Conners data for parents and children were transformed into z-scores to depict the measures on the same scale using the age- and sex-specific means and SDs for these questionnaires (Hoekstra, et al., 2008; Hoekstra, et al., 2007; Saviouk et al., 2011). Thereafter, because the distribution of scores was not completely normal, the variables were normalized using the Van der Waerden transformation (SPSS 16; IBM Corporation, Armonk, New York).

To examine the presence of (cross-)assortative mating, Pearson correlation analyses with the AQ and CAARS z-scores were performed to examine whether symptoms within and between parents were correlated. To examine the presence of parent-of-origin effects, Generalized Estimation Equations (GEE) with an exchangeable working correlation matrix (all measurements were equally correlated), scale parameter method on deviance and robust estimators were used. Family number was used as subject effect to account for clustered data. This allowed us to evaluate the relationship between parental and offspring symptoms but with correction of clustered data (i.e. multiple parent-offspring correlations were calculated per family). GEE-analyses are a convenient and general approach to analyze clustered (family) data (Liang & Zeger, 1986). Predictors were sex and age of the child, parents' age, parents' symptoms, and the two-way interactions between parental pathology and sex or age of the parent. Dependent variable was the child's symptoms. When the two-way interactions (between parental pathology and sex or age of the parent) were non-significant, these were dropped from the model and the model was rerun. The model was run separately for ADHD symptoms within families, ASD symptoms within families, and lastly for the relationship between parental ASD and offspring ADHD symptoms and vice versa. In the latter two analyses, when a significant effect of parental ASD on offspring ADHD symptoms was found, the model was rerun with parental ADHD symptoms added to the model to examine whether the observed effect was partially accounted for by parental ADHD pathology.

Table 1 Characteristics participants

	(1) Fathers		(2) Mothers		(3) population	SD
	N=121		N=121		parents	
	M	SD	M	SD	M	
% male						
Age in years	45.8	5.8	43.0	5.3		
Education	4.5 ¹	1.0	4.4 ¹	.87	4.3 ²	
Social Communication Questionnaire						
Autism Quotient	115.5	18.6	109.1	22.2	♀102.9 ♂105.7 ⁴	♀11.5 ♂11.0 ⁴
Conners inattentive scores	5.8	4.7	4.6	5.3	♂5.3 ♀5.3 ⁶	♀ 3.2 ♂ 3.1
% Above cut-off T>63	4.1		4.1		♀6.8 ♀7.4 ⁷	
Conners hyperactive scores	5.4	3.7	5.1	4.1	♂6.7 ♀7.0 ⁶	♀ 3.3 ♂ 2.9
% Above cut-off T>63	4.1		4.1		♀6.8 ♀7.4 ⁷	
% ASD (ADI)⁸						
Autism						
Asperger						
PDD-NOS						
% ADHD (PACS)⁹						
inattentive subtype						
hyperactive subtype						
combined subtype						
% Total ADHD only						
% Total ASD+ADHD						

¹1= nursery school 2= primary education 3= secondary education, first phase 4= secondary education, second phase 5= higher education, first phase 6= higher education, second phase 7= higher education, third phase ²Central Bureau of statistics (CBS) 2009 ³Based on population cohort study (N=247) (Chandler et al., 2007) ⁴Based on Dutch population-based sample (N = 302) (Hoekstra, et al., 2008) ⁵based on Dutch population-based sample of twins (N= 464) (Hoekstra, et al., 2007) ⁶Norms from the Dutch Twin register ⁷ Based on epidemiology study (N=12.000) (Boomsma, et al., 2010) . ⁸measured with the Autism Diagnostic interview (ADI-R) ⁹Measured with the Parental Account for Childhood Symptoms (PACS).

	T- test	(4) probands N=121	SD	(5) siblings N=184	SD	(6) population children	SD	T-test contrast
		M		M		M		
		85.1		49.5				
		11.7	3.7	11.4	4.7			4 = 5
	1 & 2 = 3							
		19.9	8.0	6.4	7.2	4.7 ³	5.0 ³	4 > 6 and 5 = 6
	1 & 2 > 3	138.1	17.8	113.3	24.6	♀100.8 ♂104.0 ⁵	10.5 ⁵	4 > 6 and 5 = 6
	1 & 2 = 3	59.7	9.9	53.2	9.8	50.0	10.0	4 & 5 > 6
	1 & 2 = 3	38.0		16.3		12		4 > 6 and 5 = 6
	1 & 2 < 3	61.8	11.3	53.3	10.6	50.0	10.0	4 & 5 > 6
	1 & 2 = 3	43.8		16.8		12		4 > 6 and 5 = 6
		59.5		6.1				
		3.3		.7				
		37.2		8.8				
		15.7		5.1				
		9.9		1.4				
		13.2		2.9				
		-		9.4				
		38.8		5.4		5		4 & 5 > 6

The same procedure was undertaken for the relationship between parental ADHD and offspring ASD symptoms. For all analyses correction for multiple testing using the 95% CI, was performed using the False Discovery Rate procedure (Benjamini, 2010).

RESULTS

The relationship between ASD and ADHD pathology within and between parents

Within both fathers and mothers significant positive correlations were found between their ASD and ADHD symptom scores (Table 2). No significant correlations were found between maternal and paternal ASD and ADHD symptoms.

Table 2 Correlations of self reported ASD and ADHD symptoms between and within

parents						
	father			mother		
	ASD ¹	ADHD inatt ²	ADHD hyp-imp ³	ASD ¹	ADHD inatt ²	ADHD hyp -imp ³
<i>father</i>						
ASD	1	.48*	.43*	.00	.01	.05
ADHD inatt		1	.51*	-.11	.02	.07
ADHD hyp-imp			1	-.01	-.08	.02
<i>mother</i>						
ASD				1		
ADHD inatt				.37*	1	
ADHD hyp-imp				.28*	.58*	1

* Correlation is significant at the 0.01 level and after correction for multiple testing
¹ ASD symptoms measured with the Autism Quotient (AQ)
² ADHD inattentive symptoms measured with the Conners' Adult Rating Scales- Self-report: Long version (CAARS-S:L).
³ ADHD hyperactive-impulsivity symptoms measured with the Conners' Adult rating Scales- Self-report: Long version (CAARS-S:L).

Preferential parental transmission

Because there were no significant correlations between maternal and paternal pathology, GEE analyses could be conducted with maternal and paternal pathology as predictors in the same model. For ASD pathology, an equally strong relationship between both paternal and maternal and offspring ASD symptoms was found, regardless of the child's sex or parents' age (see Table 3 and Figure 1). No parent-of-origin effects were found for ADHD inattentive pathology, although only maternal inattentive symptoms survived correction for multiple testing and predicted both inattentive and hyperactive-impulsive symptoms in offspring regardless of the sex and age of the child. A parent-of-origin effect was present for parental hyperactive-

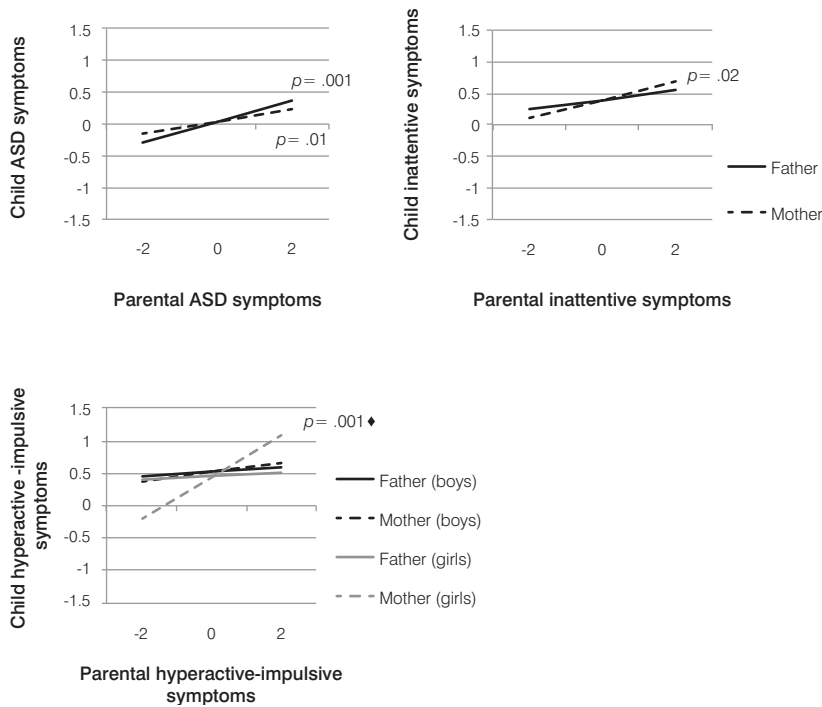


Figure 1 Illustration of parent-of-origin effects between parental and offspring pathology (Z-scores)*

* Figures are not specified for gender, unless significant gender-interaction effects were found. Child ASD, ADHD inattentive, and hyperactive-impulsive symptoms as a function of the same symptoms in parents. Higher z-scores indicate more symptoms.

♦ Indicates a significant parent-of-origin-effect

Table 3 Parent-of-origin effects of ASD and ADHD symptoms to the offspring (Z-scores)

	child ASD*		Parent-of-origin effect		child ADHD		Parent-of-origin effect		child ADHD		Parent-of-origin effect	
	child ASD*	p value		p value	inatt	p value		p value	hyp-imp	p value		p value
<i>father/ mother</i>												
ASD ¹	.16/ .15	.001/ .01	No (p = .61)		.13/ .01	.04/ .87	No (p = .20)		.10/ .03	.11/ .59	No (p = .41)	
ADHD inatt ²	♂.02/ ♂.03	♂.88/ ♂.16	No (p = .75)		.08/ .15	.79/.02	No (p = .53)		.05/ .16	.49/.01	No (p = .30)	
	♀.17/ ♀.30	♀.26/ ♀.001	No (p = .46)									
ADHD hyp-imp ³	♂.08/ ♂-.08	♂.33/ ♂.11	No (p = .11)		.07/ .13	.36/.07	No (p = .53)		♂.03/ ♂.07	♂.11/ ♂.29	No (p = .75)	
	♀-.02/ ♀.35	♀.94/ ♀.001	Yes (p = .03)						♀.03/ ♀.32	♀.24/ ♀.001	Yes (p = .03)	

Findings in bold are significant after correction for multiple testing

* Regression weights are not specified for gender, unless significant gender-interaction effects were found.

¹ ASD symptoms measured with the Autism Quotient (AQ)

² ADHD inattentive scores measured with the Conners' long version Rating Scales Revised (CRS-R)

³ ADHD hyperactive-impulsivity scores measured with the Conners' long version Rating Scales Revised (CRS-R)

impulsive symptoms, with maternal (but not paternal) symptoms being predictive for daughters' hyperactive-impulsive symptoms. Maternal or paternal hyperactive-impulsive symptoms were not related to hyperactive-impulsive symptoms in sons or offspring inattentive symptoms. Parents reported both on their own symptoms and on the symptoms of their children. To correct for a possible bias, we repeated our analyses with only the teacher score (only available for the ADHD symptoms) as the dependent variable. Doing so, we found that all results were in the same direction as before, but no longer significant (maternal inattentive symptoms with child hyperactive-impulsive symptoms $B = .02$, $p = .79$, maternal inattentive symptoms with child inattentive symptoms $B = .02$, $p = .84$, and maternal hyperactive-impulsive symptoms with daughters hyperactive-impulsive symptoms $B = .09$, $p = .37$).

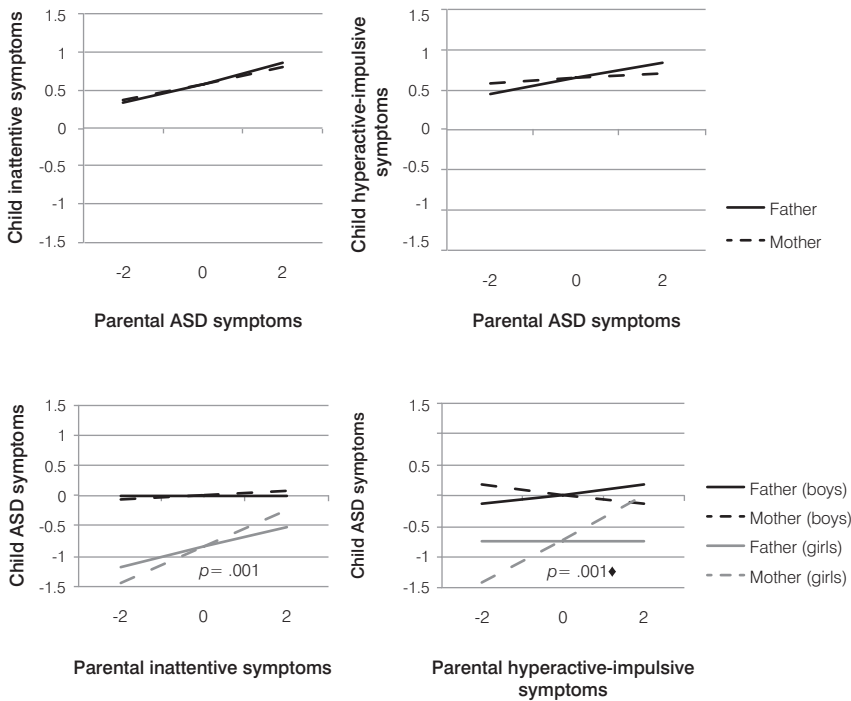


Figure 2 Illustration of cross-disorder parent-of-origin effects between parental and offspring pathology (Z-scores)*

* Figures are not specified for gender, unless significant gender-interaction effects were found. Child ASD, ADHD inattentive, and hyperactive-impulsive symptoms as a function of the same symptoms in parents. Higher z-scores indicate more symptoms.

♦ Indicates a significant parent-of origin-effect

Cross-disorder analyses revealed no significant relationship between parental ASD and offspring ADHD symptoms (see Figure 2). Vice versa, a relationship was found moderated by parent-of-origin effects. Maternal, but not paternal, ADHD inattentive and hyperactive-impulsive symptoms were predictive of daughters' ASD symptoms, but only for the latter we found a significant parent-of-origin effect. Adding maternal ASD symptoms to the model did not change this effect. For the hyperactive-impulsive symptoms in mothers and daughters, an interaction of mother's age was observed. Offspring ASD symptoms were related to the hyperactive-impulsive symptoms of younger mothers ($p = .007$), but not of older mothers ($p = .14$) when using a median split on mother's age.

DISCUSSION

In the current study we set out to examine cross-assortative mating and (cross-)parent-of-origin effects of ASD and ADHD symptoms in parents and children in order to shed more light on the frequent co-occurrence of both disorders within patients and families. No correlations were found between maternal and paternal ASD and ADHD symptoms, making (cross-)assortative mating unlikely in our sample. An equally strong relationship between paternal, maternal and offspring ASD symptoms was found, regardless of the child's sex or parents' age. Concerning ADHD, no parent-of-origin effects were found for ADHD inattentive pathology, although only maternal inattentive symptoms survived correction for multiple testing and predicted both inattentive and hyperactive-impulsive symptoms in offspring regardless of the sex and age of the child. A parent-of-origin effect was present for parental hyperactive-impulsive symptoms, with maternal (but not paternal) symptoms being predictive for daughters' hyperactive-impulsive symptoms. Parental ASD pathology was not predictive for offspring ADHD pathology, but mother's ADHD pathology was predictive for offspring ASD pathology even when corrected for maternal ASD pathology.

Our findings of moderate to strong relationships between parental and offspring symptoms are in line with previous studies (for example, Fradin, et al., 2010; Hawi, et al., 2010). The result that both paternal and maternal ASD symptoms are equally strongly related to offspring ASD symptoms, concurs with the findings from recent studies (Arking, et al., 2008; Banerjee, et al., 2006; Lauritsen, et al., 2005) and contradicts hypotheses that ASD pathology is mainly transmitted through the paternal line. In contrast, a parent-of-origin effect was present for ADHD hyperactive-impulsive symptoms, with mothers', but not fathers', symptoms predicting daughters' symptoms, suggesting that girls may be more susceptible to the inheritance of ADHD through the maternal line (Goos, et al., 2007). This may be explained by the role of

sex-chromosomes or sex-specific physiological or hormonal factors (Goos, et al., 2007). However, no parent-of-origin effect was found for parental inattentive symptom transmission, suggesting the two symptom domains in ADHD may show differential patterns of inheritance. This has indeed been recently reported in a meta-analysis on twin studies: additive genetic factors may play a more substantial role in hyperactive-impulsive symptoms than they do in inattentive symptoms (the latter more strongly influenced by dominant genetic factors) and this difference is more pronounced in girls than in boys (Nikolas & Burt, 2010). In conclusion, these findings suggest preferential parental transmission does not play an important role in ASD, but may be of relevance in ADHD hyperactive-impulsive symptoms.

Of great interest are the results that contradict the thus far never studied hypothesis of cross-assortative mating for ASD and ADHD pathology. This suggests that children are unlikely to develop both disorders as a result of a 'double-whammy' effect in which two separate sets of risk genes, an ASD set from one parent and an ADHD set from the other parent, are carried over together at a higher frequency than expected by chance. On the one hand, given the high correlations between ASD and ADHD pathology *within* parents, it may be suggested that parents transfer ASD/ADHD-common factors to their offspring, whose phenotypic expression may then depend on the parent-of-origin. On the other hand, this is contradicted by the selective effect of parental (mainly mothers') ADHD symptoms on offspring ASD symptoms, but not the other way around. In other words, the risk for developing ASD in offspring is enhanced when parents score high on ASD and/or ADHD symptoms, whereas the risk for developing ADHD in the offspring is only enhanced when the parents score high on ADHD pathology. This may suggest that risk factors underlying ASD may overlap to a larger degree with risk factors underlying ADHD than vice versa. However, we realize we only have preliminary evidence to support this hypothesis, and further research which includes a pure ADHD group is needed to clarify this issue. As we found no evidence for cross-assortative mating, this may not explain the co-occurrence of ASD and ADHD. An alternative explanation for the co-occurrence of ASD and ADHD, besides the shared underlying etiology, could be that one of the disorders produces a phenocopy of the other. It is possible that a child has a strong genetic disposition for ADHD, but when growing up in an unhealthy parenting environment this could lead to ADHD based on the genotype and ASD symptoms based on the environment (Rommelse et al., 2010). However, more research in the area of the co-occurrence of both disorders is needed.

Our findings should be interpreted in the context of several limitations. First, we relied only on self-reports of parent behavior instead of using multiple informants. Parental psychopathology may have obscured the self ratings of problem behavior, resulting in an underestimated amount of symptoms and affected parents in our sample. Parents with, for example, ADHD tend to be more positive about their own behavior

(Kooij et al., 2008; Young & Gudjonsson, 2005), perhaps due to limited self-awareness (Zucker, Morris, Ingram, Morris, & Bakeman, 2002). This would explain why the mean scores of ADHD hyperactive-impulsive symptoms in our sample were significantly lower than found in the general population, but is contradicted by the finding of increased ASD pathology in the sample. A second limitation is the possibility of informant bias, since parents reported both on their own symptoms and on the symptoms of their children. The non-significant results that were found when using only teachers reports, could be the consequence of medication use of the child at school, resulting in lower teacher scores. Nonetheless, it is important to confirm the findings of the present study through the use of multiple informants reporting about the ASD and ADHD symptoms of parents and children. A third limitation is that the child behavior questionnaires were completed mostly by mothers, therefore possibly providing a positive or negative informant bias. Though in that case, we would expect to find very different results for mother ratings than for father ratings, which was overall not the case.

In conclusion, our study suggests that there is no (cross-)assortative mating for ASD and ADHD. No parent-of-origin effects were found for both ASD and ADHD inattentive symptom transmission, though only maternal ADHD hyperactive-impulsive symptoms were predictive for daughters' hyperactive-impulsive symptoms. Parental ASD pathology was not predictive for offspring ADHD pathology, but mother's ADHD pathology was predictive for offspring ASD pathology even when corrected for maternal ASD pathology. The latter may suggest that risk factors underlying ASD may overlap to a larger degree with risk factors underlying ADHD than vice versa. However, future research is needed to clarify this issue.

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The influence of
parental and offspring Autism Spectrum
Disorder (ASD) and Attention- Deficit/
Hyperactivity Disorder (ADHD) symptoms
on family climate

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ABSTRACT

Background There is a lack of knowledge of the influence of parental and offspring Autism Spectrum Disorder (ASD) and/ or Attention Deficit/ Hyperactivity Disorder (ADHD) symptoms on the quality of family climate. The number of affected children may play an important moderating role.

Methods 103 families were recruited with at least one child with an ASD(+ADHD) diagnosis, one or more biological affected or unaffected siblings, and two participating biological parents. Parents and children were carefully screened for the presence of ASD and ADHD symptoms. Family climate (relationship and structure) was measured with the Dutch Family Environment Scale (FES).

Results No overall differences were found between ASD, ASD+ADHD families and a norm group for family relationship and family structure. However, families with at least two affected children reported lower relationship scores than families with only one affected child, which was not accounted for by family size. As reported by both fathers and mothers, paternal and maternal ASD symptoms and paternal ADHD symptoms had a negative effect on family relationships, whereas predominately maternal ADHD had a negative impact on family structure.

Conclusions No evidence was found for a negative family climate in ASD(+ADHD) families. However, families with two or more affected children and families in which parents have increased ASD/ADHD symptoms may have more difficulties in maintaining a positive family climate.

Children with Autism Spectrum Disorders (ASD), characterized by impaired communication, and social interaction skills, as well as repetitive and restricted behavior and interest (APA, 2000), and/ or Attention Deficit Hyperactivity Disorders (ADHD), characterized by severe inattention, hyperactivity and impulsivity (APA, 2000) put a larger strain on parenting skills than typically developing children (Herring et al., 2006; Rutgers et al., 2007). In previous literature, child symptoms were associated with a suboptimal parenting environment, a less optimal parenting style, and more parenting stress (Johnston, Mash, Miller, & Ninowski, 2012). Raising an ASD/ADHD affected child might also interfere with the family climate (Biederman, Faraone, & Monuteaux, 2002; Higgins, Bailey, & Pearce, 2005). The family climate involves among others the quality of the interpersonal relationships, organization, structure and social activities and is responsible for the transmission of values and skills that are important for the social behavior of the child (Jansma & Coole, 1996). The quality of the family climate is important because it may play a significant role in the severity, comorbidity and prognosis of a child's disorder (Jansma & Coole, 1996). Evidence has been found for a suboptimal family climate, lower cohesion and more family conflict in families with ASD and/ or ADHD affected children (Biederman, Faraone, & Monuteaux, 2002; Higgins et al., 2005; Johnston & Mash, 2001; Kelly, Garnett, Attwood, & Peterson, 2008; Pressman et al., 2006; Schroeder & Kelley, 2009). However, several important factors have not been examined yet that may explain these findings, such as (a) the role of ASD-ADHD comorbidity in the offspring on family climate, (b) the role of family size and the number of affected children, and (c) the role of parental symptoms (in combination with those of the offspring) that may create the suboptimal family climate. These factors will be discussed in detail below.

ASD and ADHD are disorders that frequently co-occur together within the same patient (Rommelse, Franke, Geurts, Hartman, & Buitelaar, 2010; Ronald, Simonoff, Kuntsi, Asherton, & Plomin, 2008; Rowlandson & Smith, 2009) and within the same families (Freitag, 2007; Pamploma et al., 2009). However, due to the fact that the diagnostic guidelines in the DSM-IV have so far prevented making a comorbid diagnosis, and ASD and ADHD have been studied over the past decades in isolation from each other, there is a lack of evidence for a combined effect of ASD and ADHD on family climate. It remains unclear whether there are differences in family climate in families with ASD and comorbid ADHD pathology. It is possible that the presence of comorbid ADHD pathology in families with ASD pathology may have a different effect on family climate than the presence of ASD only pathology in families. Families with offspring with only ASD may be less demanding and challenging for parents, since parents must deal with only one disorder in contrast to families dealing with the sometimes opposite upbringing demands of offspring having both ASD and ADHD pathology. Consequently, a more positive family climate may be found in families with ASD only pathology compared to families with both ASD and ADHD pathology.

Another possibility is that the family climate may be influenced by raising multiple affected children within one family. Although, this hypothesis has rarely been studied in relation to family climate before, it is not hard to imagine that it might be more difficult for parents to maintain a positive family climate when multiple children are affected compared to the situation in which only one child is affected. Parents of multiple affected children may be more stressed because they must switch between the demands of raising two or more affected children with each of their own problem behavior and needs. This has been reported before in a study of Orsmond et al. (2007) who found higher levels of depressive symptoms and anxiety and lower family adaptability and cohesion in mothers who were parenting another child with a disability in addition to a child with ASD compared with mothers with only one child with ASD. Importantly, family size may be relevant to consider in this context, since it may adversely affect family climate (Hart & Risley, 1992; Jenkins, Rasbash, & O'Conner, 2003). However, in previous literature mixed results were found, with one study reporting no effect of family size on parenting or temperament developmental processes (Bridgett et al., 2009), but several other studies reporting negative effects of increased family size parent-child interactions (Hart & Risley, 1992; Jenkins et al., 2003).

Family climate may also be influenced by parental pathology. Since both disorders are highly heritable, children with ASD and/or ADHD may have one or two parents that display subthreshold or above threshold symptoms (Constatino & Todd, 2005; Faraone, Kunwar, Adamson, & Biederman, 2009). In previous literature negative effects of parental symptoms were reported. For example, parental ADHD was associated with higher levels of family conflict and lower levels of family cohesion compared to families without parental ADHD (see for a review Johnston, Mash, Miller, & Ninowski, 2012). However, to what extent parental ASD symptoms may affect family climate is largely unknown. This may be an unexpected consequence of the in 1940's launched hypothesis of Bettelheim (1967) that the cause of autism was attributed to a lack of maternal warmth. Although, it is now universally accepted that this hypothesis is flawed, the influence of parental ASD symptoms on family climate for long remained a very sensitive and neglected area of research. Therefore, it is of great interest to examine the possible effects of parental ASD and ADHD symptoms on family climate.

The current study sets out to examine family climate in 103 families with at least one ASD affected (with/ without ADHD) and at least one sibling and two biological parents. Family climate data (operationalized as family relationship and family structure) were obtained from both fathers and mothers, as were data on their own ASD and ADHD symptoms. These data allowed us to examine (1) if the family climate differs between families with ASD only affected children and families with ASD+ADHD affected children and the norm group, (2) if the family climate is influenced by the number of affected children, and (3) if the family climate is influenced by paternal and maternal ASD and ADHD symptoms.

METHODS

Participants

Children

A subsample of 103 families was recruited as part of a large family-genetics study (Biological Origins of Autism [BOA]). Families were included in the current study if (a) they had at least one child (2-20 years) with a clinical diagnosis of ASD (with or without ADHD); diagnosis mostly based on Autism Diagnostic Interview - Revised (ADI-R) and Autism Diagnostic Observation Scale (ADOS) assessment), and (b) at least one biological sibling (regardless of possible ASD or ADHD- status), and, (c) both biological parents willing to participate. All families were of European Caucasian descent. Participants were excluded if they were nonverbal, had an IQ ≤ 60 , specific learning or language disorders, a diagnosis of epilepsy, brain disorders or known genetic disorder such as Down- syndrome, Fragile-X- syndrome or Rett's syndrome. Comorbid *DSM-IV* disorders were not excluded.

Both the children already clinically diagnosed with ASD and/or ADHD and their siblings were carefully screened for the presence of ASD symptoms with the Social Communication Questionnaire (SCQ) (Rutter, Bailey, & Lord, 2003). Children with a score above 10 on the parent version (to avoid the exclusion of children with milder ASD symptoms e.g. false negatives) or above 15 on the teacher version of the SCQ (to avoid that the often more subtle ASD symptoms reported by teachers were not confirmed by the parent SCQ or ADI-R) were included. To confirm the diagnosis of ASD, the Autism Diagnostic Interview Revised (ADI-R) (Le Couteur, Lord, & Rutter, 2003) was administered for the children scoring above clinical cut-off of the SCQ. Children were given a diagnosis of ASD if scoring above clinical cut- off on the ADI-R.

Furthermore, all children were carefully assessed for the presence of ADHD symptoms using the Conners long version Rating Scales Revised (CRS-R) (Conners, 1997) completed by both parents and teachers. For all children scoring above cut-off ($T \geq 63$: a lower cutoff for the CRS-R were chosen to avoid the exclusion of children with milder ADHD symptoms [e.g., false negatives]) on any of the parent or teacher Conners' DSM-IV Inattention, Hyperactivity-Impulsivity or Combined scales, the Parental Account for Childhood Symptoms (PACS) (Taylor, Sandberg, Thorley, & Giles, 1991), a standardized semi-structured interview for dimensionally and categorical diagnoses, was administered by a certified clinician. Thereafter, the items of the teacher rated CRS-R that were scored 2 [pretty much true] or 3 [very much true] were combined with the item scores on the PACS to confirm a formal diagnosis of ADHD (see for details, Rommelse, Oosterlaan, Buitelaar, Faraone & Sergeant, 2007a). We were able to include 47 families ($N = 114$ children) that had one or more children (probands and siblings) with an ASD diagnosis *without* clinical ADHD symptoms (ASD families) and 56 families ($N = 148$ children) that had one or more

Table 1a Characteristics children

	ASD only families (N= 47)	within comparisons	ASD+ADHD families (N= 56)
	<i>M (SD)</i>	<i>Contrast</i>	<i>M (SD)</i>
N Children per family	2.5 (.82)		2.8 (.97)
N affected children per family	1.2 (.41)		1.6 (.72)
Relative N of affected children (Ratio ¹)	.52 (.18)		.60 (.21)
	Probands (N=47)/ Siblings (N=67)		Probands (N=56)/ Siblings (N=92)
% male	85.1/ 41.8		83.9/ 55.4
Age in years	12.1 (4.0) / 12.2 (4.9)		11.3 3.7) / 10.3 (4.6)
Estimated full scale IQ	97.7 (16.2)/ 104.42 (14.1)	prob < sibs	97.2 (15.9)/ 103.7 (13.7)
SCQ (ASD symptoms)	20.0 (7.7)/ 5.3 (5.9)	prob > sibs	20.5 (6.6)/ 7.0 (7.6)
CRS-R ³ (ADHD symptoms)	58.6 (9.2)/ 53.0 (9.2)	prob > sibs	67.1 (9.2)/ 54.9 (10.6)
CRS-R: oppositional scale	57.2 (11.7)/ 54.1 (12.7)	prob > sibs	63.3 (12.1)/ 53.8 (10.0)
CRS-R anxiety scale	65.8 (14.2)/ 54.9 (12.5)	prob > sibs	66.2 (14.5)/ 56.3 (15.2)
% ASD (ADI) ⁴	100/ 13.4		19.6/ 13.0
% ADHD (PACS) ⁵	0/ 0		0/ 13.0
% ASD+ADHD (ADI and PACS)	0/ 0		80.4/ 8.7

*prob and sibs= probands and siblings ¹ratio= amount of children per family/ affected children per family.

²Social Communication Questionnaire, norms based on population cohort (N=247) (Chandler et al., 2007).³Conners long version Rating Scales Revised. ⁴Autism Diagnostic Interview (ADI-R). Parental Account for Childhood Symptoms (PACS).

children with an ASD diagnosis and/ or clinical ADHD symptoms (probands and siblings) (ASD+ADHD families), see Table 1a for sample characteristics. Behavioral measures of parents (ASD and ADHD symptoms) were compared with control families (N= 73 fathers and 74 mothers) recruited in the same way as ASD families of the BOA-study.

Full scale IQ of the children was estimated by using four subtest (Similarities, Block Design, Vocabulary and Picture Completion) of the Dutch version of the Wechsler Preschool and Primary Scale of Intelligence (WPSSI-III: 2;6 -7; 11 years), Wechsler Intelligence Scale of Children (WISC-III: 6- 16 years), or the Wechsler Adult Intelligence scale (WAIS-III: 16- 84;11 years) (Wechsler, 1989, 2000, 2002).

	within comparisons	norms (n)		
	<i>Contrast</i>	<i>M (SD)</i>	<i>Contrast</i>	<i>Contrast</i>
			ns	
			asd < asd+adhd	
			ns	
			between probands	between siblings
			ns	asd < asd+adhd
			ns	asd > asd+adhd
	prob < sibs		ns	ns
	prob > sibs	4.7 (5.0) ²	asd = asd+adhd > n	asd+adhd > n
	prob > sibs	50 (10)	asd < asd+adhd > n	asd = asd+adhd > n
	prob > sibs	50 (10)	asd < asd+adhd > n	asd = asd+adhd > n
	prob > sibs	50 (10)	asd = asd+adhd > n	asd = asd+adhd > n

Parents

All parents were assessed for the presence of ASD symptoms with the self report Autism Spectrum Quotient (AQ; Baron-Cohen, Wheelwright, Skinner, Martin, & Clubley, 2001). The AQ consist of 50 items rated on a 4-point rating scale. The total score was used as indication of ASD symptom severity (Hoekstra, Bartels, Cath, & Boomsma, 2008; Hoekstra, Bartels, Verweij, & Boomsma, 2007). Self reported ADHD symptoms of the parents were assessed with the DSM raw total score for ADHD on a 4-points scale of the Conners Adult Rating Scales- Self-report: Long version (CAARS-S:L; Conners, Erhardt, & Sparrow, 1998, 1999). In total, self reported ASD and ADHD data were available for 99/103 fathers and 103/103 mothers. See Table 1b for sample characteristics.

Table 1b Characteristics parents

	ASD only families (N= 47)	within comparisons	ASD+ADHD families (N= 56)
	<i>M (SD)</i>	Contrast	<i>M (SD)</i>
Education	4.8 (1.0)/ 4.4 (.88) ¹	fath > moth**	4.5 (.99)/ 4.4 (.89)
Autism Quotient (ASD symptoms)	104.4 (17.4)/ 95.2 (18.4)	fath > moth	107.8 (20.7)/ 96.4 (21.0)
ADHD DSM-IV raw inatt scores ⁴	4.2 (4.0)/ 3.9 (4.3)	ns	6.9 (5.0)/ 5.2 (6.3)
ADHD DSM-IV raw hyp-imp scores ⁴	5.0 (3.9)/ 5.1 (3.8)	ns	5.6 (3.7)/ 5.7 (4.9)

** fath and moth= father and mother ¹1= nursery school 2= primary education 3= secondary education, first phase 4= secondary education, second phase 5= higher education, first phase 6= higher education, second phase 7= higher education, third phase. ²Central Bureau of statistics (CBS, 2009). ³Scores were based on N=73 fathers and N= 74 mothers of control families of the BOA-study. ⁴ADHD DSM-IV raw inattentive scores and raw hyperactive-impulsive symptoms, scores were based on N=73 fathers and N= 74 mothers of control families of the BOA- study.

To assess the family environment, the Dutch version of the Family Environment Scale (FES) (Jansma & Coole, 1996) was used. The FES consists of 77 yes/ no questions (for example, 'we fight a lot in our family', 'family members often keep their feelings to themselves') related to 7 subscales: 1) cohesion (family commitment and support), 2) expressiveness (expression of feelings), 3) conflict (expression of anger and aggression), 4) organization (structure and planning of family life), 5) control (rules used in family life), 6) family values (opinion about norms and behavior) and 7) social orientation (involvement in the social environment). Each subscale consists of 11 questions and scores range from 0 to 11, higher scores indicating a more positive environment, (vice versa for the conflict scale). In this study two index scores were used: the Family Relationships Index (FRI), based on three subscales (i.e. cohesion, expressiveness and conflict) and the Family Structure Index (FSI), based on two subscales (i.e. organization and control). Higher scores indicate better family relationships and parental structure (Gazendam-Donofrio et al., 2007). Both FES indices and subscales have shown good test- retest reliability and adequate internal consistency (>.60) and has been extensively tested by normal controls, families with/ without behavioral problems and families with/ without parenting problems (Jansma & Coole, 1996). The two subscales which are not linked to the two indices i.e. family values and social orientation, are not included in this study. Both mothers and fathers completed the FES under supervision of the researchers. Data was available for

	within comparisons	norms (n)		
	Contrast	M (SD)	Contrast	Contrast
			between fathers	between mothers
	ns	4.3 ²	asd > n	ns
	fath > moth	95.4 (16.3)/ 84.1 (12.9) ³	asd = asd+adhd > n	asd = asd+adhd > n
	fath > moth	4.4 (3.1)/ 3.3 (2.5) ⁴	asd+adhd > n	asd+adhd > n
	ns	4.9 (3.2)/ 4.4 (2.4) ⁴	ns	asd+adhd > n

N= 97 fathers and N= 102 mothers regarding the family relation scale and N= 97 fathers and N= 102 mothers regarding the family structure scale.

No FES-data was obtained from the control families recruited at the BOA- study. However, norm data of the FES were available for the two indices based on N= 1,707 Dutch families without psychopathology (Jansma & Coole, 1996) with secondary education or higher education level comparable with the BOA- families. No differences were found between scores of fathers and mothers regarding both indices (Jansma & Coole, 1996).

Procedure

Eligible ASD (with/ without ADHD) families registered at an outpatient clinic specialized in ASD and ADHD pathology (Karakter Child and Adolescent Psychiatric University Center) and members of the Dutch Autism Association (NVA) received a brochure containing information about the BOA study and were requested to return a pre-stamped response card. A short telephone screening and, subsequently, screening questionnaires were used to verify if families were eligible to participate. These families were invited to visit Karakter Child and Adolescent Psychiatry Nijmegen, where a researcher conducted the diagnostic interview(s) (ADI-R and/ or the PACS). Children who score above clinical cut-off on the SCQ and CRS-R receive both the ADI-R and PACS interviews. Children who score above clinical cut-off on the

SCQ or CRS-R receive only the ADI-R or the PACS interview. All researchers were extensively trained in the ADI-R and PACS by a certified trainer. The ADI-R and PACS training consisted of watching and coding several videotapes of interviews and discussions about coding and administration. The trained researchers must achieve at least 80% agreement in coding with the certified trainer. As part of a larger study, additional data was collected, including blood samples of all family members and neuropsychological data of the children. The study was approved by the local medical ethics board and parents and children (above 12 years of age) signed for informed consent.

Data-analyses

Analyses were performed with SPSS 20. The Expectation Maximization (EM) algorithm (Tabachnick & Fidell, 2001) was used to impute the missing values (<5%). Correction for multiple testing using the 95% CI, was performed with the False Discovery Rate procedure (Benjamini, 2010). One sample T-tests were performed for comparisons with the norm data of the FES. First, effects of possible confounders of child's age (by calculating the absolute age by adding up all ages to correct for the discrepancy between ages and by calculating the mean age of children) and IQ, were examined using Pearson correlations. To examine the effect of family type (ASD or ASD+ADHD) on the family relationship and family structure, two separate (regarding the two indices) repeated measure ANOVAs were used. Variables included into the model were (1) family type (ASD and ASD+ADHD), and (2) parent (father/mother) as repeated measure (to account for within family measurements), and (3) the two-way interaction effect (parent by family type).

To examine the effect of the absolute number of affected children, repeated measure ANOVAs were used with the absolute number of affected children and family type (ASD versus ASD+ADHD) as factors, and parent (father/mother) as repeated measure. Since there were only 4 families with 3 or more affected children, the absolute number of affected children was used as dichotomous factor (1 versus 2 or more affected children).

Additionally, we include the factor relative number of affected children in our analyses to rule out the effect of the ratio of affected children and the total number of children in one family. This was calculated by dividing the number of affected children by the total number of children within one family (for example, 2:4= 0.5). We also included the effect of absolute family size in our analyses to rule out the effect of the total number of children within one family. Both additional factors were examined in a similar way as the absolute number of affected children.

Further, to examine to what extent own and spouse ASD and ADHD symptoms were related to family climate, ANOVAs were used. Dependent variable was the family relationship index or the family structure index of the FES. Variables included in the

model were (1) paternal and maternal ASD symptoms (total AQ score), (2) paternal and maternal ADHD symptoms (DSM-IV ADHD raw subscales scores), (3) family type (ASD versus ASD+ADHD) and (4) all two- and three way interactions. The two and three -way interactions were dropped from the model in case of non-significance and the model was rerun. We repeated the above analyses with the subcomponents of the two indices (cohesion, expressiveness, conflict, organization and control) to explore which component is especially impacted by own and spouse ASD and ADHD symptoms.

RESULTS

Fathers and mothers of ASD and ASD+ADHD families reported significant higher ASD symptoms than the control group whereas only parents of ASD+ADHD families reported significantly higher scores on inattentive and hyperactive symptoms than the control group (see Table 1). Moderate to large correlations were found between spouses' family relationship index scores ($r = .58, p < .001$) and family structure index scores ($r = .47, p < .001$), indicating that fathers and mothers reported relatively similar on the indices. Moderate correlations were also found between the family relationship index and family structure index within fathers ($r = .31, p = .001$) and mothers ($r = .28, p = .01$), indicating that the two indices within parents are related to each other. Overall no effects of age (all p 's were between .06 and .81) were found regarding the family relationship and family structure index. Only one exception was found, the mean age ($r = -.23, p = .02$) and absolute age ($r = -.20, p = .04$) were negatively related to the family structure index as reported by mothers. Since there was overall no main effect, age was omitted from further analyses to reduce the complexity of the results.

Differences in family climate in ASD and ASD+ADHD families

Comparisons with the norm data of the FES revealed that both fathers and mothers of ASD only families reported higher relationship index scores than the norm ($t(46) = 3.04, p = .004$ and $t(46) = 2.95, p = .01$, respectively) whereas this was not the case for fathers and mothers of ASD+ADHD families ($t(55) = 0.69, p = .50$ and $t(55) = 0.32, p = .75$, respectively) (see Figure 1). Next, examining the differences in family climate between ASD and ASD+ADHD families, no significant two-way interaction was found between parent by family type (ASD and ASD+ADHD) ($F(1,101) = .02, p = .89$) regarding the family relationship index. This implies that there were no differences in family climate between fathers and mothers and ASD only and ASD+ADHD families. No main effects of parent ($F(1,101) = .07, p = .78$) or family type ($F(1,101) = 2.70, p = .10$) were found, indicating there were no differences between fathers and mothers or between family types regarding the relationship index.

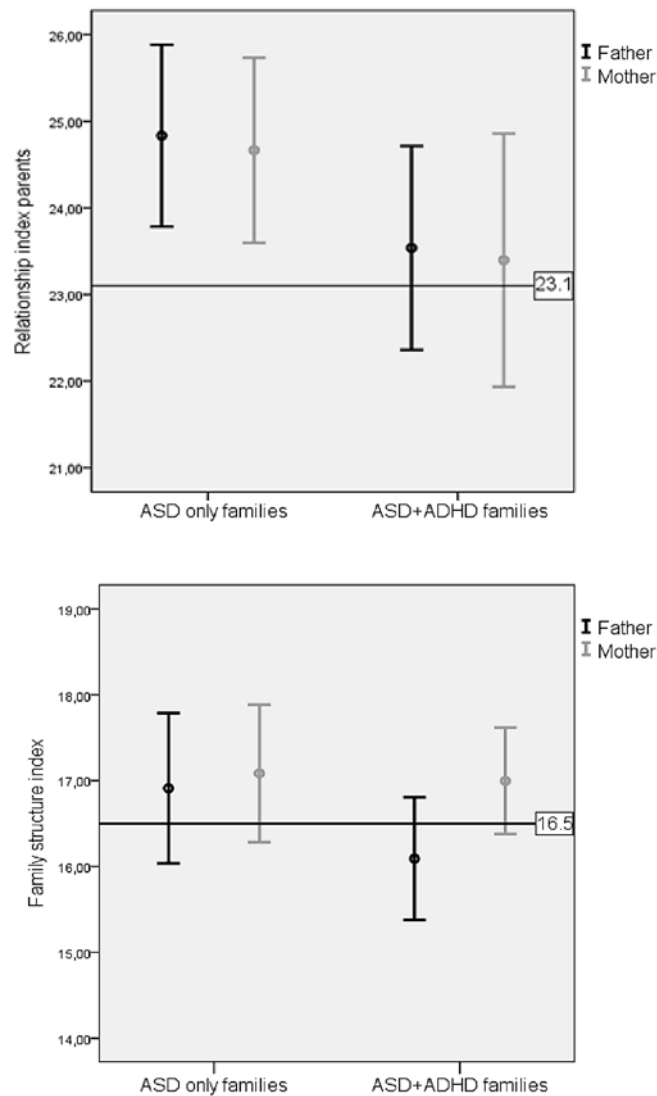


Figure 1 Comparison of the Dutch version of the Family Environment Scale (FES) index scores between and within ASD (N= 47) and ASD+ADHD (N= 56) families and the norm group

Norms relationship scale 23.1 (5.2) and family structure 16.5 (3.8) for both fathers and mothers (Jansma & Coole, 1996). The error bars represented the 95% Confidence Interval (CI) using one-sample T-test in comparison to the population norm value.

Comparisons with the norm data of the FES and family structure index scores revealed that both fathers and mothers of ASD only families ($t(46) = 1.41, p = .17$ and $t(46) = -1.46, p = .15$, respectively) and ASD+ADHD families ($t(55) = -1.32, p = .19$ and $t(55) = 1.53, p = .13$, respectively) reported similar family structure index scores (see Figure 1). Further, no significant two-way interaction (parent by family type) was found ($F(1,101) = 3.17, p = .08$) and no main effects of parent ($F(1,101) = 3.33, p = .07$) or family type ($F(1,101) = 1.62, p = .21$) were present, indicating that there were no difference between fathers and mothers and ASD only and ASD+ADHD families.

Effects of family size on family climate

Regarding both the family relationship and family structure index, no three-way ($F(1,99) = .44, p = .51$ and $F(1,99) = .10, p = .76$, respectively) or two-way interaction effects (all p 's were between .21 and .96) were found between family type, family size and parent. No significant main effect of family size was found regarding both the family relationship ($F(1,99) = 1.60, p = .21$) and the family structure index ($F(1,99) = .24, p = .62$), indicating that family size has no effect on family climate.

Effects of raising multiple affected children within one family

Absolute number of affected children

A total of $N=68$ families with one affected child (ASD with/ without ADHD) and $N=35$ families with at least two affected children (ASD and/ or ADHD) were included in the analyses. Comparisons with the norm data of the FES revealed that both fathers and mothers of families with one affected child reported higher family relationship scores than the norm ($t(67) = 3.47, p = .001$ and $t(67) = 2.24, p = .03$, respectively), whereas fathers and mothers of families with at least two affected children reported similar scores as the norm ($t(34) = -0.58, p = .57$ and $t(34) = -0.22, p = .83$, respectively). Regarding the family structure index, fathers and mothers of both families of one affected child and families with at least two affected children reported similar scores as the norm data of the FES (all p 's were between .45 and .65), except mothers of families of one affected child that scored higher than the norm ($t(67) = 2.34, p = .02$). Next, examining the differences in family climate between fathers and mothers of families with one affected child and at least two affected children, no three-way (absolute number by parent by family type) ($F(1,99) = 2.05, p = .16$ and $F(1,99) = .05, p = .82$, respectively) and two-way interaction effects (parent by family type, absolute number of affected children by family type and, absolute number of affected children by parent) were found regarding the family relationship and family structure index, (all p 's were between .13 and .82). A main effect of the absolute number of affected children was found for the family relationship index ($F(1,99) = 4.41, p = .04$), but no main effect was found for the family structure index ($F(1,99) = 0.17, p = .68$). This

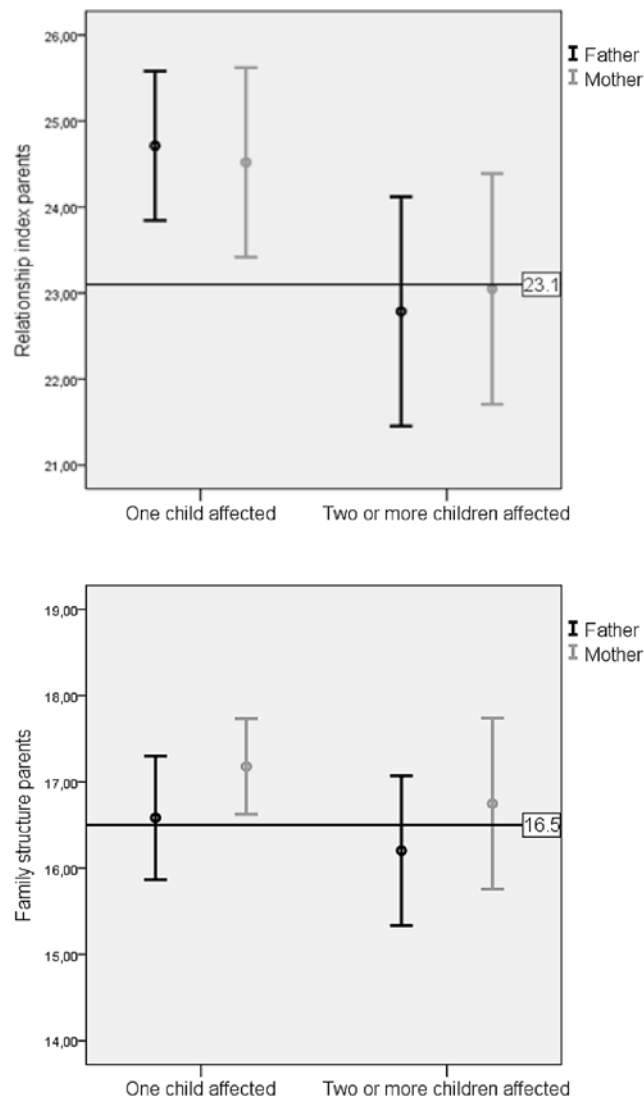


Figure 2 Comparison of the Dutch version of the Family Environment Scale (FES) index scores between and within families with one affected child (N= 68) and families with at least two affected children (N=35)

Norms relationship scale 23.1 (5.2) and family structure 16.5 (3.8) for both fathers and mothers (Jansma & Coole, 1996). The error bars represented the 95% Confidence Interval (CI) using one-sample T-test in comparison to the population norm value.

means that families with at least two affected children reported lower family relationship scores than families with one affected child (see Figure 2). In addition, when repeating these analyses with the relative number of affected children in the family (the total number of affected children by the total number of children within one family), no significant two-way interactions or main effects were found regarding family relationship and family structure, indicating that the relative number of affected children has no effect on family climate.

Effects of paternal and maternal ASD and ADHD symptoms on family climate

ANOVAs with paternal and maternal ASD symptoms, paternal and maternal ADHD symptoms, family type and all two- and three-way interaction effects between these variables were used to examine the effect of parental symptoms on family climate (family relationship and structure as reported by fathers and mothers). The most parsimonious model for the family relationship index for both fathers and mothers was a model with one two-way interaction between paternal and maternal ASD symptoms (as reported by fathers: $F(1,102) = 5.98, p = .02 [\eta^2 = .06]$ and mothers: $F(1,102) = 4.74, p = .03 [\eta^2 = .05]$), main effects of paternal ASD (as reported by fathers: $F(1,102) = 8.40 [\eta^2 = .08]$, $p = .01$ and mothers: $F(1, 102) = 5.14, p = .03 [\eta^2 = .05]$) and maternal ASD symptoms (as reported by fathers: $F(1, 102) = 6.04, p = .02 [\eta^2 = .06]$ and mothers: $F(1, 102) = 4.70, p = .03 [\eta^2 = .05]$), and paternal ADHD symptoms (only reported by mothers: $F(1, 102) = 7.72, p = .01 [\eta^2 = .07]$) (see Figure 3). The two-way interaction indicated that the effect of paternal ASD on the family relationship index was stronger than the effect of maternal ASD. Analyses with the subscales of the family relationship index revealed that paternal ASD symptoms impacted especially the subscales expressiveness ($F(1,102) = 7.01, p = .01$) and conflict ($F(1,102) = 3.99, p = .05$) and maternal ASD symptoms the subscale conflict ($F(1,102) = 4.89, p = .03$). Paternal ADHD (only reported by mothers) impacted all three subscales: cohesion ($F(1, 102) = 6.87, p = .01$), expressiveness ($F(1,102) = 5.19, p = .03$) and conflict ($F(1,102) = 8.40, p = .005$). The most parsimonious model for the family structure index for both fathers and mothers was a model with maternal ADHD (as reported by fathers: $F(1,102) = 5.07, p = .03 [\eta^2 = .05]$ and mothers: $F(1,102) = 5.81, p = .02 [\eta^2 = .06]$), but not paternal ADHD (as reported by fathers: $F(1,102) = 3.01, p = .09$ and mothers: $F(1,102) = 1.86, p = .18$). Analyses with the subscales of the family structure index revealed that maternal ADHD impacted especially the subscale organization ($F(1,102) = 5.24, p = .02$).



Figure 3 Family relationship and structure index measured with the Family Environment Scale (FES) in relation to parent ASD and ADHD symptoms (N= 103)

Family relationship and structure as a function of paternal and maternal symptoms of ASD and ADHD. Higher Z-scores on the X-axis indicate more parental or maternal symptoms. Higher scores on the Y-axis indicate a higher score on the family relationship and structure index.

DISCUSSION

The main aim of this study was to examine the possible influence of offspring and parental ASD and ADHD symptoms, as well as the possible effect of raising multiple affected children, on family climate. We found no evidence that in general, compared with the Dutch norm data of the FES, family climate in families with offspring with ASD or ASD+ADHD was more negative. The absolute number of affected children negatively impacted the family climate which was not explained by family size per se. However, within ASD and ASD+ADHD families negative effects of both paternal ASD, maternal ASD and paternal ADHD symptoms on family relationships were found, as well as negative effects of maternal (but not paternal) ADHD symptoms on family structure.

The most intriguing finding of this study is that there was no evidence for a suboptimal family climate *per se* in families with ASD/ADHD affected offspring. This is remarkable, given that previous studies (Biederman et al., 2002; Higgins et al., 2005; Johnston & Mash, 2001; Kelly et al., 2008; Pressman et al., 2006; Schroeder & Kelley, 2009) found a lower cohesion and more family conflict in families with ASD and/or ADHD affected children. However, other studies are in line with the current study, documenting on a similar positive family climate in families of children with ASD on a measure of emotional closeness (Hoffman, Sweeney, Lopez-Wagner, & Looney, 2009). These authors suggested that the diagnosis of ASD itself may serve as a protective factor in the parent-child relationship, in that parents view the child as less responsible for his or her behavior. This view was supported by two other studies that have found that parents of children with ASD were less likely to be angry with their child - despite reporting that they were bothered by their child's behavior - and attributed most of their child's misbehavior to ASD symptoms, rather than their child's personality or temperament (Montes & Halterman, 2007; Whittingham, Sofronoff, Sheffield, & Sanders, 2008). As suggested by Weiss et al. (2012) parent's psychological acceptance of the child diagnosis may serve as a partial mediator between problematic child behavior and parent mental health problems. Nevertheless, a negative effect of raising multiple affected children on the family climate (family relationship index) was found, which could not be explained by family size *per se*. Parents of families with at least two affected children reported lower family relationship scores than families with one affected child, but not lower than Dutch norm data, suggesting that even in these families an adequate family climate appears to exist.

This study provides evidence for negative effects of parental ASD and ADHD symptoms. Both fathers and mothers reported that paternal ASD and maternal ASD symptoms were negatively related with the relationship index, aspects of the family climate that are related to parent-child relationships (especially the subscales expressivity and conflict). In contrast, parental ASD symptoms did not influence family structure (organization, structure and control), and these contrasting effects are comparable for fathers and mothers. In contrast, paternal ADHD symptoms negatively influenced family *relationships*, whereas maternal ADHD symptoms negatively influenced family *structure* (especially the subscale organization). This may possibly be explained by the different roles and functioning in family life fulfilled by fathers and mothers: although there are fathers as primary caregivers, mothers are usually more involved in organizing day-to-day activities (making sure all children arrive on time at school, and overview what groceries are needed to be bought) compared to fathers (Craig, 2006) and ADHD symptoms characterized by disorganized, chaotic lifestyle may negatively affect these day-to-day activities; In contrast, fathers are usually more involved in play, talking and recreational activities and paternal ADHD may negatively affect these activities resulting in a more negative

family relationship. In other words, it seems that ASD symptoms have a negative effect on family relationships for mothers and fathers alike, whereas the negative effect of ADHD on family functioning depends on which parent is affected.

Our findings should be interpreted in the context of several limitations. First, we relied on parents' self ratings of family climate instead of objective measurements. Our findings may be the results of parents' perception of the family climate and may not be an accurate reflection of the actual home situation. Nevertheless, because previous studies suggest that self reported family climate correlates highly with observation of family climate in the home situation (Hinshaw, Han, Erhardt, & Huber, 1992; McHale, Kuersten-Hogan, Lauretti, & Rasmussen, 2000; Morrongiello & House, 2004; Zaslou et al., 2006), and the results were quite consistent across reporter, it is unlikely that reporter bias explained our findings. However, repeating this study with more objective home climate assessments is needed to clarify this issue. Second, it is unclear to what extent results are equally applicable to children affected with an ADHD-only diagnosis. Future research should clarify whether the results found in this study were also present in ADHD only families.

In conclusion, this is one of the first studies that reports on the influence of parental and offspring ASD and ADHD symptoms and the effect of raising multiple affected children on family climate. No evidence was found for a more negative family climate in families with ASD (+ADHD) affected offspring. Maternal and particularly paternal ASD symptoms have a negative effect on family relationships. Further, maternal ADHD symptoms appear to be negatively related to family *structure* whereas paternal ADHD symptoms were negatively related to family *relationships*. Child diagnosis (ASD or ASD+ADHD affected) does not appear to influence family climate, but raising two or more affected children does have a negative effect on the family relationship compared to raising one affected child (albeit the family climate is still not worse compared to Dutch norms). The results suggest that, although parental ASD or ADHD and raising multiple affected children were negatively related to family climate, still a positive family climate were found in families with ASD (+ADHD) affected offspring.

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Are parental Autism Spectrum Disorder and/or Attention- Deficit/Hyperactivity Disorder symptoms related to parenting styles in families with ASD (+ADHD) affected children?

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ABSTRACT

Background An understudied and sensitive topic nowadays is that even subthreshold symptoms of Autism Spectrum Disorder (ASD) and Attention-Deficit/Hyperactivity Disorder (ADHD) in parents may relate to their parenting styles. The aim of this study was to explore the influence of (the combined) effect of child diagnosis (ASD or ASD+ADHD affected/ unaffected children) and parental ASD and/ or ADHD on parenting styles.

Methods 96 families were recruited with one child with a clinical ASD(+ADHD) diagnosis, and one unaffected sibling. Parental ASD and ADHD symptoms were assessed using self-reports. The Parenting Styles Dimensions Questionnaire (PSDQ) self- and spouse report were used to measure the authoritative, authoritarian and permissive parenting styles.

Results Fathers and mothers scored significantly higher than the norm data of the PSDQ on the permissive style regarding affected children, and lower on the authoritative and authoritarian parenting style for affected and unaffected children. Self- and spouse report correlated modestly to strongly. Higher levels of paternal (not maternal) ADHD symptoms were suboptimally related to the three parenting styles. Further, two parent-child pathology interaction effects were found, indicating that fathers with high ADHD symptoms and mothers with high ASD symptoms reported to use a more permissive parenting style only towards their unaffected child.

Conclusions The results highlight the negative effects of paternal ADHD symptoms on parenting styles within families with ASD(+ADHD) affected offspring and the higher permissiveness towards unaffected offspring specifically when paternal ADHD and/or maternal ASD symptoms are high. Parenting training in these families may be beneficial for the well being of all family members.

Autism Spectrum Disorder (ASD) and Attention-Deficit/Hyperactivity Disorder (ADHD) are highly heritable disorders and often co-occur in the same patient and/or family (Rommelse, Franke, Geurts, Hartman, & Buitelaar, 2010). By consequence, children with ASD or ASD+ADHD may have one or two parents that show subthreshold (Broader Autism Phenotype, BAP) or above threshold symptoms of ASD or ADHD (Bishop et al., 2004; Constatino & Todd, 2005; Faraone, Kunwar, Adamson, & Biederman, 2009; Groen et al., 2012). These parental ASD and/ or ADHD symptoms may affect their parenting skills. This is reported regarding parental personality (Clark, Kochanska, & Ready, 2000; Prinzie, Stams, Dekovi, Reijntjes, & Belsky, 2009) and psychopathology, such as depression (Cummings, Keller, & Davies, 2005; Wilson & Durbin, 2010) and anxiety disorder (Bruggen, Stams, & Bögels, 2008; Woodruff-Borden, Morrow, Bourland, & Cambron, 2002). For instance, depression in parents was associated with decreased positive emotions, warmth, sensitivity, and responsiveness, and increased negative emotions, hostility and disengagement (Wilson & Durbin, 2010). This may also apply for parental ASD and/or ADHD symptoms and in this way provide a suboptimal environment for these already vulnerable children. However, it is possible that the presence of parental ASD symptoms may have a different effect on the environment than the presence of parental ADHD symptoms. Since ASD and ADHD often co-occur within the same patient or family, it is of great relevance to study the effect of parental ASD and ADHD symptoms together. Although the study of ASD or ADHD symptoms in parents and the impact thereof on child development is important, it is also a very sensitive area of research. Bettelheim claimed in the 1940's that the cause of autism was attributed to a lack of maternal warmth (Bettelheim, 1967). As a result of this view, mothers were found responsible for their children's autism and many mothers suffered from feelings of guilt and doubt about their parenting skills. It is universally accepted that autism is nowadays a complex neurobiological disorder and not *caused* by parenting styles (Silver & Rapin, 2012). Nevertheless, the importance of research regarding parenting styles is highlighted by the fact that a child with ASD may have a negative effect on parenting styles since the lack of reciprocal relationships and the communication deficits may decrease parental warmth and increase more protective and controlling behavior of parents (Baumrind, 1996; Gau et al., 2010; Rutgers et al., 2007; Woolfson & Grant, 2006). In turn, negative parenting styles may increase the child (additional) behavioral problems (Gau et al., 2010; Reed, Osborne, McHugh, & Saunders, 2008; Siller & Sigman, 2002; Wachtel & Carter, 2008). For example, an association has been found between suboptimal parenting and more thought problems, social problems, inattentive, hyperactive, disruptive and maladaptive behavior in children with ASD (Gau et al., 2010). However, parenting seems nowadays a relatively neglected area of research in ASD, and it may be relevant to examine whether parental ASD and/ or ADHD symptoms relate to parenting styles. Further since that ASD and ADHD

symptoms often co-occur (Freitag, 2007; Pamploma et al., 2009; Rommelse, Jansen, & Heemink, 2010; Ronald, Simonoff, Kuntsi, Asherton, & Plomin, 2008; Rowlandson & Smith, 2009), it is relevant to examine their combined effect on parenting styles in ASD or ASD+ADHD.

Before further discussing the studies that have examined parenting styles in relation to ASD and ADHD pathology, it is relevant to first define the term 'parenting style'. Baumrind (1973) has conceptualized various parenting styles, including the authoritative, authoritarian, and the permissive parenting style. The *authoritative* parenting style is characterized by a large amount of control and high responsiveness of the parents towards the child. Parents express affection, approval and acceptance towards their child, and set reasonable rules adapted to the wishes and needs of their child. The *authoritarian* parenting style is also characterized by a large amount of control, but little responsiveness of the parents towards the behavior of the child. These parents dominate the child and his/her behavior, do not explain rules to the child and are insensitive to the child's needs or displaying hostile or a negative attitude towards the child. In comparison with the authoritative parenting style, parents with a *permissive* parenting style are also responsive and give the child a lot of positive attention. However these parents tend to use little control and adjust their parenting behavior too much to the wishes of their child. It has been shown that little control in combination with less responsiveness (permissive parenting style) or a large amount of control in combination with less responsiveness (authoritarian parenting style) are important risk factors for the cognitive and social development (e.g. lower self-concept and lower locus of control, lower math and reading scores, less proficient psychosocial competence and maturity) in typically developing children, but also in children with psychopathologies (Baumrind, 1991; Lee, Daniels, & Kissinger, 2006; Rogers, Wiener, Marton, & Tannock, 2009). Although a large amount of control (authoritarian parenting style) may be positive for a child with ASD (with/ without ADHD) since the rules are strict and clear, the insensitivity for the child's needs and the tendency to react hostile towards the child may not be very beneficial.

Given the previously mentioned sensitive history of ASD and parenting, it bears no surprise that we only were able to find studies on parental ADHD symptoms in relation to parenting practices, and not parental ASD symptoms. A recent review shows that there is considerable evidence that fathers and mothers with subthreshold or above threshold ADHD symptoms may use a more permissive parenting style, because they are less able to monitor, provide structure, effective discipline, and warmth towards their children (Johnston, Mash, Miller, & Ninowski, 2012). However, this review finds also evidence that particularly fathers with high compared to low levels of ADHD symptoms used a large amount of control and less warmth, equivalent to a more authoritarian parenting style. Since both strategies are less effective parenting styles in relation to positive child outcomes, this suggest that high levels of

ADHD symptoms might interfere with effective parenting. Of great interest is to examine whether these effects can be replicated within families with ASD in relation to parental ASD and ADHD symptoms.

The greatest challenge in studies targeting parenting styles in relation to parental ASD or ADHD symptoms is to disentangle the effects of child pathology and parental pathology on parenting practices. It is well known that children with developmental pathology such as ASD and ADHD put a larger strain on parenting skills than typically developing children (Harpin, 2005; Herring et al., 2006; Rutgers et al., 2007). For instance, several studies have found that parents of children with ASD reported lower levels of the more responsive authoritative parenting style than parents in non clinical groups (Baumrind, 1996; Gau et al., 2010; Rutgers et al., 2007; Woolfson & Grant, 2006). Studies in the area of ADHD reported that parents of children with ADHD have the tendency to use a more authoritarian parenting style instead of an authoritative parenting style (Alizadeh & Andries, 2002; Bögels, Lehtonen, & Restifo, 2010; Hinshaw, 2002; Johnston & Mash, 2001; Lange et al., 2005) or a more permissive parenting style (Goldstein, Harvey, & Friedman, 2007; Keown & Woodward, 2002; Robledo-Rámon & García-Sánchez, 2012). These results imply that both ASD and ADHD in children may evoke a more suboptimal parenting style, which then negatively influences the further development of the child. However, none of the above described studies about the effect of child ASD and ADHD on parenting skills include unaffected siblings *and* take parental pathology into account, leaving open the question if the suboptimal parenting styles were related to child pathology, parental pathology or a combination of both.

Therefore, the main aim of the current study was to explore the influence of (the combined) effect of child diagnosis (ASD or ASD+ADHD) and parental ASD and/ or ADHD on parenting styles. Based on the literature, we expected to find an effect of child diagnosis on parenting styles, but also an effect of parental symptoms on parenting styles. In addition, the combination of child and parental symptoms may also be related to parenting styles. We had the opportunity to select 96 families from an ongoing ASD genetics study for whom both self reported and spouse reported parenting style data was available from both father and mother in relation to both the affected and an unaffected child. These data allowed us to tease apart effects of parent and child pathology on parenting styles and examine their possible interaction effect, by using parenting styles towards the unaffected sibling as a reference point. The data of unaffected siblings allowed us to correct for possible confounders (such as family environment) that may vary between families with psychopathology and without psychopathology, but not between affected and unaffected siblings within one family since they share the same environment (Cartwright et al., 2011). If related to parental pathology, it was expected that the parenting style was expressed both towards the affected and the unaffected child. If related to child pathology, the

parenting style was only expressed towards the affected child. In addition, data was available from spouses to examine the robustness of the findings.

METHODS

Participants

Children

A subsample of 96 families were recruited as part of a large family-genetics study (Biological Origins of Autism [BOA]), that aims at detecting the genetic, biochemical and cognitive origins of ASD and study the overlap between ASD and ADHD on these levels. Families were included in the current subsample if they had at least one child between 2 and 20 years of age, with a clinical diagnosis of ASD (probands), one unaffected sibling (no ASD and ADHD diagnosis), and at least two participating biological parents. All families were of European Caucasian descent. Exclusion criteria were epilepsy, a diagnosis of a defined genetic or non-genetic cause of ASD (Rett's syndrome, fragile X syndrome) or a genetic disease such as Down-syndrome. Comorbid *DSM-IV* disorders were not excluded.

Both the children already clinically diagnosed with ASD and their siblings were carefully screened for the presence of ASD symptoms with the Social Communication Questionnaire (SCQ) (Rutter et al., 2003) (for the fully described procedure of the SCQ, see van Steijn et al., 2012). The Autism Diagnostic Interview Revised (ADI-R) (Le Couteur, Lord, & Rutter, 2003) was administered for all children scoring above clinical cut-off of the SCQ. All children were also carefully screened for the presence of ADHD symptoms using the Conners long version rating Scales Revised (CRS-R) (Conners, 1997) completed by parents and teachers. From 18 years of age, participants also filled out the Conners Adult Rating Scales- Self-report: Long version (CAARS-S:L). For all children scoring above cut-off on one of three *DSM-IV* ADHD scales (≥ 63), the Parental Account for Childhood Symptoms (PACS) (Taylor, Sandberg, Thorley, & Giles, 1991) was administered by a certified clinician. Thereafter, a standardized algorithm was applied with the scores of the PACS and the teacher version of the CRS-R to construct a formal diagnosis of ADHD (for details see, Rommelse, Oosterlaan, Buitelaar, Faraone, & Sergeant, 2007a).

We were able to include 96 children with an ASD (+ADHD) diagnosis. For each affected child, one unaffected sibling closest in age to the affected child was selected. This resulted in 46 same-sex sibpairs and 50 different sex sibpairs with a mean absolute age difference of 2.96 years ($SD = 1.54$) (see Table 1).

Parents

All parents were screened for the presence of current ASD symptoms with the self report Autism Spectrum Quotient (AQ; Baron-Cohen, Wheelwright, Skinner, Martin, & Clubley, 2001). This questionnaire has been found reliable and valid (Auyeung, Baron-Cohen, Wheelwright, & Allison, 2008; Baron-Cohen et al., 2001; Hoekstra, Bartels, Cath, & Boomsma, 2008; Woodbury-Smith, Robinson, Wheelwright, & Baron-Cohen, 2005). The questionnaire consists of 50 items rated on a 4-point rating scale. A total score for parents was obtained by summing up all items resulting in a score between 50 and 200 (Hoekstra, Bartels, Cath, & Boomsma, 2008; Hoekstra, Bartels, Verweij, & Boomsma, 2007). Current self reported ADHD symptoms of the parents were assessed with the DSM index scale for ADHD on a 4-points rating scale of the Conners Adult Rating Scales- Self-report: Long version (CAARS-S:L; Conners, Erhardt, & Sparrow, 1998, 1999). This questionnaire has found to be reliable and valid (Conners et al., 1998, 1999).

Instruments

To assess parenting styles of parents, the Parenting Styles and Dimensions Questionnaire (PSDQ) was used. This questionnaire contains a list of 62 parent behaviors, developed to measure the authoritative, authoritarian and permissive parenting style. Responses were given on a 5-point scale with; (1) representing never; (2) sometimes; (3) half of the time; (4) often; and (5) always. The PSDQ has been shown to demonstrate adequate reliability and validity (Robinson, Mandleco, Olsen, & Hart, 2001) and very good internal consistencies across all three subscales (Robinson, Mandleco, Olsen, & Hart, 1995). The PSDQ was completed by parents four times, once for their own parenting style towards the affected child, once for their own parenting style towards the unaffected child, once for the parenting style of their spouse towards the affected child, and once for the parenting style of their spouse towards the unaffected child. Parents completed the PSDQ under supervision of the researchers and were instructed not to exchange answers when completing the questionnaire. Norm data of the PSDQ were available from the unpublished Dutch study of Wierda-Boer (2009) (N= 298), which included mean scores of parents of typically developing children.

Procedure

Eligible families registered at an outpatient clinic specialized in ASD and ADHD pathology (Karakter Child and Adolescent Psychiatry University Center) and members of the Dutch Autism Association (NVA) received a brochure containing information about the BOA study and were requested to return a pre-stamped response card. A short telephone screening and, subsequently, screening questionnaires were used to verify if families were eligible to participate. The families were invited to visit

Table 1 Characteristics participants

	(1) Fathers N = 96		(2) Mothers N = 96		Norms	
	<i>M</i>	<i>SD</i>	<i>M</i>	<i>SD</i>	<i>M</i>	<i>SD</i>
% male						
Age in years	45.5	5.8	43.0	5.5		
Education ¹	4.6	1.0	4.5	.89	♂4.1 ♀4.1 ²	♂.88 ♀.82
SCQ						
CRS-R ⁴						
% Above cut-off T > 63						
% ASD (ADI) ⁵						
% ADHD (PACS) ⁶						
Autism Quotient	114.2	18.5	108.6	2.1	♂105.7 ♀102.9 ⁷	♂11.0 ♀11.5 ⁷
ADHD DSM-IV index scale	10.9	7.5	9.9	9.1	♂ 8.6 ♀9.1 ⁸	♂3.7 ♀3.9 ⁸

¹1 = nursery school 2 = primary education 3 = secundair education, first phase 4 = secundair education, second phase 5 = higher education, first phase 6 = higher education, second phase 7 = higher education, third phase. ²Central Bureau of Statistics (CBS), 2010. ³Social Communication Questionnaire, norms based on population cohort study (N= 247) (Chandler et al., 2007) ⁴Measured with the Conners long version Rating Scales Revised. ⁵Measured with The Autism Diagnostic Interview (ADI-R). ⁶Measured with the Parental Account for Childhood Symptoms (PACS). ⁷Norms from (Hoekstra et al., 2008). ⁸Norms from the Dutch Twin Register (Boomsma et al., 2010).

the clinic, where a trained researcher conducted the ADI-R and the PACS. Additional data was collected including blood samples of all family members and neuropsychological data of the children. The study was approved by the local medical ethics board and parents and children (above 12 years of age) signed for informed consent.

Data-analyses

Analyses were performed with SPSS 20. Less than 8% of the CRS-R and SCQ data of children, < 8% of the CAARS-S:L and AQ data of fathers, < 4% of the self report of the CAARS-S:L and AQ data of mothers, and < 8% of the data on the PSDQ was missing. For the missing data we used the Expectation Maximization (EM) algorithm (Dempster, Laird, & Rubin, 1977) to impute the missing values.

	T-test	(4) ASD (+ADHD) affected children N = 96		(5) Unaffected children N = 96		Norms		T-test
	<i>contrast</i>	<i>M</i>	<i>SD</i>	<i>M</i>	<i>SD</i>	<i>M</i>	<i>SD</i>	<i>contrast</i>
		86.5		44.8				
	1 = 2	11.4	3.9	11.0	4.6			4 = 5
	1 > n & 2 > n							
		18.9	7.7	4.3	4.9	4.7 ³	5.0 ³	4 > n & 5 = n
		62.8	10.5	51.6	8.3	50	10	4 > & 5 > n
		48.4		8.6		12	4	4 > n & 5 = n
		100		0				
		37.5		0				
	1 > n & 2 > n							
	1 > n & 2 = n							

To examine the effect of child diagnosis (affected or not) on the parenting styles, three separate (authoritative, authoritarian and permissive parenting style) repeated measure ANOVAs were used. Variables included into the model were (1) family type (ASD and ASD+ADHD), (2) parent (father / mother), and (3) child diagnosis (affected or not). Both the factors parent and child diagnosis were included as repeated measure (i.e. the same mother or father reported on both children). In addition, all two-way and three-way interaction effects were included and dropped from the model if not significant. In addition, one sample T-test were performed for comparisons with the norm data of the PSDQ. Correlations analyses with continuous child ASD (SCQ) and ADHD (CRS-R) were used to examine the robustness of the findings. To examine the relation between the PSDQ scales within observers and between

spouses, Pearson correlation analyses were conducted. To examine to what extent, parental symptoms, diagnosis of the child and the combination between parent and child symptoms were related to the parenting styles, also repeated measure ANOVAs were used. The analyses were performed separate for authoritative, authoritarian and permissive parenting style, and for fathers and mothers. Variables included into the main model were (1) parents' ASD symptoms (continuous), (2) parent's ADHD symptoms (continuous), and (3) child diagnosis (affected or not) as repeated measure (to prevent duplicating parental symptom data for children within the same family). In addition to the main effects, two-way (interaction between child diagnosis and parental symptoms) and three-way interactions (interaction between parental ASD, parental ADHD and child diagnosis) were tested. Variables also included initially as effects to correct for possible confounders were: (1) family type (ASD and ASD+ADHD), (2) sex difference (same sex/ different sex), and (3) the absolute age difference between the affected and unaffected child. Self reported and spouse reported parenting styles were separately used for analyses to examine the robustness of the findings. Correction for multiple testing using the 95% CI, was performed with the False Discovery Rate procedure (Benjamini, 2010).

RESULTS

Correlations within and between reporters

Positive, significant correlations between the authoritarian and permissive parenting style were found for both fathers and mothers, although the effect for mothers was only present with regard to their affected child. All correlations between self-report and spouse report for comparable indices were small to large and significant (see Table 2).

The relationship between self reported ASD and ADHD symptoms within parents

Significant small to medium positive correlations were found between parental ASD and ADHD symptom scores in both fathers ($r = .26, p = .01$) and mothers ($r = .22, p = .03$).

Main effect of child diagnosis

Authoritative parenting style

No significant three-way interaction (child diagnosis by family type by parent) was found regarding the authoritative parenting style ($F(1,94) = 0.56, p = .64$) and this effect was dropped from the model. The two-way interactions of child diagnosis by parent, child diagnosis by family type, and parent by family type were not significant

Table 2 Correlations between parenting scales, and between self report and spouse report in ASD (+ADHD) families (N = 96) measured with the Parenting styles and Dimension Questionnaire (PSDQ)

	Authoritative parenting style	Authoritarian parenting style	Permissive parenting style
Affected children (N = 96)			
Authoritative parenting style	.46 \ .51	-.15	.12
Authoritarian parenting style	.06	.31 \ .56	.30
Permissive parenting style	.07	.30	.46 \ .29
Unaffected children (N = 96)			
Authoritative parenting style	.41 \ .73	.14	-.11
Authoritarian parenting style	.03	.53 \ .70	.23
Permissive parenting style	-.19	.19	.62 \ .59

Correlations above the diagonal: Self report father. Correlations below the diagonal: Self report mother. On the diagonal: Self report mother with spouse report father \ Self report father with spouse report mother. **Findings in bold are significant after correction for multiple testing.**

($F(1,94) = 1.06, p = .31$, $F(1,94) = 0.55, p = .46$ and $F(1,94) = 0.10, p = .57$, respectively). No main effects of family type ($F(1,94) = 0.03, p = .85$) or child diagnosis ($F(1,94) = 0.71, p = .40$) were found. Correlation analyses with continuous child symptom data indeed indicated no correlations between severity of symptoms and the authoritative parenting style (all r 's were between $-.03$ and $.08$, all p 's were between $.27$ and $.74$). However a main effect of parent was present ($F(1,94) = 40.02, p < .001$) revealing that mothers reported a higher authoritative parenting style than fathers (see Figure 1). Both fathers and mothers scored significantly lower on the authoritative parenting style compared to the norm data of the PSDQ, regardless the affected status of their children.

Authoritarian parenting style

No significant three-way interaction (child diagnosis by family type by parent) was found regarding the authoritarian parenting style ($F(1,94) = 0.12, p = .37$) and this effect was dropped from the model. The two-way interactions of child diagnosis by parent and parent by family type were not significant ($F(1,94) = 1.59, p = .21$ and $F(1,94) = 2.49, p = .12$). However, a significant two-way interaction effect between child

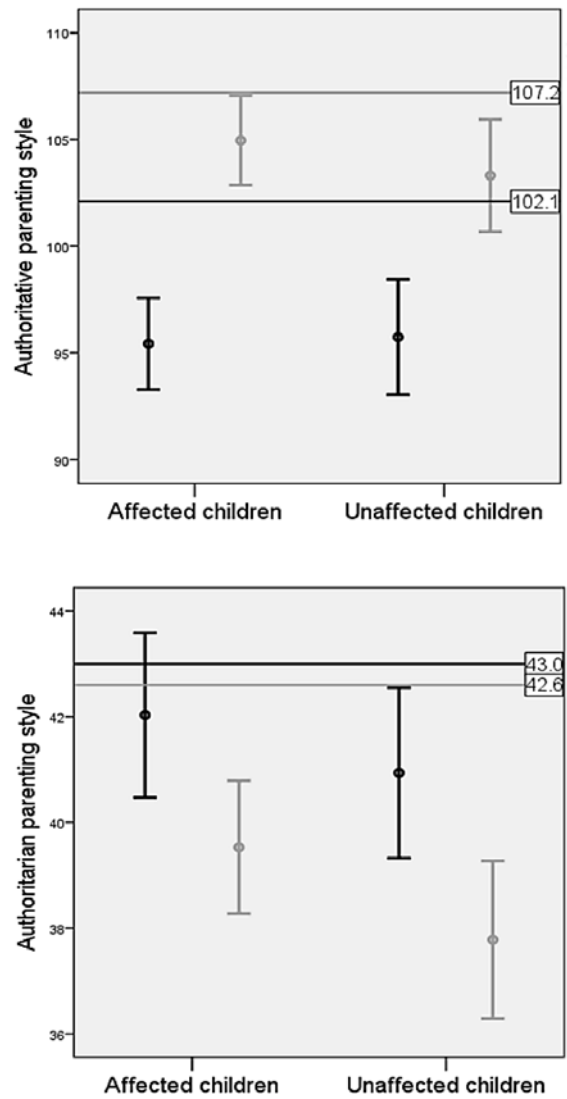


Figure 1 Comparison of parenting styles measured with the Parenting Styles and Dimension Questionnaire (PSDQ) between and within ASD and ASD+ADHD affected and unaffected families (N= 96) and the PSDQ norm data

Black line indicate the PSDQ norm value of fathers and the grey line the PSDQ norm value of mothers of typically developing children (Wierda-Boer, 2009). The error bars represented the 95% Confidence Interval (CI) using one-sample t-test in comparison to the population nom value.

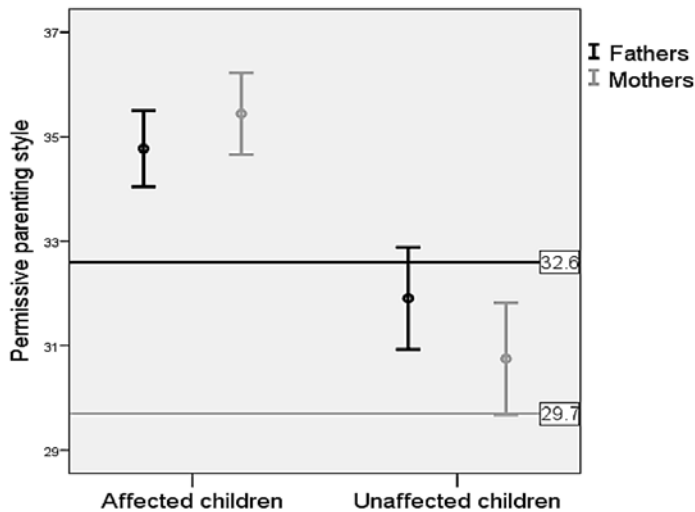


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diagnosis and family type was present ($F(1,94) = 3.95, p = .05$) indicating that there were differences in ratings regarding affected and unaffected children in the two types of families. Post hoc analyses revealed that larger differences between affected and unaffected children were present in the families with ASD+ADHD offspring (fathers $t(35) = 2.09, p = .04$, mothers $t(35) = 3.44, p = .002$) compared to families with ASD only offspring (fathers $t(59) = -.28, p = .78$, mothers $t(59) = 1.67, p = .10$). Correlation analyses indeed indicated that higher ASD symptoms in children were related to higher authoritarian parenting styles in fathers ($r = .16, p = .04$). Last, a main effect of parent was present ($F(1,94) = 18.52, p < .001$) revealing that fathers reported a higher authoritarian parenting style than mothers. Furthermore, both fathers and mothers scored also significantly lower than the norm data of the PSDQ on the authoritarian parenting style, although for fathers only regarding unaffected children.

Permissive parenting style

No significant three-way interaction (child diagnosis by family type by parent) was found regarding the permissive parenting style ($F(1,94) = 0.01, p = .94$) and this effect was dropped from the model. The two-way interaction between child diagnosis by family type were not significant ($F(1,94) = 1.45, p = .23$). However, a significant parent by family type interaction was found ($F(1,94) = 4.78, p = .03$) indicating that there were differences in ratings between fathers and mothers in the two types of families. Post hoc analyses revealed that fathers of ASD+ADHD families reported a more permissive

parenting style than mothers ($t(71) = 2.07, p = .04$.) whereas this was not the case in ASD families ($t(119) = -.93, p = .35$). A significant two-way interaction effect was also present between child diagnosis and parent ($F(1,94) = 7.47, p = .01$) indicating that there were differences in ratings between fathers and mothers and affected and unaffected children. Post hoc analyses revealed that both fathers and mothers reported a higher permissive parenting style towards affected children in comparison with unaffected children ($t(95) = 5.91, p < .001$) and $t(95) = 9.31, p < .001$, respectively). These effects were also reflected in differences in the norm data of the PSDQ (see Figure 1). In accordance to our results, significant effects of child ASD and ADHD were found regarding both parents and the permissive parenting style using continuous data.

Effects of parental symptoms and the combination of parent and child symptoms

A repeated measure ANOVA with parents' ASD symptoms, parents' ADHD symptoms and child diagnosis (repeated measure to account for identical parent symptom information in two siblings), the two-way and three-way interactions between these variables and the confounding effects of absolute sex and age differences, and family type, was used to examine the combined effect of child and parent pathology on the three parenting styles. No three-way interactions were found between child diagnosis by parental symptoms by type of diagnosis on the three parenting styles, indicating that the effects were present in both families with ASD-only and ASD+ADHD affected children. Significant two-way interactions were found between paternal ADHD by child diagnosis ($F(1, 90) = 8.32, p = .01$) and maternal ASD by child diagnosis ($F(1,90) = 7.11, p = .01$) regarding the permissive parenting style indicating that there was an effect of a particular combination of parental symptoms and child pathology on permissiveness (see Figure 2). Post hoc analyses revealed that paternal ADHD symptoms related to increased permissiveness towards their unaffected child ($F(1,90) = 10.69, p < .001$) but less so towards their affected child ($F(1,90) = 4.82, p = .03$). Maternal ASD symptoms were also related to a more permissive parenting style towards their unaffected child ($F(1,90) = 2.87, p = .09$) than their affected child ($F(1,90) = 0.91, p = .34$). Overall, no main effects of paternal and maternal **ASD** symptoms were found (all p 's were between .16 and .99) (see Figure 2), but main effects of paternal (but not maternal) **ADHD** symptoms were present (authoritative ($F(1,90) = 6.05, p = .02$; authoritarian $F(1,90) = 8.52, p = .003$; and permissive $F(1,90) = 6.03, p = .02$) (all maternal p -values were between .07 and .19). Analyses were repeated using spouse-report data on parenting styles. Most effects were not significant anymore, except for maternal ADHD symptoms being related to a more permissive parenting style as reported by their spouse ($F(1,90) = 7.56, p = .01$). Further, paternal ASD symptoms were now negatively related to their authoritative parenting style as reported by their spouses ($F(1,90) = 4.67, p = .03$).

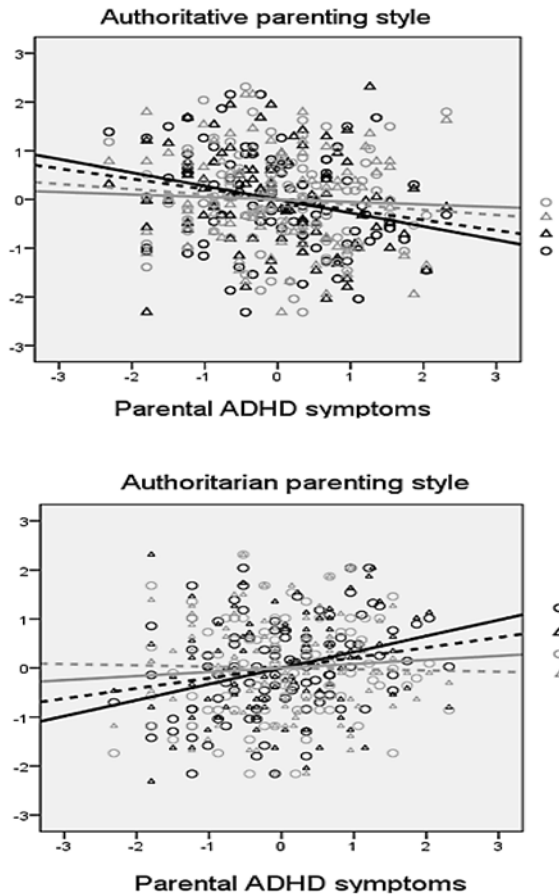


Figure 2 Authoritative, Authoritarian and permissive parenting style measured with the Parenting Styles and Dimensions Questionnaire (PSDQ) self-report in relation to parent and offspring symptoms in ASD (+ADHD) families (N = 96) (Z-scores)

Parenting style as a function of paternal and maternal symptoms of ASD and ADHD in their ASD (+ADHD) affected and unaffected offspring. Higher Z-scores on the X-axis indicate more paternal or maternal symptoms. Higher Z-scores on the Y-axis indicate a higher score on the parenting style.

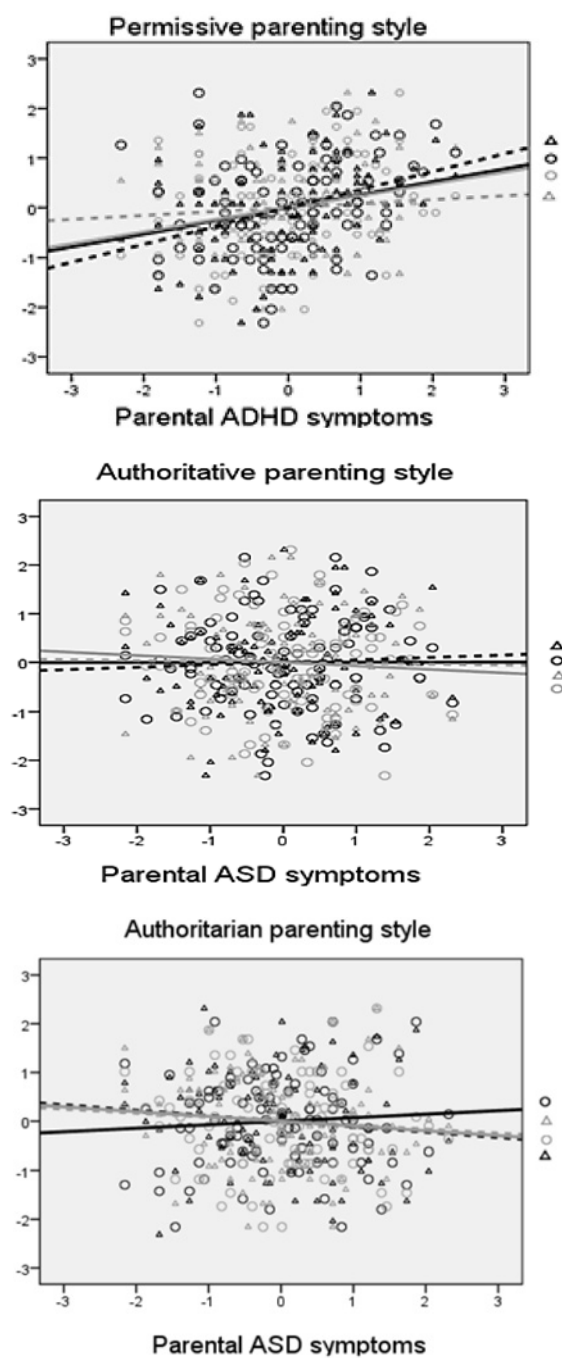


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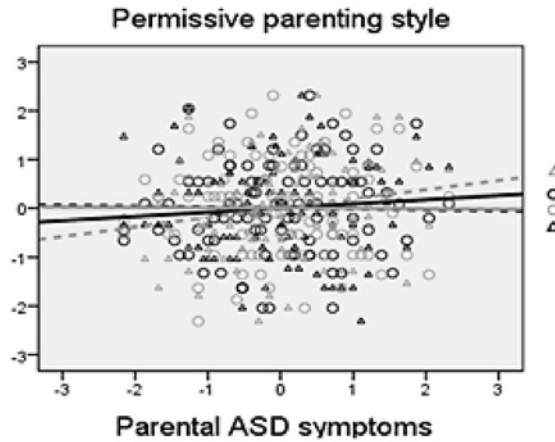


Figure 2 Continued

DISCUSSION

The main aim of this study was to explore the influence of (the combined) effect of child diagnosis (ASD or ASD+ADHD) and parental ASD and/ or ADHD on parenting styles. Our results indicate that both fathers and mothers alike tend to apply a less authoritative parenting style towards affected and unaffected children, and a more permissive parenting style towards affected children. This suggests that only the permissive (and not the authoritative and authoritarian) parenting style is evoked by child pathology. Overall higher levels of ADHD symptoms in fathers (not mothers) were related to suboptimal scores on authoritative, authoritarian and permissive parenting styles. Importantly, higher permissiveness towards unaffected (but not affected) children was found when fathers scored high on ADHD symptoms and mothers on ASD symptoms.

The finding of a less authoritative parenting style for fathers, and especially mothers, regarding their affected and unaffected children, and a more permissive parenting style, mothers and fathers alike, towards their affected child, corresponds with previous studies that found a less authoritative parenting style in families with ASD affected children (Baumrind, 1996; Rutgers et al., 2007; Woolfson & Grant, 2006), a more authoritarian style instead of an authoritative parenting style in families with ADHD affected children (Alizadeh & Andries, 2002; Bögels et al., 2010; Hinshaw, 2002; Johnston & Mash, 2001; Lange et al., 2005) and a more permissive parenting style in families with ADHD affected children (Goldstein et al., 2007; Keown & Woodward, 2002; Robledo-Rámon & García-Sánchez, 2012). There was also a

positive correlation between authoritarian and the permissive parenting style, indicating parents who tend to be more authoritarian on some occasions, are also more permissive on other occasions. Thus, even though both styles are opposites by definition, apparently they are used by the same individual at the cost of the authoritative style. Based on the literature, a less authoritative and a more permissive and authoritarian parenting style is associated with cognitive and social development problems in affected children (Baumrind, 1991; Lee et al., 2006; Rogers et al., 2009). This is not surprising if you consider that children with ASD or ASD+ADHD with their desire for routine, predictability and organization, may not benefit from an environment with little control and organization such as a permissive parenting style. Although it was often suggested that these suboptimal parenting styles may be evoked by the pathology of the children (Baumrind, 1996; Gau et al., 2010; Harpin, 2005; Herring et al., 2006; Johnston et al., 2012; Reed et al., 2008; Rogers et al., 2009; Woolfson & Grant, 2006), our results suggest that only the permissive (and not the authoritative and authoritarian) parenting style was evoked by child pathology. Apparently, fathers and mothers alike, tend to use less control and punishments towards their affected child, possibly to avoid confrontations or because parents may develop feelings of not being able to influence the child's development (Baumrind, 1991; Kendall & Shelton, 2003). Permissive parents may also be influenced by the lack of reinforcement that they perceive during child rearing (Goldstein et al., 2007; Keown & Woodward, 2002; Robledo-Rámon & García-Sánchez, 2012). However, since we found also a less authoritative parenting style regarding unaffected children, it seems like that the presence of a child with ASD(+ADHD) may put a burden on the family as a whole, thereby negatively influencing parenting styles for the entire offspring.

It was further examined if parental symptoms or a combination of parental symptoms and child symptoms were related to parenting styles. Findings indicated that paternal, and not maternal, ADHD was related to a less authoritative, more authoritarian and more permissive parenting style. It is surprising that we did not find this in mothers, although an effect emerged for increased permissiveness when fathers documented on maternal parenting style. It may thus be suggested that fathers with a disorganized and chaotic life style and who struggle with paying attention to their surroundings (ADHD symptoms) have more problems with the use of an optimal parenting style adapted to the needs of the child (Johnston et al., 2012) than mothers. Paternal ASD symptoms were not associated with parenting, except when spouse reports were used (higher paternal ASD related to authoritativeness). The discrepancy between self- and spouse-report may be explained by a relative lack of reflection on his own parenting style by the father with high ASD symptoms (see for example Baron-Cohen, 1989, 1991; Baron-Cohen et al., 1994; Noriuchi et al., 2010). In any case, it appears that parental ASD symptoms may have a less profound impact on parenting styles than paternal ADHD symptoms. Intriguingly though, was

the finding that particularly unaffected offspring seem at risk to be raised permissively when their father's score high on ADHD and/or when their mothers' scored high on ASD. On the one hand this finding implies the possibility that having similar type (ASD or ADHD) symptoms as your mother/ father may in some cases be more optimal for children than being unaffected. On the other hand, this may not necessarily be negative but a compensatory strategy of the mother/ father for the many strains already put upon siblings of affected children having to cope with the burden of disease in their family. However, we realize that we have only preliminary evidence to support this hypothesis, so further research is needed to clarify this issue. Nevertheless, in studies regarding parenting it is important to include both measurements of parental and child pathology to disentangle the (combined) effect of parent and child pathology on parenting.

Our findings should be interpreted in the context of several limitations. First, despite the small to large correlations between self- and spouse-report parenting style data, almost all results were only present using self-reported parenting data and not spouse-reported parenting data. This concurs with previous studies showing that questionnaire data within reporters generally correlates more strongly than between reporters (Ende van der & Verhulst, 2005; Kooij et al., 2008; Wolraich et al., 2004), but underlines the need for replication of our findings using more objective assessments of parenting styles. Nevertheless, because previous studies suggest self reported parenting styles correlate highly with observations of parenting styles in the home setting and it is unlikely that reporter bias can explain the difference in ASD versus ADHD parental symptoms in relation to parenting styles, we believe our main conclusions are still valid. A second limitation is that no formal ASD or ADHD diagnosis in the parents was made. However, our findings are relevant in showing that relationship between parental ADHD symptoms and suboptimal parenting is present across the ADHD symptom continuum and not only in a small clinically impaired subgroup of parents. A third limitation is that this study does not provide evidence for the possible longitudinal outcomes of the suboptimal parenting style in ASD(+ADHD) families. However, we intend to conduct a follow-up study in this sample to examine the outcomes of parenting styles on child functioning. A fourth limitation is that it is unclear to what extent results are equally applicable to children affected with an ADHD-only diagnosis. Results indicated that the effects were present in families with ASD-only and ASD+ ADHD affected children, but future studies should clarify whether parental ADHD and maybe ASD, symptoms relate to parenting styles in families with ADHD-only affected children. A fifth limitation is that it is possible that the findings of this study are only attributable to families of Caucasian descent since, for example, the level of parental warmth and control differ across cultures (Deater-Deckard et al., 2011). Replicating our findings among different cultures may help to clarify this issue.

To the best of our knowledge this is the first study that reports on the negative effects of paternal ADHD symptoms on parenting styles within ASD (+ADHD) affected families and the higher permissiveness towards unaffected offspring specifically when paternal ADHD and/or maternal ASD symptoms are high. Given that suboptimal parenting styles may form a higher risk for developing (additional) behavior problems and parents in ASD (+ADHD) families may have subthreshold or above subthreshold symptoms, parenting training in these families may be beneficial for the well being of both parents and their offspring. As suggested by Chronis-Tuscano (2011) directly treating the ADHD and ASD symptoms in parents before implementing a parenting intervention may be much more beneficial. Although not sufficient for all families (Chronis-Tuscano & Stein, 2012), pharmacological treatment may be considered for treating ADHD or ADHD-like symptoms in parents with ASD (Cortese, Castelnau, Morcillo, & Bonnet-Brilhault, 2012; Autism Network Participants, 2005) and in parents with ASD (targeting the commonly associated ASD symptoms such as irritability, anxiety, withdrawal), besides appropriate psychological interventions (Tchacoukian & Adelman, 2013).

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Match or mismatch?
Influence of parental and offspring
ASD and ADHD symptoms on the
parent-child relationship

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ABSTRACT

Few studies have examined the influence of parental ASD and ADHD symptoms in combination with child pathology on the parent- child relationship as perceived by the child. A sample of 132 families was recruited with one child with ASD (with/without ADHD), and one unaffected sibling. Affected children (regardless of diagnosis) reported lower acceptance and conflict resolution scores than their unaffected siblings, with conflict resolution scores (but not acceptance) being lower than the norm according to both affected and unaffected children in both fathers and mothers. Higher paternal, but not maternal, ASD and ADHD symptoms were related to poorer scores regarding acceptance and conflict resolution, respectively. Treatment targeting conflict resolution skills of parents and the feeling of being less accepted in children with ASD/ADHD may be beneficial.

It is now widely acknowledged that Autism Spectrum Disorder (ASD) and Attention Deficit- Hyperactivity Disorder (ADHD) frequently co-occur together within the same patient (Rommelse, Franke, Geurts, Hartman & Buitelaar, 2010; Ronald, Simonoff, Kuntsi, Asherton, & Plomin, 2008; Rowlandson & Smith, 2009) and within the same families (Freitag, 2007; Pamplo et al., 2009). ASD is characterized by impaired communication and social interaction skills, as well as repetitive and restricted behavior and interests (APA, 2000), ADHD by severe inattention, hyperactivity and impulsivity (APA, 2000). Both disorders appear to share at least a substantial proportion of their genetic influences, as well as related functional and structural brain abnormalities (see for a review Rommelse, Geurts, Franke, Buitelaar & Hartman, 2011). In addition, in both disorders it has been reported that parents of affected children often display subthreshold or above threshold symptoms (Constatino & Todd, 2005; Faraone, Kunwar, Adamson, & Biederman et al., 2009). Parental symptom information has often been used to unravel family-genetic transmission of ASD and ADHD symptoms. However, to what extent these parental symptoms may influence the family environment is largely unknown. Particularly in ASD, the influence of parental symptoms on parenting is a very neglected area, most likely due to the sensitive nature of this topic since Bettelheim (1967) unleashed his idea that the cause of autism was a lack of maternal warmth towards the child. Though this idea was based on clinical impressions and has never been confirmed, it is of great relevance to study the influence of parental symptoms since the family environment can have a substantial impact on the child's social and cognitive development functioning (Reed, Osborne, McHugh, & Saunders, 2008; Wachtel & Carter, 2008),

Given the previously mentioned dark history of ASD and parenting, it bears no surprise that we only were able to find a few studies on family environment influenced by parental ADHD (see for a review Johnston, Mash, Miller, & Ninowski, 2012), and not parental ASD symptoms. Parental ADHD symptoms appear to be associated with suboptimal parenting; a less optimal parenting style, higher levels of family conflict and less family cohesion. However, it is unclear to what extent these parental symptoms relate to suboptimal parent- child relationships independent from, or in combination with, child pathology. It is well known that children with developmental pathology such as ASD and ADHD put a larger strain on parenting skills than typically developing children (Harpin, 2005; Herring et al., 2006; Rutgers et al., 2007). Child ASD and ADHD symptoms were both, for example, related to more family conflict (Biederman et al., 1995; Higgins, Bailey, & Pearce, 2005; Kelly, Garnett, Attwood, & Peterson, 2008; Wells et al., 2000) and strained parent- child relationships (Harpin, 2005; Kaminsky & Dewey, 2002; Weiss & Hechtman, 2000). Thus, previous literature clearly suggests that both parental and offspring ASD and ADHD symptoms may have a negative effect on parenting, but the combination of both is scarcely investigated. It could be hypothesized that the most difficult rearing situation exists

when families have a parent with high ASD or ADHD symptoms and an unaffected child, or vice versa (a discordant pair). This has been reported in two recent studies that have found that parental ADHD symptoms were associated with poorer school performance or prosocial behavior in offspring without ADHD, but not in offspring with ADHD (Biederman et al., 2002; Griggs & Mikami, 2011). Vice versa, behavioral and emotional problems of a child in combination with a parent with low or no symptoms, contribute significantly to parental stress, parent mental health, family dysfunction and marital problems (Berg- Nielsen, Vikan, & Dahl, 2002; Herring, et al., 2006 ; Piven et al., 1991). Another possibility is that the most difficult rearing situation may be evoked by children having the *same* symptoms as their parents (a homotypic concordant pair) as has been observed for parental ADHD and child ADHD which contributes to the reciprocal negative interactions in these families (Chronis-Tuscano et al., 2008). However, it has also been suggested that mothers with high ADHD symptoms may be more positive and affectionate with their children with high ADHD symptoms (Psychogiou, Daley, Thompson, & Sonuga-Barke, 2008).

A rather unexplored area of parent-child pathology in relation to family environment is the issue of heterotypic concordance. We refer to heterotypic concordancy in situations in which both parent and child are displaying symptoms, but of *different* disorders. For instance, having a child with ADHD that is talkative, distractible, demanding, and less cooperative may be particularly straining for parents having high levels of ASD symptoms, such as being rigid and poorer in social skills (Ornstein- Davis & Carter, 2008). Vice versa, a child with high ASD symptoms requiring a predictable and organized family environment may probably be worst off having a parent with high levels of ADHD symptoms. It may be suggested that these particular combinations may negatively impact each other, as has for instance been shown in depressed mothers rearing a child with emotional and behavioral disturbances (Civic & Holt, 2000; Harrison & Sofronoff, 2002). It thus remains to be determined which combination of parent-child pathology is related to the most suboptimal family environment.

In this study we explore the influence of parental ASD and ADHD symptoms in combination with offspring ASD and ADHD symptoms on the parent-child relationship as perceived by the child. These child perceptions may be influenced by various factors such as child gender (Sentse, Veenstra, Verhulst, & Ormel, 2009) and child age (Berkien, Louwerse, Verhulst, & Van der Ende, 2012; Taber, 2010). In addition, gender of the parent (Phares, Renk, Duhig, Fields, & Sly, 2009; Smetana, Metzger, Gettman, & Campione-Barr, 2006; Yahav, 2006) may also have an effect on child perception. For example, children reported more positive affect and less negative affect towards their mother compared with their father (Phares et al., 2009). However, in general the importance of child perception towards the parent- child relationship is highlighted by the fact that a negative perception of this relationship may provide

higher levels of the child emotional behavioral problems (Phares & Renk, 1998), whereas a more positive perception of the parent-child relationship are associated with less problem behavior (Bosco, Renk, Dinger, Epstein, & Phares, 2003; Lange, Blonk, & Schaar van der, 1997; Nelson, Patience, & MacDonald, 1999). Although the perception of the child may not reflect the 'actual' situation, previous studies indicate that the behavior of the child is more influenced by the child's *perception* of parenting, rather than by the *actual* parenting behaviors of the parent (Yahav, 2006). In order to disentangle the effects of parent and offspring ASD and ADHD symptoms on the parent-child relationship, we included families from two ongoing ASD and ADHD genetics studies for whom childrens' self reported parent-child relationship data concerning fathers and mothers was available for both affected children and their unaffected siblings. These data allowed us to tease apart the effects of parent and child ASD and ADHD pathology, parent and offspring gender, and examine their possible interaction effect on the child perception of the parent-child relationship. If related to parental pathology, it was expected that affected and unaffected siblings rated the same parent similarly. If related to child pathology, a positive or negative perception towards the parent was only expressed by the affected child. If related to the combination of parental and child pathology, a positive or negative perception towards the parent was expressed by an affected child, but only in combination with parental symptoms. In general, more favorable scores towards mothers than fathers were expected, regardless of the child's gender. By comparing these effects in the three types of families (proband with ASD-only, ADHD-only or ASD+ADHD), both homotypic and heterotypic concordant parent-offspring effects could be examined.

METHODS

Participants

Children

A total of 132 families were recruited from two ongoing ASD and ADHD family-genetics studies (*Biological Origins of Autism [BOA]* and *International Multicenter ADHD Genes study [IMAGE]*). Families were included in the studies if (a) they had at least one child between 2-20 years with a clinical ASD (+ADHD) diagnosis (*BOA*) or if they had at least one child between 5-19 years with a clinical ADHD (combined subtype) diagnosis (*IMAGE*), (b) at least one biological sibling (regardless of possible ASD or ADHD-status) and, (c) at least one biological parent willing to participate. In the current study only families with two participating biological parents were included. All families were of European Caucasian descent. Participants were excluded if they had an IQ \leq 60, specific learning or language disorders, a diagnosis of epilepsy, a defined genetic or non-genetic cause of ASD or ADHD (Rett's syndrome, fragile X

syndrome) or a genetic disease such as Down-syndrome. Comorbid *DSM-IV* disorders were not excluded, with the exception of a diagnosis of autistic disorder in the *IMAGE* study (other ASD subtypes were allowed).

Both the children already clinically diagnosed with ASD or ADHD and their siblings were carefully screened for the presence of ASD symptoms with the Social Communication Questionnaire (SCQ: Rutter et al., 2003) (for the fully described procedure of the SCQ in the *BOA* and *IMAGE* studies, see van Steijn et al., 2012). The Autism Diagnostic Interview Revised (ADI-R) (Le Couteur, Lord, & Rutter, 2003) (*BOA*) or the Children 's Social Behavior Questionnaire (CSBQ) (Luteijn, Minderaa, & Jackson, 2002) (*IMAGE*), a parental 49 item questionnaire measuring social problem behavior with adequate reliability and validity (Luteijn, et al., 2002) were administered for all children scoring above clinical cut-off of the SCQ. Children were given a diagnosis of ASD if scoring clinically on the ADI-R (*BOA*) or above clinical cut off on the SCQ (>15) in addition to a score above the 95th percentile on the CSBQ (*IMAGE*) (Hartman, Luteijn, Moorlag, de Bildt, & Minderaa, 2007). All children were also carefully screened for the presence of ADHD symptoms using the Conners long version Rating Scales Revised (CRS-R) (Conners, 1997) completed by parents and teachers. For all children scoring above the cut-off on one of three *DSM-IV* ADHD scales (≥ 63), the Parental Account for Childhood Symptoms (PACS) (Taylor, Sandberg, Thorley, & Giles, 1991) was administered by a certified clinician. Thereafter, a standardized algorithm was applied with the scores of the PACS and the teacher version of the CRS-R to construct a formal diagnosis of ADHD (for details see, Rommelse, Oosterlaan, Buitelaar, Faraone & Sergeant, 2007a).

We were able to include 47 children with an ASD diagnosis without clinical ADHD symptoms (all from the *BOA* study), 52 children with an ADHD diagnosis without clinical ASD symptoms (all from the *IMAGE* study), and 33 children with ASD+ADHD diagnosis (24 from the *BOA* study and 9 from the *IMAGE* study). For each affected child, one unaffected sibling closest in age was selected. This resulted in 70 same-sex sibpairs and 62 different sex sibpairs with a mean age difference of 2.68 years ($SD=1.5$) (See Table 1).

Parents

In the *BOA* sample, all parents were screened for the presence of ASD symptoms with the self report Autism Spectrum Quotient (AQ; Baron-Cohen, Wheelwright, Skinner, Martin, & Clubley, 2001). In total, self reported ASD data was available for 71 fathers and 71 mothers having a child with ASD (with/without ADHD) (not available for parents with a child with ADHD only). In the *IMAGE* sample, parents were screened for ASD using the spouse report Adult's Social Behavior Questionnaire (ASBQ; Hartman et al., in press) Spouse reported ASD data was available for 48 fathers and 44 mothers having a child with ADHD (with/without ASD) (not available for parents with a child with ASD

only). The AQ consists of 50 items rated on a 4-point rating scale. The ASBQ contains 49 items on a 3-point scale and measures the social problem behavior of adults (Horwitz, Sytema, Ketelaars, & Wiersma, 2005). Both total scores were used as indication of ASD symptom severity (Hoekstra, Bartels, Cath, & Boomsma, 2008; Hoekstra, Bartels, Verweij, & Boomsma, 2007). The psychometric qualities of both instruments are good (Hartman, et al., in press; Hoekstra et al., 2008). Self-reported ADHD symptoms of the parents were assessed with the DSM raw total score for ADHD on a 4-point rating scale of the Conners Adult Rating Scales- Self-report: Long version (CAARS: Conners, Erhardt, & Sparrow, 1998; Conners, Erhardt, & Sparrow, 1999) in the *BOA* sample and the self report questionnaire for ADHD (Kooij, Boonstra, Swinkels, Bekker, de Noord & Buitelaar, 1997) in the *IMAGE* sample.

Instruments

To assess the perception of children regarding the parent-child relationship, the Dutch version of the Parent- Child Interaction Questionnaire –revised (PACHIQ-R; Lange, 2001) was used. The Dutch version of the PACHIQ-R has been shown to demonstrate adequate reliability and validity (Lange, 2001; Lange, Evers, Jansen, & Dolan, 2002) and consists of 25 items developed to measure the perception of each child regarding the relationship with their fathers and mothers. The PACHIQ-R contains two scales: acceptance and conflict resolution. The subscale *acceptance* consists of 8 items (for example 'my father/mother and I get on well', 'my father/mother is proud of me'), and refers to the level of warmth, comfort and protection that a child experiences at home. The subscale *conflict resolution* consists of 17 items (for example 'when my father/mother tells me not to do something, I do it anyway', 'my father/ mother thinks that I cannot do anything for myself') and refers to the quality of preventing and solving problems by parents. For both the subscales, a higher score refers to a more positive relationship between parent and child. Responses were given on a 5-point scale with for the first 14 items representing (1) completely not true for me; (2) not true for me; (3) in between; (4) true for me; (5) completely true for me. The latter 11 items were scored as (1) never; (2) almost never; (3) sometimes; (4) almost always; (5) always. Children filled out the PACHIQ-R under supervision of the researcher, who verified after each question if the child had understood the question correctly. Children completed the PACHIQ-R separately for fathers and mothers. Norm data of the PACHIQ-R were available for each subscale and for both fathers and mothers regarding N=372 families without psychopathology (Lange, 2001).

Procedure

Eligible ASD and ADHD families registered at an outpatient clinic specialized in ASD and ADHD pathology (Karakter Child and Adolescent Psychiatry University Center), members of the Dutch Autism Association (NVA), and families in other pediatric

Table 1 Characteristics participants

	ASD families (N= 47)		ADHD families (N= 52)	
	<i>probands/ siblings</i>	<i>within families T-tests</i>	<i>probands / siblings</i>	<i>within families T-tests</i>
	<i>M (SD)</i>	<i>Contrast</i>	<i>M (SD)</i>	<i>Contrast</i>
% male	83.0 / 42.6	prob > sib*	75.5 / 59.2	prob > sibs
Age in years	13.0 (3.3) / 12.6 (3.6)	ns	12.2 (3.0) / 11.9 (3.0)	ns
SCQ	17.5 (7.8) / 3.8 (3.7)	prob > sibs	6.2 (3.3) / 4.1 (2.8)	prob > sibs
CSBQ			29.2 (15.3) / 14.4 (9.1)	prob > sibs
CRS-R ³	58.5 (9.0)/ 53.5 (6.9)	prob > sibs	72.5 (8.4)/ 53.1 (9.6)	prob > sibs
% ASD (ADI) ⁴	100/ 0		0 / 0	
% ADHD (PACS) ⁶	0/ 0		100 / 0	
	<i>fathers/ mothers</i>		<i>fathers/ mothers</i>	
Autism Quotient	114.6 (19.0) / 11.2 (23.0)	ns	-	
ASBQ ⁸	-		12.2 (12.4)/ 12.9 (13.1) ⁹	ns
ADHD DSM-IV raw inattention scores	5.1 (4.4)/ 3.5 (2.9)	ns	5.8 (3.7)/ 5.7 (4.6)	ns
ADHD DSM-IV raw hyperactive scores	5.0 (3.3)/ 4.9 (3.0)	ns	7.0 (4.9)/ 7.2 (5.5)	ns

*prob and sibs= probands and siblings. ¹Social Communication Questionnaire, norms based on population cohort (N= 247) (Chandler et al., 2007). ²Children's Social Behavior Questionnaire, norms based on a study of Luteijn (N= 232) (1998). ³Conners long version Rating Scales Revised. ⁴Autism Diagnostic Interview (ADI-R). ⁵Based on N= 24, the other 12 children were included if they scored above cutoff on the SCQ (> 15) and CSBQ (>Based on 95th percentile Hartman, Luteijn, Moorlog, de Bildt & Minderaa, 2007)). ⁶Parental Account for Childhood Symptoms (PACS). ⁷Hoekstra, Bartels, Cath & Boomsma (2008). Mean scores of ASD+ADHD families were based on N= 24 parents. ⁸Adult's Social Behavior Questionnaire. Mean scores of ASD+ADHD families were based on N= 9 parents. ⁹About 21% of father data and 28% of mother data were missing. ¹⁰Norms from the Dutch Twin Register (Boomsma et al., 2010).

	ASD+ADHD families (N= 33)		<i>norms (n)</i>	<i>between probands</i>	<i>between siblings</i>
	<i>probands / siblings</i>	<i>within families T-tests</i>			
		<i>Contrast</i>			
	<i>M (SD)</i>		<i>M (SD)</i>	<i>Contrast</i>	<i>Contrast</i>
	91.7 / 38.9	prob > sibs		ns	ns
	12.4 (3.1) / 12.2 (3.9)	ns		ns	ns
	18.2 (6.1) / 4.3 (3.7)	prob > sibs	4.7 (5.0) ¹	asd+adhd > adhd > n	ns
	42.6 (16.9) / 6.5 (10.0)	prob > sibs	8.3 (2.7) ²	asd+adhd > adhd > n	adhd > asd+adhd
	72.1 (7.6)/ 49.9 (6.6)	prob > sibs	50 (10)	asd+adhd > asd > n	adhd > asd+adhd
	100 ⁵ / 0				
	100 / 0				
	<i>fathers/ mothers</i>			<i>between fathers</i>	<i>between mothers</i>
	108.5 (16.2) / 104.9 (24.2)	ns	105.7 (11.0) / 102.9 (11.5) ⁷	asd > asd+adhd	asd > n
	17.1 (14.4) / 14.2 (17.0) ⁹	ns		adhd < asd+adhd	ns
	6.0 (4.4)/ 4.1 (4.9)	ns	5.3 (3.2) / 5.3 (3.1) ¹⁰	ns	adhd > asd; asd > n
	6.3 (4.7)/ 4.7 (5.1)	ns	6.7 (3.3) / 7.0 (2.9) ¹⁰	asd < adhd; asd+adhd < n; ns	adhd < asd < asd+adhd < n; asd+adhd < n

clinics received a brochure containing information about the BOA and IMAGE study and were requested to return a pre-stamped response card. A short telephone screening and, subsequently, screening questionnaires were used to verify if families fulfilled inclusion criteria. The families were invited to visit Karakter or Radboud University Nijmegen Medical Centre, where a trained researcher conducted the ADI-R and/or the PACS. Additional data was collected including blood samples of all family members and neuropsychological data of the children. Both studies were approved by the local medical ethics board and parents and children (above 12 years old) signed for informed consent.

Data-analyses

Analyses were performed with SPSS 20. The Expectation Maximization (EM) algorithm (Tabachnick & Fidell, 2001) was used to impute the missing values when less than 5% of the parent data and the PACHIO-R was missing. To examine the effect of child diagnosis (affected or not) on the parent-child relationship, two separate (regarding acceptance and conflict resolution) repeated measure ANOVAs were used. Variables included into the model were (1) family type (ASD, ADHD and ASD+ADHD) as between subjects measure and (2) child diagnosis (affected or not) and (3) parent (father/ mother) as repeated measures (to account for within family measurements). In addition, all two-way interaction effects were included and dropped from the model if not significant. In addition, one sample T-test were performed for comparisons with the norm.

To examine to what extent, parental symptoms, diagnosis of the child and the combination between parent and child symptoms were related to the child perception of the parent-child relationship, also repeated measure ANOVAs were used (separately for acceptance and conflict resolution). To combine self (total AQ-score [BOA])- and spouse reported (total ASBQ [IMAGE]) ASD data of parents, both scales were separately standardized using the Van der Waerden transformation (SPSS 20; IBM Corporation, Armonk, New York) and merged into one ASD parent variable. A dummy code was created (self versus spouse report) and used in further analyses. Variables included into the main model were (1) parents' ASD symptoms (continuous), (2) parents' ADHD symptoms (continuous), and (3) child diagnosis (affected or not) as repeated measure (to prevent duplicating parental symptom data for children within the same family). In addition to the main effects, two-way (interaction between child diagnosis and parental symptoms) and three-way interactions (the interaction between parental ASD symptoms, parental ADHD symptoms and child diagnosis) were tested, to examine the match or mismatch between parental and child ASD and ADHD symptoms in relation to the parent-child relationship. Variables also included initially as effects to correct for possible confounders were: 1) family type (ASD, ADHD, ASD+ADHD), (2) self- versus spouse reported ASD data (to examine if type

of report influenced the results), (3) sex difference (same sex / different sex) and (4) the absolute age difference between the affected and unaffected child. Correction for multiple testing using the 95% CI was performed for all analyses using the False Discovery Rate procedure (Benjamini, 2010).

RESULTS

Main effect of child diagnosis

Acceptance

No significant two-way interaction (child diagnosis by family type and parent by family type) were found regarding the *acceptance scale* ($F(2,129) = 2.59, p = .08$ and $F(2,129) = 2.51, p = .09$, respectively) indicating that there were overall no differential effects of family type on the difference in rating between affected and unaffected children and fathers and mothers. No main effect of family type were found ($F(2,129) = .77, p = .46$). However, a main effect of parents was found ($F(1,129) = 14.47, p < .001$), indicating that mothers were rated higher than fathers. Last, a main effect of child diagnosis was present ($F(1,129) = 7.37, p = .01$) revealing that affected children reported lower acceptance scores than unaffected children. These effects were also reflected in differences with the norm (see Figure 1). Affected children reported lower acceptance scores regarding fathers and mothers ($t(131) = -4.24, p < .001$ and $t(131) = -1.72, p = .09$, whereas unaffected children reported similar acceptance scores as the norm ($t(131) = -1.43, p = .16$ and $t(131) = 0.05, p = .96$, respectively).

Conflict resolution

Regarding the *conflict resolution scale* no two-way interaction effects (child diagnosis by family type and parent by family type) were found ($F(2,129) = 2.07, p = .13$ and $F(2,129) = 1.45, p = .24$, respectively). In addition, no main effect of parents ($F(1,129) = .24, p = .63$) or family type ($F(2,129) = 0.15, p = .86$) were found, indicating that overall fathers and mothers were rated comparably regarding their conflict resolution skills and this did not depend on the type of disorder of their offspring. However, a main effect of child diagnosis was present ($F(1,129) = 15.70, p < .001$), indicating that probands rated their parents poorer in conflict resolution than unaffected children (see Figure 2). Analyses with the norm revealed that, for both fathers and mothers alike, affected children (father $t(131) = -6.89, p < .001$ and mother $t(131) = -5.13, p < .001$) and their unaffected siblings (father $t(131) = -3.52, p = .001$ and mother $t(131) = -2.73, p = .01$) scored significantly lower than the norm.

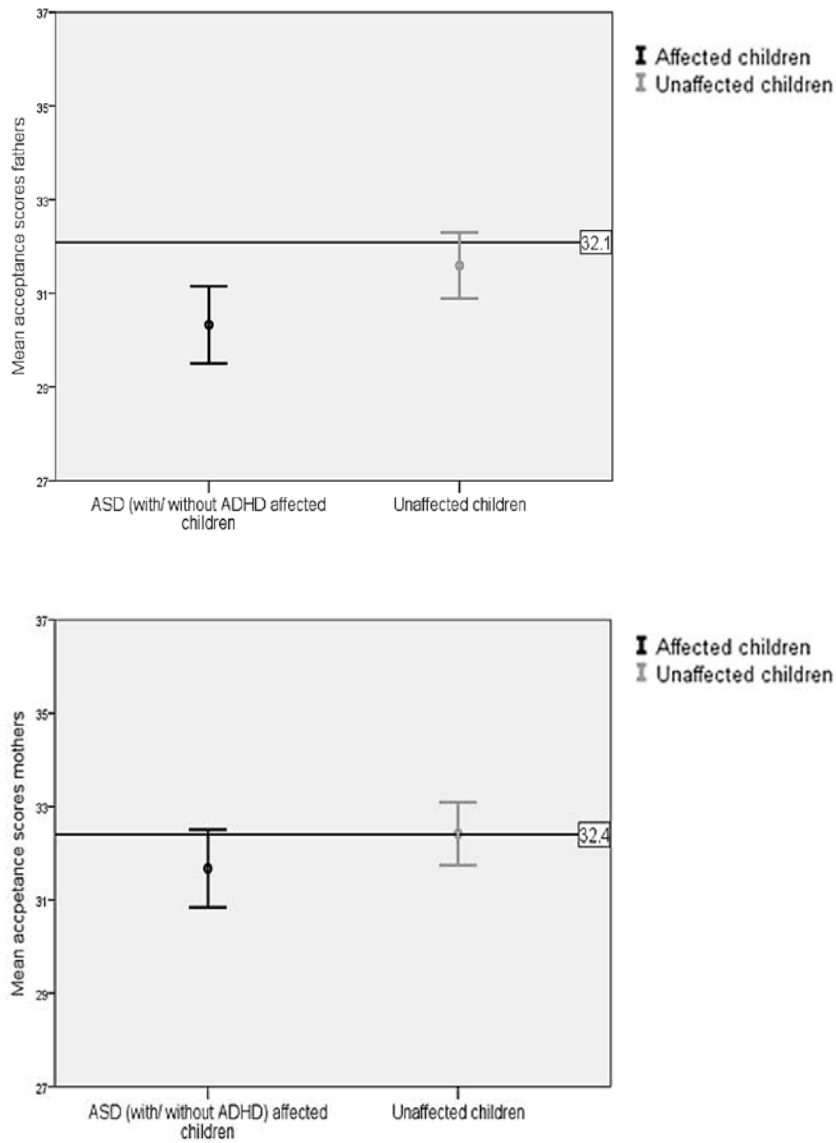


Figure 1 Comparison of Parent- Child Interaction Questionnaire –Revised (PACIIQ-R) acceptance scores between ASD (with/ without ADHD) affected children and their unaffected siblings and the norm group

Norms fathers acceptance scale 32.1 (4.5) (N= 352), norms mothers acceptance scale 32.4 (4.2) (N= 372) (Lange, 2001). The error bars represent the 95% Confidence Intervals (CI) using one-sample t-test in comparison to the population norm value.

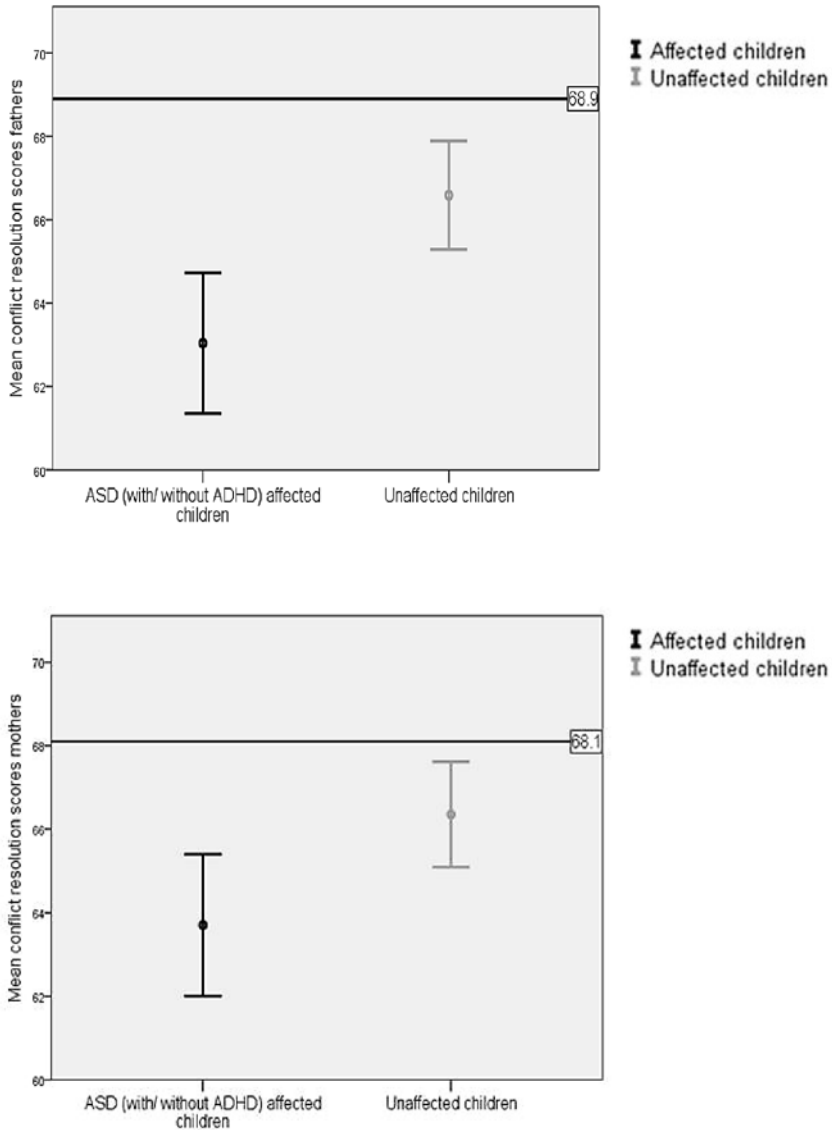


Figure 2 Comparison of Parent- Child Interaction Questionnaire –Revised (PACIQ-R) conflict resolution scores between ASD (with/ without ADHD) affected children and their unaffected siblings and the norm group

Norms fathers conflict resolution scale 68.9 (7.7) (N= 341), norms mothers conflict resolution scale 68.1 (7.5) (N= 326) (Lange, 2001). The error bars represent the 95% Confidence Intervals (CI) using one-sample t-test in comparison to the population norm value.

Effects of parental symptoms and the combination of parent and child symptoms

A repeated measure ANOVA with parents' ASD symptoms, parents' ADHD symptoms, and child diagnosis (within family repeated measure to account for identical parent symptom information in two siblings), the two- and three-way interactions between these variables, and the confounding effects of absolute sex and age differences between siblings, family type and self versus spouse report, was used to examine the combined effect of child and parent pathology on the acceptance and conflict resolution scales. Overall, no interaction or main effects of the confounders were found, except a two-way interaction between child diagnosis and sex difference regarding the acceptance scores of mothers ($F(1,127)=7.51, p=.01$). Post-hoc analyses revealed that unaffected children from different-sex-sibpairs reported significant higher maternal acceptance scores than their affected sib ($t(63)=3.10, p=.003$), whereas no significant differences were found between sibpairs from the same sex ($t(69)=-.64, p=.53$). No two-way interactions between child diagnosis and parental

Table 2 Parent- child relationship measured with the Parent-Child Interaction Questionnaire- Revised (PACIIQ-R) in relation to child pathology (affected/ unaffected) and parental ASD and ADHD symptoms (N=132)

	Main effect parent symptoms		Parent-child pathology interaction	
	ASD symptoms ¹ parents	ADHD symptoms ² parents	parental ASD symptoms	parental ADHD symptoms
	(continuous)	(continuous)	X child diagnosis	X child diagnosis
	F (p-values)	F (p-values)	F (p-values)	F (p-values)
Fathers				
Acceptance	6.31 (.01)	1.07 (.30)	.23 (.63)	1.92 (.17)
Conflict resolution	1.35 (.25)	5.05 (.03)	1.07 (.30)	.14 (.71)
Mothers				
Acceptance	.00 (.99)	.32 (.57)	.42 (.52)	.54 (.47)
Conflict resolution	.34 (.56)	1.82 (.18)	.01 (.91)	.06 (.81)

¹Parental ASD symptoms measured with the Autism Quotient (AQ) self report and Adult's Behavior Questionnaire (ASBQ) spouse report. ²Parental ADHD symptoms measured with the Conners Adult Rating Scales- Self-report: Long version (CAARS-S:L).

Findings in bold are significant after correction for multiple testing.

ASD or ADHD symptoms were found (all p 's were between .17 and .91), indicating that there was no effect of a particular combination of parental symptoms and child pathology on the parent-child relationship (see also Table 2). However, main effects were found for paternal ASD symptoms on the acceptance scale ($F(1, 127) = 6.31, p = .01$) and of paternal ADHD symptoms on the conflict resolution scale ($F(1, 127) = 5.05, p = .03$), but not vice versa ($F(1, 127) = 1.35, p = .25, F(1, 127) = 1.07, p = .30$, respectively), with higher symptom scores relating to poorer relationship scores. No main effects of maternal ASD or ADHD symptoms were found regarding the acceptance and conflict resolution scale (all p 's were between .18 and .99).

DISCUSSION

The main aim of this study was to examine the influence of (a particular combination of) parental and child ASD and ADHD symptoms on parent-child relationships through the perspective of the child. One of the key findings that stood out is that regardless of diagnosis, affected children reported lower acceptance and conflict resolution scores compared to their unaffected siblings, with fathers receiving somewhat poorer scores than mothers regarding acceptance towards especially fathers, but also mothers and lower conflict resolution scores towards both fathers and mothers, compared to their unaffected siblings. It is possible that this is not an accurate reflection of parenting practices, because affected children may have more problems with reporting accurate parenting skills regarding acceptance and conflict resolution or may react more strongly to parenting practices than their unaffected siblings (Belsky & Pluess, 2009). However, it may also be a true indicator of differential parenting practices towards the offspring with parents displaying a less positive parenting style towards their ASD (with/ without ADHD) affected offspring compared to their unaffected offspring. A possible explanation for this might be that affected offspring may evoke more negative feelings by parents because of their talkative, distractible, demanding, moody, less adaptable, and less cooperative and more challenging behavior than their unaffected brothers and sisters (Anastopoulos, Sommer, & Schatz, 2009; Pimentel, Vieira- Santos, Santos, & Vale, 2011). In any case, it seems of great clinical relevance to be aware of these issues in ASD (with/without ADHD) families, since the feeling of being less accepted than other children in the family is a strong predictor of future maladaptive behavior (Bosco et al., 2003; Lange et al., 1997; Nelson et al., 1999; Phares & Renk, 1998).

Another interesting finding is that mainly the conflict resolution skills, but not the acceptance of their offspring, of the parents were rated lower by their offspring compared to norm scores. This suggests that in these families both fathers and mothers may have difficulties with preventing and solving problems, more so than

with providing a warm and accepting environment for their children. This loving, nurturing and protective environment may serve as a protection towards the potential disadvantages of the difficulties of preventing and solving problems of their parents. It is also associated with positive outcomes such as the development of social behavior (empathy, helpfulness) in children, positive peer relations in adolescence and psychological well-being in adulthood (Khaleque & Rohner, 2002; Rohner & Khaleque, 2010). In other words, this study provides another piece of evidence against Bettelheims' (1967) hypothesis that the cause of autism was a lack of maternal warmth towards the child. However, differential feelings of acceptance do appear to exist, with affected children feeling generally less accepted by their parents, which may be a cause for clinical concern.

It was further examined if parental symptoms were related to child's perception of the parent-child relationship. Findings indicated that paternal ASD, but not ADHD, was related to poorer acceptance, whereas paternal ADHD, but not ASD, was related to poorer conflict resolution. It is surprising that we did not find this in mothers, yet overall scores for mothers and fathers were very similar in contrast to previous literature (Phares et al., 2009; Smetana et al., 2006; Yahav, 2006). It may thus be suggested that fathers with rigid and poorer social skills (ASD symptoms) have more problems in maintaining a positive relationship with their children than mothers with ASD symptoms and fathers without ASD symptoms, and that fathers characterized by a disorganized and chaotic life style (ADHD symptoms) have less conflict resolution skills than mothers with ADHD symptoms and fathers without ADHD symptoms (see for a review Johnston et al., 2012). A possible explanation for this might be that paternal ASD and ADHD symptoms may evoke more negative feelings in the children, since fathers are –more than mothers– more involved in –for the child– important activities such as play, talking and recreational activities (Craig, 2006). Importantly though, no evidence was found for a particular combination of parent-child pathology influencing the parent-offspring relationship, suggesting discordant or concordant parent-child pairs do not pose an even higher risk for a poor relationship above and beyond the main effects of child diagnosis and parental symptoms.

Our findings should be interpreted in the context of several limitations. First, the percentages boys in the proband groups were larger than the percentage boys in the sibling groups. It is possible that boys have the tendency to score lower than girls, resulting in a significantly difference between the probands and sibling group. However, earlier research (Gerlsma, Snijders, Duijn van, & Emmelkamp, 1997; Phares et al., 2009) has found that ASD affected children and their unaffected siblings score comparable on the perception regarding parental warmth and conflict resolution skills. Second, parental symptoms were assessed with self (ADHD) or self and spouse (ASD). Self reported symptoms may be less valid in high scoring individuals due to limited self awareness (Berthoz & Hill, 2005; Kooij et al., 2008; Mazefsky, Kao,

& Oswald, 2011; Young & Gudjonsson, 2005). This may result in an underestimation of ASD and ADHD symptoms in parents which might have hampered the lack of findings regarding the match/ mismatch between parental symptoms and child symptoms. Further research with objective diagnoses or spouse reported symptoms is needed to clarify this issue. Third, it may be possible that some self-selection bias may have occurred: parents wanting to participate may have been more accepting of their child's diagnosis and therefore may have better parent-child relationships than parents who refused participation. However, that does not explain the overall lower ratings of probands compared to unaffected siblings.

In conclusion, this is the first study that reports on the influence of parental ASD and ADHD symptoms in combination with child pathology on the parent- child relationship as perceived by the child. The results show that regardless of diagnosis, affected children are more negative regarding perceived acceptance and conflict resolution skills of their parents, than their unaffected siblings, with conflict resolution scores being lower than the norm. It is possible that this is not an accurate reflection of real parenting practices, but the feeling of being less accepted than other children in the family may be a strong predictor of future maladaptive behavior and reason for concern. Furthermore, paternal (and not maternal) ASD and ADHD were related to poorer acceptance and conflict resolution scores, respectively, but no evidence was found for a specific detrimental combination of parent and child pathology on the parent-child relationship. In any case, treatment targeting conflict resolution skills of parents of ASD/ADHD affected children may be beneficial, and clinical awareness in treatment for feelings of differential parental acceptance in affected offspring is required. Longitudinal studies may reveal the outcomes of differential parenting practices and parental symptoms and may indicate whether child diagnosis may moderate this.

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The reciprocal relationship
of ASD, ADHD, depressive symptoms
and stress in parents of children with
ASD and/ or ADHD

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ABSTRACT

The current study sets out to examine, using Generalized Linear Models and Structural Equations Models, the role of parental ASD, ADHD and depressive symptoms on parenting stress in 174 ASD and/or ADHD families. Fathers and mothers reported more parenting stress towards ASD and/or ADHD affected offspring than unaffected offspring and a norm population. Depressive symptoms were most pronounced in parents of ASD and ASD+ADHD families. Spouse correlations were found for ASD, depression and parenting stress. Paternal ASD and maternal ADHD symptoms were related to increased parenting stress. Parental ADHD symptoms were found to be related to depressive symptoms and in turn to parenting stress. The results highlight the increased burden on a parent raising a child with ASD and/or ADHD and the reciprocal relationship this has with their own ASD, ADHD, depressive symptoms and stress levels.

Autism Spectrum Disorder (ASD) and Attention-Deficit/Hyperactivity Disorder (ADHD) often co-occur in the same child and/or family (Rommelse, Franke, Geurts, Hartman, & Buitelaar, 2010). Children with Autism Spectrum Disorder (ASD) have deficits in social and communicative skills and odd ritualistic and rigid behaviors which makes them less cooperative and more challenging to raise (APA, 2000; Fombonne, 2009). Children with Attention-Deficit/Hyperactivity Disorder (ADHD) present a pattern of inattention, hyperactivity and impulsivity which makes them usually talkative, distractible, demanding, moody, less cooperative and also more challenging to raise (APA, 2000). It bears no surprise that these behaviors make a strong appeal on the strategies used by parents to raise their offspring adequately. Consequently, parents of children with one (or both) of these disorders experience increased levels of stress compared to parents of typically developing children (see for example Hayes & Watson, 2013). Parenting stress is significantly associated with more negative parent-child interactions, harsh authoritarian parenting styles, more child behavior problems and reduced effectiveness of implementing interventions (Harpin, 2005; Hastings, 2002; van IJzendoorn et al., 2007). Therefore, reducing parenting stress has been recognized as an important goal of successful treatment for children with behavioural problems (Nezu, Nezu, & Perri, 2006; Osborne, McHugh, Saunders, & Reed, 2008) and as a prerequisite for parent-mediated intervention programs (Herring et al., 2006).

Parents of children with psychiatric problems such as ASD and ADHD experience even higher levels of stress than parents of children with other developmental or somatic disorders, such as Down syndrome, Fragile X, cerebral palsy or specific learning disorders (Blacher & McIntyre, 2006; Eisenhower, Baker, & Blacher, 2005; Gupta, 2007). Apparently, ASD and ADHD affected children place a higher burden on their parents due to their challenging behavioral characteristics. The literature provides evidence that both inattentive and hyperactive-impulsive symptoms are predictive for parenting stress (Theule, Wiener, Tannock, & Jenkins, 2010) and that the deficits in social communication and the odd ritualistic and rigid behaviors are particularly stressful for parents (Hayes & Watson, 2013). However, parenting stress appears to be largely similar in severity for ASD and ADHD (Theule et al., 2010). This suggest that parenting stress may result from other factors common to having a child with any clinical diagnosis such as increased costs for health care or constraints on leisure time (Theule et al., 2010). However, what is unknown is the burden of parents with offspring affected by *both* disorders. Due to classification limitations in the *DSM-IV* preventing a comorbid diagnosis of ASD and ADHD (APA, 2000), very little is known about this topic. For example, a child with ASD and ADHD may show demanding, moody and less cooperative behavior, and this behavior may be enhanced by ASD characteristics such as rigidity. Thus, the presence of comorbid ADHD and ASD pathology in offspring may have a stronger negative effect on parenting stress than the presence of ASD only pathology in these children.

Parenting stress may further arise from other factors that are not directly linked to child pathology such as child age and gender (Seltzer, Shattuck, Abbeduto, & Greenberg, 2004; Theule et al., 2010; Tomeny, Barry, & Bader, 2012). Importantly, following family system theories, children cannot be understood in isolation from other family members, but rather as a part of their family (for a review, see Head & Abbeduto, 2007). The well being of family members may also impact child pathology and parenting stress. Rather neglected in these theories is the role of psychiatric disorders in the parents. Parents of ASD and/or ADHD children often show subthreshold (Broader Autism Phenotype, BAP) or above threshold symptoms of ASD and ADHD (Constatino & Todd, 2005; Faraone, Kunwar, Adamson, & Biederman, 2009), most likely explained by the highly heritable nature of both disorders (Rommelse et al., 2010; Ronald, Simonoff, Kuntsi, Asherton, & Plomin, 2008). These parents may experience more stress than parents with few or no symptoms (Berg-Nielsen, Vikan, & Dahl, 2002). Moreover, the rearing situation can be further complicated by parental depressive symptoms, being elevated in adults with ADHD (Theule et al., 2010) and ASD (Sterling, Dawson, Estes, & Greenson, 2008) and being related to parental stress. Depressive symptoms in adults reduce emotional involvement, parental competence, effectiveness of communication and the use of directives in guiding child behavior (Dix & Meunier, 2009; Lee et al., 2012). In other words, emotional difficulties in parents influence the degree of parental stress and vice versa, parenting stress influences depressive symptoms (Leigh & Milgrom, 2008; Ornstein- Davis & Carter, 2008).

To take the issue even further, it is known that the well being of spouses is also related. For instance, mothers' parenting stress was predictive of fathers' parenting stress in Down syndrome families (Roach, Orsmond, & Barratt, 1999) and mothers' parenting stress was associated with fathers' depressive symptoms in ASD families (Hastings, 2003; Hastings et al., 2005). These relationships between partners' symptoms and parenting stress is not surprising when considering that one's wellbeing depends on the amount of support received from their partner when handling a difficult to rear child (Hastings, 2003). This interdependence of symptoms may act as a catalyst in increasing one's own and their spouses' parenting stress, which in turn results in more behavioral problems from the child and in more parents mental health symptoms displayed by the parents (Hastings, 2003).

The current study aimed to examine several interrelated and largely neglected research questions. (1) Does parenting stress differ between parents having a child with ASD only, ADHD only, or if the child has both ASD and ADHD? (2) Do parental ASD and/ or ADHD with or without depressive symptoms contribute to parental stress? (3) Are symptoms and parenting stress levels related between spouses? Based on the literature, it was uncertain whether or not depression could best be modeled as mediating between parental ASD/ADHD symptoms and parenting stress

(Figure 1, Model 2), or as a dependent variable only (Figure 1, Model 1), so both models were tested.

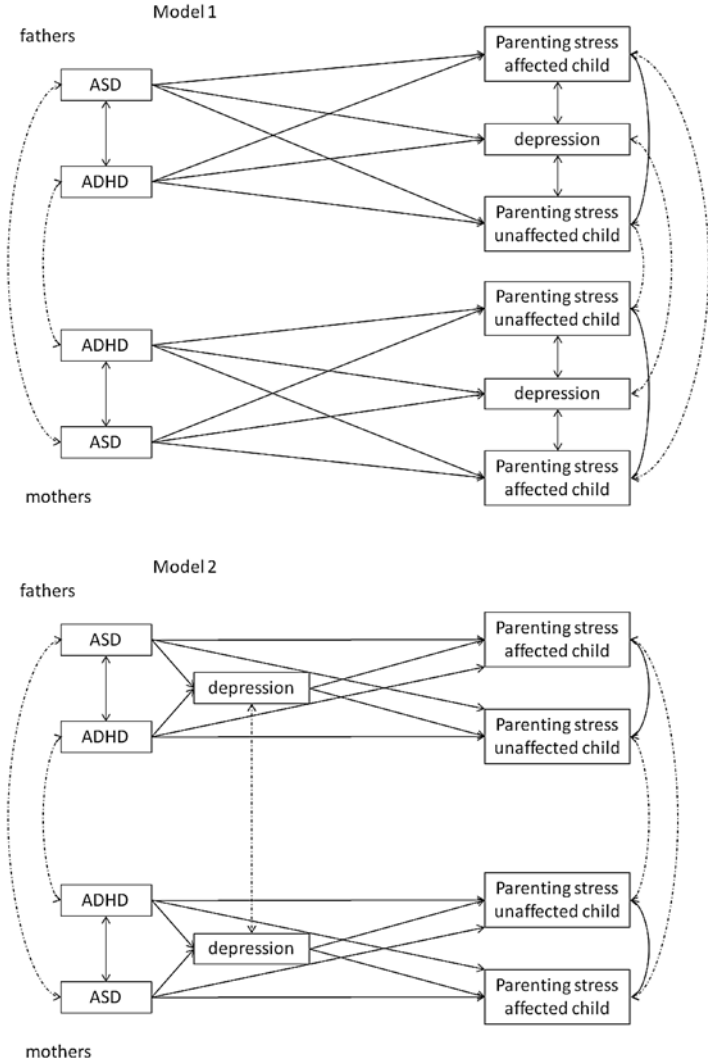


Figure 1 Two potential models linking parental ASD/ADHD symptoms with depression and parenting stress regarding affected and unaffected offspring. The models only differ in the mediating effect of depression, which is included in Model 2, but not in Model 1

Arrows between parents in dotted lines.

METHODS

Participants

Children

A total of 174 families were recruited from two ASD and ADHD family-genetics studies (*Biological Origins of Autism [BOA]* and *International Multicenter ADHD Genes study [IMAGE]*). Families were included in the studies if (a) they had one child (2-20 years) with a clinical ASD (+ADHD) diagnosis (*BOA*) or if they had one child (5-19 years) with a clinical ADHD (combined subtype) diagnosis (*IMAGE*), (b) at least one biological sibling (affected or not) and (c) at least one biological parent willing to participate. The data of unaffected siblings allowed us to correct for possible confounders (such as family environment) that may vary between families with psychopathology and without psychopathology, but not between affected and unaffected siblings within one family since they share the same environment (Cartwright et al., 2011). In the current study only families with two participating biological parents were included where the children still lived at home. All families were of European Caucasian descent. Exclusion criteria for all families were epilepsy, a diagnosis of a defined genetic or non-genetic cause of ASD or ADHD (Rett's syndrome, fragile X syndrome) or a genetic disease such as Down syndrome. Comorbid *DSM-IV* disorders were not excluded, with the exception of a diagnosis of autistic disorder (other ASD subtypes were allowed) in the *IMAGE* study. All families received their usual care such as treatment in day care centers, motor therapy and speech and language therapy, sessions with a psychologist and/ or intensive support in the home environment.

The children clinically diagnosed with ASD or ADHD and their siblings were carefully screened for the presence of ASD symptoms with the Social Communication Questionnaire (SCQ) (Rutter et al., 2003), (for the fully described procedure of the SCQ in the *BOA* and *IMAGE* studies, see Steijn van et al., 2012). The Autism Diagnostic Interview Revised (ADI-R) (Le Couteur, Lord, & Rutter, 2003) (*BOA*) or the Children's Social Behavior Questionnaire (Luteijn, Minderaa, & Jackson, 2002) (*IMAGE*), a parental 49 item questionnaire measuring social problem behavior with adequate reliability and validity (Lutteiijn, et al., 2002), was administered for all children scoring above clinical cut-off of the SCQ. Children were given a diagnosis of ASD if scoring clinically on the ADI-R (*BOA*) or above cut-off on the SCQ (>15) in addition to a score above the 95th percentile on the CSBQ (*IMAGE*) (Hartman, Luteijn, Moorlag, de Bildt, & Minderaa, 2007).

All children were carefully screened for the presence of ADHD symptoms using the Conners long version Rating Scales Revised (CRS-R) (Conners, 1997) completed by parents and teachers. For all children scoring above the cut-off on one of three *DSM-IV* ADHD scales ($T \geq 63$), the Parental Account of Childhood Symptoms (PACS) (Taylor, Sandberg, Thorley, & Giles, 1991) was administered by a certified clinician.

Thereafter, a standardized algorithm was applied using the scores of the PACS and the teacher version of the CRS-R to construct a formal diagnosis of ADHD (for details see, Rommelse, Oosterlaan, Buitelaar, Faraone & Sergeant, 2007a).

We were able to include 48 children with an ASD diagnosis without clinical ADHD symptoms (all from the *BOA* study) and 72 children with an ADHD diagnosis without clinical ASD symptoms (all from the *IMAGE* study). The ASD+ADHD diagnose group contained children that were given an ASD and ADHD diagnosis as described above. A total of 54 children with ASD+ADHD diagnosis (39 from the *BOA* study and 15 from the *IMAGE* study) were included. For each affected child, one unaffected sibling closest in age was selected. This resulted in 86 same-sex sib pairs and 88 different sex sibpairs with an absolute mean age difference of 2.88 years ($SD = 1.6$) (See Table 1a).

Parents

In the *BOA* sample, all parents were screened for the presence of ASD symptoms with the self-report Autism Spectrum Quotient (AQ; Baron-Cohen, Wheelwright, Skinner, Martin, & Clubley, 2001) (*BOA*) (see Table 1b). In total, current self-reported ASD data was available for 87/87 fathers and 87/87 mothers having a child with ASD or ASD+ADHD. In the *IMAGE* sample, parents were screened for ASD using spouse report Adult's Social Behavior Questionnaire (ASBQ; Hartman et al., in press). Spouse reported data was available for 65/87 fathers and 67/87 mothers having a child with ADHD or with ADHD+ASD. The AQ consists of 50 items rated on a 4-point rating scale. The ASBQ contains 49 items and measures the social problem behavior of adults (Horwitz, Sytema, Ketelaars, & Wiersma, 2005). Both total scores were used as indication of ASD symptom severity (Hoekstra, Bartels, Cath, & Boomsma, 2008).

Current self-reported ADHD symptoms of the parents were assessed with the raw total score for the 18 DSM-IV ADHD items on a 4-points scale of the Conners Adult Rating Scales- Self-report: Long version (CAARS:Conners, Erhardt, & Sparrow, 1999) in the *BOA* sample (available for 87/87 fathers and 87/87 mothers) and the self-report questionnaire for ADHD (Kooij et al., 2004) in the *IMAGE* sample (available for 83/87 fathers and 83/87 mothers).

To assess the depressive symptoms of parents, short versions of the GHQ-60 were used (Koeter & Ormel, 1991); the GHQ-12 (*BOA*) or GHQ-28 (*IMAGE*) (Koeter & Ormel, 1991). Data was available for 72/87 fathers and 78/87 mothers of the *BOA* sample and for 77/87 fathers and 83/87 mothers of the *IMAGE* sample. Although, commonly treated as a subjective psychological health index of adults, the GHQ is also a useful screening instrument for the detection of depression (Boothby, Holcombe, Clark, Fisher, & Salmon, 2010; Ozdemir & Rezaki, 2007). The GHQ consists of 12 or 28 items (for example 'Have you recently lost much sleep over worry?', 'Have you recently felt constantly under strain?'). Responses were given on a 4-point scale representing: (0) not at all; (1) no more than usual; (2) rather more than

Table 1a Characteristics children

	ASD families (n= 48)		ADHD families (n= 67)	
	<i>probands/ siblings</i>	<i>within families T-tests</i>	<i>probands/ siblings</i>	<i>within families T-tests</i>
	<i>M (SD)</i>	<i>Contrast</i>	<i>M (SD)</i>	<i>Contrast</i>
% male	85.4/ 41.7	prob > sibs*	80.6/ 50.7	prob > sibs
Age in years	12.0 (4.2)/ 11.4 (4.7)	prob > sibs	11.9 (2.8)/ 10.9 (3.3)	prob > sibs
SCQ	19.7 (7.7)/ 4.1 (3.4)	prob > sibs	6.6 (3.2)/ 4.6 (3.5)	prob > sibs
CSBQ			29.9 (14.4)/ 15.6 (10.9)	prob > sibs
CRS-R ³	59.2 (9.1)/ 49.6 (7.0)	prob > sibs	72.5 (7.4)/ 52.6 (9.5)	prob > sibs
% ASD (ADI) ⁴	100 / 0		0 / 0	
%ADHD (PACS) ⁶	0 / 0		100 / 0	

*prob and sibs= probands and siblings. ¹Social Communication Questionnaire, norms based on population cohort (N= 247) (Chandler et al., 2007). ²Children's Social Behavior Questionnaire, norms based on a study of Luteijn (N= 232) (1998). ³Conners long version Rating Scales Revised. ⁴Autism Diagnostic Interview (ADI-R). ⁵Based on N= 24, the other 12 children were included if they scored above cutoff on the SCQ (> 12) and CSBQ (> 14). ⁶Parental Account for Childhood Symptoms (PACS).

usual; (3) much more than usual (for other 4-points scales see Koeter & Ormel, 1991). A total higher score refers to more depressive symptoms. Total scores of both versions were made comparable by multiplying the obtained score by 60/12 (GHQ-12) or 60/28 (GHQ-28). Norm data of the GHQ was available for both fathers and mothers (Koeter & Ormel, 1991). The short version of the Parental Stress Index (PSI-SF; De Brock, Vermulst, Gerris, & Abidin, 1992) was used to measure parenting stress of parents. The PSI-SF consists of 25 items that refer to parenting stress regarding a particular child (for example, 'I find that I am not able to take care of this child as well as I thought I could'). Responses were given on a 6-point scale representing; (1) strongly disagree; (2) slightly disagree; (3) tend to disagree; (4) tend to agree; (5) fairly agree; (6) strongly agree. A total parenting stress score could be obtained by summing up the item scores with a higher score referring to more stress. The PSI-SF has been shown to demonstrate adequate validity and reliability (De Brock et al., 1992). The PSI-SF was completed by both fathers and mothers of the BOA and IMAGE sample for the probands (174/174 fathers and 174/174 mothers). The fathers

	ASD+ADHD families (n= 59)				
	<i>probands / siblings</i>	<i>within families T-tests</i>			
	<i>M (SD)</i>	<i>Contrast</i>	<i>norms (n)</i>	<i>between probands</i>	<i>between siblings</i>
	83.1/ 44.1	prob > sibs		asd = adhd = asd+adhd	asd = adhd = asd+adhd
	10.9 (3.3)/ 10.8 (4.8)	prob = sibs		asd = adhd = asd+adhd	asd = adhd = asd+adhd
	18.8 (5.4)/ 4.6 (4.6)	prob > sibs	4.7 (5.0) ¹	asd = asd+adhd > adhd > n	asd = adhd = asd+adhd = n
	49.9 (13.9)/ 15.7 (13.9)	prob > sibs	8.3 (2.7) ²	adhd < asd+adhd > n	adhd = asd+adhd > n
	69.8 (9.1)/ 50.4 (5.6)	prob > sibs	50 (10)	adhd = asd+adhd > asd > n	asd = adhd = asd+adhd = n
	100 ⁵ / 0				
	100 / 0				

and mothers of the *IMAGE* sample also completed the PSI-SF for the unaffected siblings (fathers 79/87 and mothers 86/87). Dutch norm data of the PSI-SF was available separately for fathers and mothers (De Brock et al., 1992).

Procedure

Eligible ASD and ADHD families registered at an outpatient clinic specializing in ASD and ADHD pathology (Karakter Child and Adolescent Psychiatric University Center), members of the Dutch Autism Association (NVA) and families in other pediatric clinics, all received a brochure containing information about the *BOA* and *IMAGE* study and were requested to return a pre-stamped response card. A short telephone screening and subsequently, screening questionnaires were used to verify if families fulfilled inclusion criteria. The families were then invited to visit three clinical sites (Karakter Child and Adolescent Psychiatry Nijmegen, Radboud University Nijmegen Medical Centre or the VU University Amsterdam), where a trained researcher

Table 1b Characteristics parents

	ASD families (n= 48)		ADHD families (n= 67)		
	<i>fathers/ mother</i>	<i>within families T-tests</i>	<i>fathers/ mothers</i>	<i>within families T-tests</i>	
	<i>M (SD)</i>	<i>Contrast</i>	<i>M (SD)</i>	<i>Contrast</i>	
Autism Quotient	103.1 (17.5)/ 95.5 (19.1)	fath > moth**			
ASBQ ²			15.1 (13.1)/ 11.0 (10.8)	ns	
ADHD DSM-IV raw inattentive scores	4.4 (4.0)/ 3.6 (3.8)	ns	6.0 (4.6)/ 5.9 (4.9)	ns	
ADHD DSM-IV raw hyperactive scores	5.1 (3.9)/ 4.9 (3.8)	ns	7.4 (4.9)/ 7.6 (5.6)	ns	

** fath and moth= fathers and mothers. ¹Hoekstra, Bartels, Cath & Boomsma (2008). Mean scores of ASD+ADHD families were based on N= 39 parents. ²Adult's Social Behavior Questionnaire. Mean scores of ASD+ADHD families were based on N= 15 fathers and mothers. ³Norms from the Dutch Twin Register (Boomsma et al., 2010).

conducted the diagnostic interviews and parents filled out the questionnaires. Additional data was collected including blood samples of all family members and neuropsychological data of the children. Both studies were approved by the local medical ethics board and parents and children (> 12 years) signed consent forms. Children younger than 12 years of age were asked to give their assent for participation.

Data-analyses

Data was normally distributed adequately based on skewness and curtosis parameters and visual inspection. For all analyses correction for multiple testing was applied using a q-value setting of 0.05 using the False Discovery procedure (Benjamini, 2010). First, effects of possible confounders of parenting stress, child's age and gender, were examined using Pearson correlations and independent t-tests respectively. To examine the effect of family type and parent on parenting stress in affected and non-affected offspring separately, repeated measure ANOVAs were used separately for affected and non-affected children with (1) family type (affected children: ASD, ADHD and ASD+ADHD; non-affected children: ADHD and ASD+ADHD) as between subjects measure, and (2) parent (father/ mother) as a repeated measure (to account for reporting stress regarding the same child). The

	ASD+ADHD families (n= 59)					
	<i>fathers/ mothers</i>	<i>within families T-tests</i>				
	<i>M (SD)</i>	<i>Contrast</i>	<i>M (SD)</i>	<i>Contrast</i>		<i>Contrast</i>
	108.2 (17.5)/ 95.4 (17.9)	fath > moth	105.7 (11.0)/102.9 (11.5) ¹	ns		n > asd+adhd < n
	19.0 (16.1)/ 16.0 (16.1)	ns		ns		asd+adhd > adhd
	6.7 (4.7)/ 4.8 (4.7)	fath > moth	5.3 (3.2)/ 5.3 (3.1) ³	n > asd		n > asd
	5.8 (4.2)/ 5.3 (4.0)	ns	6.7 (3.3)/ 7.0 (2.9) ³	n > asd		n > asd

two-way interaction effect of parent by family type was included and dropped from the model if not significant. To examine the effect of type of family (ASD, ADHD and ASD+ADHD) on parental depressive symptoms, an ANOVA was used. Variables included into the model were (1) family type (ASD, ADHD and ASD+ADHD), and (2) parent (fathers/mother). The two-way interaction effect of parent by family type was included and dropped from the model if not significant. One sample t-tests were performed for comparisons with the norm data of the PSI-SF and GHQ regarding parenting stress and depressive symptoms. Analyses were conducted in SPSS 20.

Structural equation modeling (Mplus 6.11, Muthén & Muthén, 1998–2010) was used to estimate the best fitting model linking parental ASD and ADHD and depressive symptoms, with self-reported parenting stress towards affected and unaffected offspring. Basic assumptions were (a) parental ASD and ADHD symptoms would influence parental stress and depression, (b) ASD and ADHD were correlated *within* parents, (c) parenting stress was related within (affected and unaffected) offspring, and (d) congruent measures were related *between* parents (i.e. correlation between fathers' and mothers' depression, between fathers' and mothers' parental stress etc.). All analyses were performed on a family-based level, with each family contributing one degree of freedom to the analyses.

Because parental ASD symptoms were measured by self-report (*BOA* sample) or spouse report (*IMAGE* sample), both measures were transformed into z-scores using the Van der Waerden transformation (SPSS 18; IBM Corporation) and thereafter combined into one ASD variable. Since analyses were carried out within families, and within families the same measure was always used, it was hypothesized not to influence the results significantly. To verify this, a dummy variable was created indexing self versus spouse report and used in the model fitting a group variable when examining the relationships between ASD, ADHD and depression within and between parents.

Based on previous literature, it was uncertain whether or not depression could best be modeled as mediating between parental ASD/ADHD symptoms and parenting stress (Figure 1, Model 2), or as a dependent variable only (Figure 1, Model 1). Therefore, in the first instance, these models were compared regarding goodness of fit. Thereafter, the most parsimonious model was determined, by excluding any redundant parameters in a set-wise fashion. In this way, the model incorporating the fewest number of assumptions was selected, without resulting in a significantly poorer explanation of the data. In first instance, parameters that were not significant were dropped from the model as well as constraining means/intercepts and (residual) variances to be equal for congruent measures in fathers and mothers, unless model fit indices indicated a poorer fit. In the second instance, it was examined whether measures regressed on the same construct (such as parenting stress regarding affected and unaffected offspring on ADHD symptoms) could be construed to be equal. Finally, if these steps did not result in an acceptable model fit, modification indices were calculated with a minimum value of 6.64 (i.e. resulting in a $p < .01$ significantly better model fit if included in the model). The stability of parameter estimation and of the structural equation model results were evaluated via bootstrapping procedures with 10.000 repeats.

Goodness of fit indices included (a) chi square (χ^2), (b) the χ^2 to degrees of freedom ratio (good fit is below a 2 to 3 ratio) (Wheaton, Muthen, Allwin, & Summers, 1997), (c) the Comparative Fit Index (CFI) and the Tucker-Lewis Index (TLI) with very good fit indicated by scores $> .95$ (Bentler, 1990; Hu & Bentler, 1998), (d) the Root Mean Square Error Approximation (RMSEA) with values $< .05$ indicating good fit (Hu & Bentler, 1998), and (e) the Standardized Root Mean Squared Residual (SRMR) where good fit is indicated by a score of $< .08$ (Hu & Bentler, 1998). Families with incomplete data were included in the analyses, as Mplus provides a method for handling incomplete data by using raw maximum likelihood estimation, in which a likelihood statistic ($-2LL$) of the data for each observation is calculated (Múthen and Múthen, 1998–2010)). The best fitted model was used for further analyses in which the model was maximally simplified.

RESULTS

Checking the possible effects of child's age and gender on parenting stress

The correlations between child age and parenting stress were all small and non-significant (all p -values $> .28$). No differences were found between boys and girls regarding parenting stress, except that mothers reported significantly higher parenting stress regarding ASD affected girls compared to ASD affected boys (see Figure 2). Based on the results of these analyses, gender and age were omitted from further analyses.

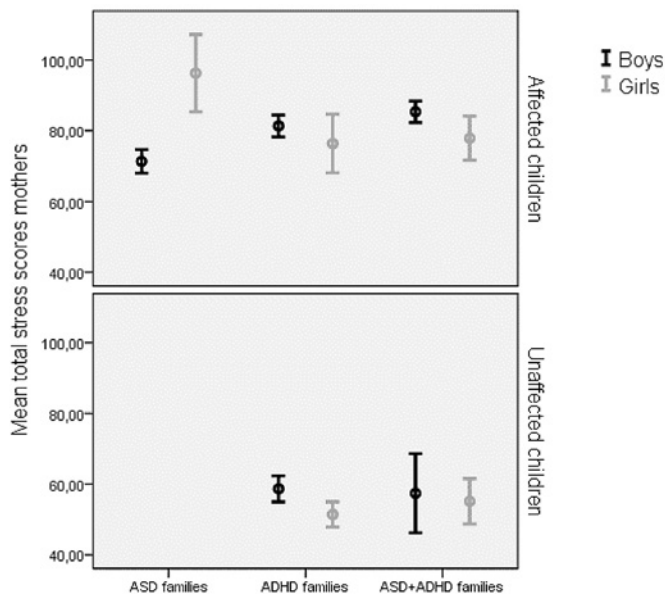


Figure 2 Differences between ASD, ADHD and ASD+ADHD affected and unaffected boys and girls regarding parenting stress scores

Main effects of child diagnosis on parenting stress

A significant two-way interaction was found between parent and family type for parenting stress regarding affected and unaffected children ($F(1,170) = 3.13, p = .05$ and $F(1,84) = 5.58, p = .02$, respectively), indicating that there were differences in parenting stress between parents across the types of families. Post hoc analyses

revealed that **affected children** mothers reported more parenting stress than fathers towards ASD ($t(45) 2.00, p = .05$) and ADHD affected offspring ($t(63) 2.75, p = .01$), which was not found in families with ASD+ADHD affected offspring ($t(53) .40, p = .69$). Regarding **unaffected children**, mothers reported more parenting stress than fathers towards unaffected siblings of ASD+ADHD children ($t(15) 2.79, p = .01$), which was not found for unaffected siblings of ADHD probands ($t(61) 0.21, p = .83$). Compared to the norm data of the PSI-SF, fathers and mothers reported significantly more parenting stress towards their ASD, ADHD and ASD+ADHD affected children whereas parenting stress regarding unaffected children was comparable with the norm (see Figure 3a). An exception was fathers reporting significantly more parenting stress regarding unaffected children of ADHD probands.

Main effects of child diagnosis on depressive symptoms

No two-way interaction between family type and parent was present ($F(2, 345) = 0.50, p = .60$), indicating that there were no differences in depressive symptoms between parents across the three types of families. No main effect of parent was found ($F(1, 345) = 0.32, p = .57$). However, a main effect was found for family type ($F(2, 345) = 15.85, p < .001$) revealing that parents of ASD families reported more depressive symptoms than parents of ADHD families ($t(220) = 12.70, p < .001$) and ASD+ADHD families ($t(184) 4.25, p < .001$). Parents of ASD+ADHD families reported more depressive symptoms than ADHD families ($t(238) = 6.84, p < .001$). These effects were also reflected in differences with the norm data of the GHQ (see Figure 3b).

Parental ASD, ADHD and depressive symptoms and parenting stress in ASD and/or ADHD families

Results are presented in Table 2. The relationships between ASD, ADHD and depression within and between parents as depicted in Figure 1 were similar for families with ASD self-report versus spouse report, as indicated by a non-significant worse model fit with and without fitting separately for both groups ($\Delta\chi^2 = 4.35, df = 6, p > .50$). Therefore, further models were fitted for the complete sample. The model with a mediating effect of depressive symptoms (Fig.1, model 2) was 1.47 times more likely and obtained slightly better fit indices than the model without this effect (Fig.1, model 1). Model 2 was therefore used for further analyses. After dropping non-significant paths from the model and constraining means/intercepts and (residual) variances to be equal in congruent measures in fathers and mothers (step 1), fit indices improved significantly, but did not result in an acceptable fit. Therefore, measures regressed on the same construct (such as parenting stress regarding affected and unaffected offspring on ADHD symptoms) were constrained to be equal for further simplification (step 2). This was indeed the case for the effect of maternal depression on parenting stress regarding affected and unaffected offspring, paternal

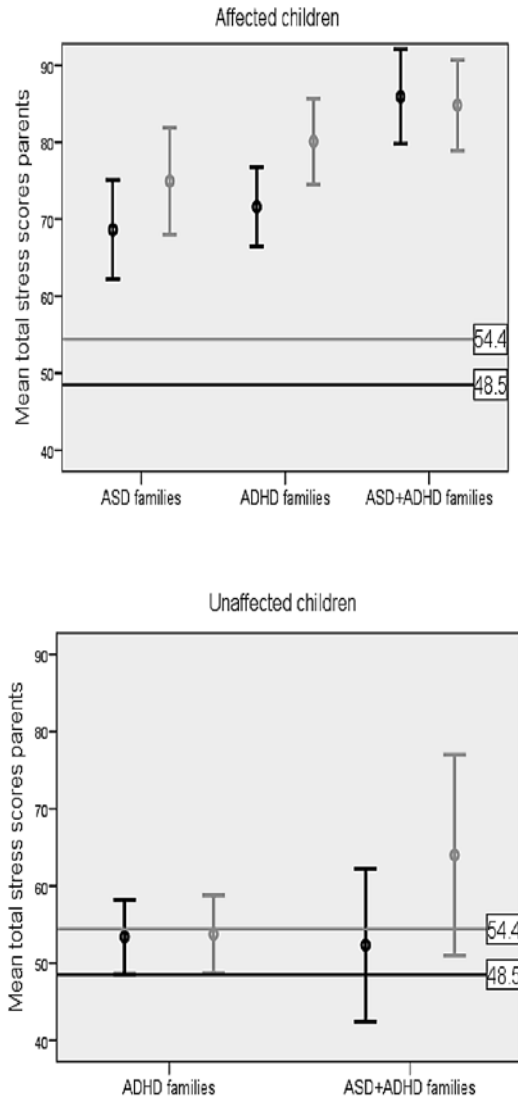


Figure 3a Comparison of the Parental Stress Index (PSI-SF) scores between ASD, ADHD and ASD+ADHD families (N=174) and the norm group

Norms Parental stress Index (PSI-SF) mean total score fathers 48.5 and norms mean total score mothers 54.4 (PSI manual, 1992). The error bars represented the 95% Confidence Intervals (CI) using one sample T-test in comparison to the population value. The means of the unaffected children of the ASD+ADHD families were based on a subsample (n= 20) of the *IMAGE* cohort.

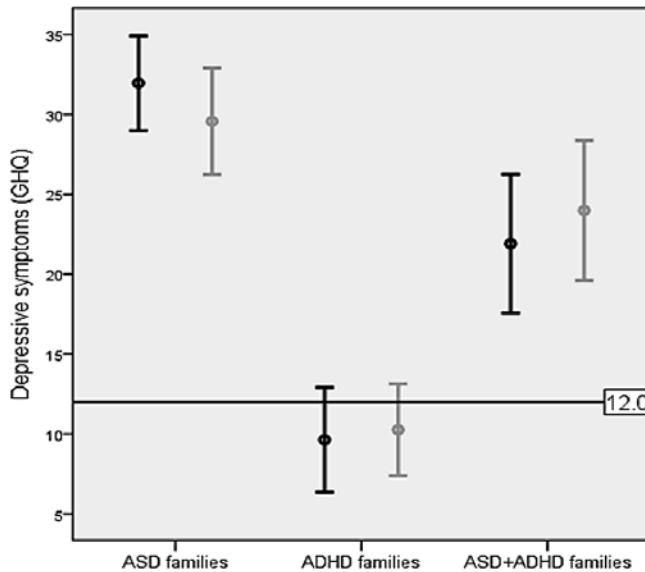


Figure 3b Comparison of the General health Questionnaire (GHQ) scores between ASD, ADHD, and ASD+ADHD families (N=174) and the normgroup.

Cut off norms of the General Health Questionnaire (GHQ) regarding mothers and fathers is 12 (GHQ-manual, 1991). The error bars represented the 95% Confidence Intervals (CI) using one sample T-test in comparison to the population value.

ASD on parenting stress regarding affected and unaffected offspring, and maternal ADHD on parenting stress regarding affected and unaffected offspring, but not for ASD and ADHD on depression in mothers. Model fit was further improved with these adjustments, but was still not completely satisfactory. Modification indices (MI) (step 3) indicated that including paternal parenting stress regarding unaffected offspring influencing maternal depression would result in a strong and significant improvement of fit (Modification Index 11.16, $p < .001$), which was indeed the case. Because excellent model fit was not yet achieved, one further adjustment was made based on MI (6.848, $p < .01$), namely an effect of maternal ASD on paternal parenting stress regarding unaffected offspring. The final model had excellent model fit according to all parameters.

In summary, as expected, positive correlations between spouses were found regarding ASD, ADHD and depressive symptoms and particularly parenting stress (see Figure 4). However, a higher correlation existed between parenting stress

regarding affected and unaffected offspring in fathers than in mothers (constraining both to be equal results in poorer fit ($\Delta\chi^2 = 6.24$, $df = 1$, $p = .01$). Second, only paternal ASD (but not maternal ASD) and maternal ADHD (but not paternal ADHD) symptoms appeared to have a direct effect on parenting stress. Third, in both fathers and mothers, ADHD symptoms (but not ASD symptoms), had an effect on depressive symptoms and in turn on parenting stress. Fourth, in most instances, child diagnosis did not moderate the relationship between parental symptoms and parenting stress, except for the effect of paternal ADHD influencing depression and thereby parenting stress only regarding affected offspring (but note that parenting stress was higher regarding affected children than regarding unaffected children, intercepts could not be constrained to be equal). Last, post-hoc analyses indicated that an unexpected path was present linking maternal ASD symptoms to parenting stress in fathers back to depressive symptoms in mothers.

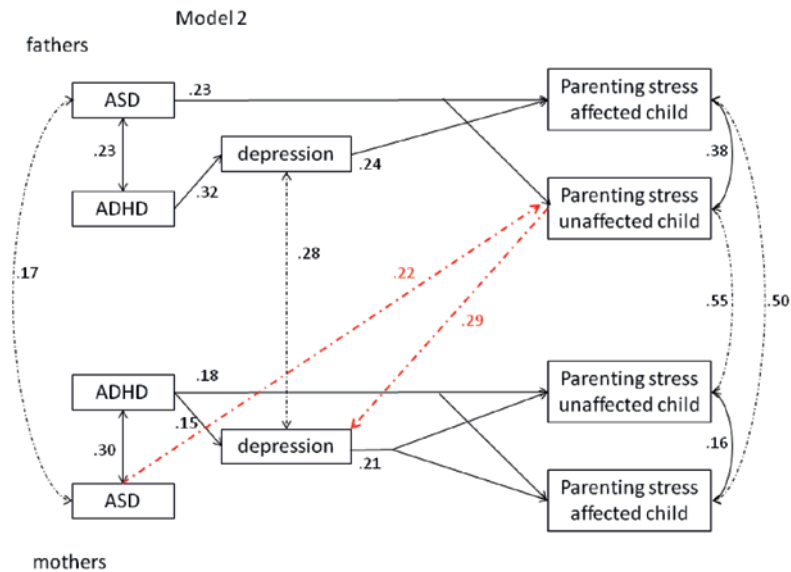


Figure 4 Best fitting model linking parental ASD/ADHD symptoms with depression and parenting stress regarding affected and unaffected offspring.

One-way arrows represent standardized (-1 to +1) structural regression coefficients and indicate the impact of one variable on another. Double-headed arrows represent correlations between variables (without inferring a direction). Arrows between parents in dotted lines. Red arrows indicate paths that were not hypothesized, but had to be added in order to obtain good model fit.

Table 2 Fit indices for the tested models.

	RMSEA (90% CI)	SRMR	CFI
Step 0: Comparing fit of both full models			
Model 1	.089 (.057-.122)	.113	.881
Model 2	.084 (.051-.118)	.108	.894
Step 1: Simplifying model 2 by excluding non-significant parameters and equalizing means, intercepts and variances			
1.1 Excluding non-significant parameters	.071 (.039-.101)	.108	.899
1.2 Constraining means z-scores ASD fathers and mothers to zero	.065 (.033-.095)	.108	.908
1.3 Constraining means ADHD fathers and mothers to be equal	.065 (.033-.094)	.109	.907
1.4 <i>Constraining intercepts depression fathers and mothers to be equal</i>	.069 (.039-.097)	.111	.890
1.5 Constraining intercepts stress affected child to be equal for fathers and mothers	.063 (.031-.092)	.111	.907
1.6 <i>Constraining intercepts stress unaffected child to be equal for fathers and mothers</i>	.071 (.043-.099)	.122	.879
1.7 Constraining variances to be equal for similar measures in fathers and mothers	.056 (.021-.084)	.114	.919
Step 2: Simplifying model 2 by constraining parameters regressed on the same construct to be equal			
2.1 Constraining parameters maternal depression on stress affected and unaffected child to be equal	.054 (.018-.082)	.114	.923
2.2 Constraining parameters paternal ASD on stress affected and unaffected child to be equal	.053 (.018-.081)	.113	.922
2.3 Constraining parameters maternal depression on stress affected and unaffected child to be equal	.051 (.013-.079)	.113	.927
2.4 <i>Constraining maternal parameters ASD and ADHD on depression be equal</i>	.054 (.021-.081)	.116	.915
Step 3: improving fit of model 2 based on modification indices			
3.1 Adding path from maternal ASD to father's stress regarding unaffected offspring	.034 (.000-.066)	.095	.969
3.2 Adding path from paternal stress regarding unaffected offspring to maternal depression	.013 (.000-.056)	.085	.995

RMSEA = Root Mean Square Error Approximation (good fit <.05); SRMR = the Standardized Root Mean Squared Residual (good fit <.08); CFI = Comparative Fit Index (good fit >.95); TLI = Tucker-Lewis Index (good fit >.95); AIC = Akaike Information Criterion (lower AIC implies a better fit); BIC = Bayesian Information Criterion (lower BIC implies either fewer explanatory variables, better fit, or both).

Steps in italics indicate a worse fit that was not carried forward in further model fitting.

	TLI	AIC	BIC	χ^2 , df, p	(AIC _{m1} -AIC _{m2})/2
	.768	10541.55	10683.45	47.53, 20, .0005	Model 2 is 1.47 more likely
	.793	10538.61	10680.51	44.59, 20, .001	
ances of congruent measures in fathers and mothers					
	.854	10530.35	10650.18	50.34, 27, .004	5.75, 7, > .50
	.876	10526.40	10639.92	50.38, 29, .008	0.04, 2, > .95
	.879	10525.61	10635.98	51.60, 30, .008	1.22, 1, > .25
	.861	10528.54	10635.76	56.53, 31, .003	4.93, 1, < .05
	.883	10524.47	10631.68	52.45, 31, .009	0.85, 1, > .25
	.852	10530.09	10634.15	60.08, 32, .002	7.63, 1, < .01
	.910	10517.70	10612.30	53.68, 35, .023	1.23, 4, > .75
	.916	10515.96	10607.41	53.94, 36, .028	0.26, 1, > .50
	.918	10514.98	10603.27	54.96, 37, .029	1.02, 1, > .25
	.925	10513.01	10598.15	54.99, 38, .037	0.03, 1, > .75
	.915	10514.80	10596.79	59.78, 39, .022	4.79, 1, < .05
	.967	10504.30	10592.59	44.28, 37, .192	10.71, 1, < .001
	.995	10499.15	10590.59	37.13, 36, .417	7.15, 1, < .01

DISCUSSION

The current study indicates that fathers, and especially mothers, reported more parenting stress towards ASD only, ADHD only and ASD+ADHD affected than unaffected offspring and norm data. Fathers and mothers of ASD families reported more depressive symptoms than ADHD and ASD+ADHD families and the norm data. Parents of ASD+ADHD families reported more depressive symptoms than ADHD families and the norm data. Positive correlations between spouses were found regarding symptoms and parenting stress. Paternal *ASD* and maternal *ADHD* symptoms, related directly to increased parenting stress. In both fathers and mothers, ADHD (not ASD) symptoms related to depressive symptoms and in turn to parenting stress. Interestingly, maternal ASD symptoms related to paternal parenting stress and in return to depressive symptoms in mothers.

In accordance with our expectations, no differences were found for parenting stress between ASD only and ADHD only families (Theule et al., 2010). However, in contrast to our expectations, the presence of comorbid ADHD pathology in offspring with ASD did not have an increased negative effect on parenting stress. It seems that, in accordance with previous literature, parenting stress may result from other factors common to having a child with any clinical diagnosis such as increased costs for health care or constraints on leisure time (Theule et al., 2010). The increased levels of parenting stress regarding affected children replicates a recent meta-analysis (Hayes & Watson, 2013) and indicates raising a child with ASD and/or ADHD puts a heavy burden on the parents, especially on mothers. An explanation for this finding may be that mothers are usually more involved in day-to-day care activities with the affected child than fathers (Herring et al., 2006; Little, 2002). Our findings also suggest that parenting stress levels generally do not relate to all children within the family, as parenting stress levels were mostly normal regarding unaffected offspring. Nevertheless, in line with previous studies depressive symptoms were equally elevated in both fathers and mothers, and in turn influenced the experiencing of parenting stress (Sterling et al., 2008; Theule et al., 2010). Especially parents of families with ASD (with or without ADHD) reported more depressed symptoms than parents of offspring with ADHD only. It is possible that depressive symptoms were higher in parents of children with ASD because ASD is a life-time diagnosis whereas ADHD is outgrown (or at least is often associated with symptom improvement) in a number of cases (Cherkasova, Pondé & Hechtman, 2012).

A novel finding was the influence of parental ASD/ADHD symptoms on one's own depressive symptoms and parenting stress as well as on the spouses' depressive symptoms and parenting stress. Apparently, parents with ASD/ ADHD symptoms have more problems or less parenting skills to cope with the behavior of their child and as a consequence are reporting more parenting stress and depressive

symptoms. The explanation for the differential effect of paternal ASD symptoms influencing fathers' parental stress, yet maternal ADHD symptoms influencing mothers' parental stress, may possibly be sought in the different roles and functions both parents fulfill within the family. Oversimplified, mothers are typically more involved in organizing the household, making sure all children arrive on time at school, and in ensuring needed groceries are bought (Craig, 2006). A higher level of maternal ADHD symptoms may significantly hinder these aspects (Mokrova, O'Brien, Calkins, & Keane, 2011). Fathers are usually somewhat less involved in these organizing and structuring tasks but more involved in play, talking, educational and recreational activities (Craig, 2006); higher levels of ASD symptoms may then work counterproductively. In any case, higher parental levels of either ASD or ADHD symptoms appear to have a negative impact on the family environment by directly (a) influencing the level of depressive symptoms (paternal and maternal ADHD), (b) influencing parenting stress (paternal ASD, maternal ADHD) or (c) influencing the parenting stress of the spouse (maternal ASD).

Our findings should be interpreted in the context of several limitations. First, due to methodological issues parenting stress was only completed for the affected children in the *BOA*-cohort. It is possible that this lack of an unaffected sibling group may have influenced the results of the model fitting. However, because most effects on experienced stress were comparable regarding affected and unaffected offspring and group comparisons indicated that parental stress scores were largely similar for the three types of families, we do not believe this has strongly influenced the outcome of the model fitting. Nevertheless, further research with data of unaffected siblings of ASD only families is recommended. A second limitation is that parental ASD symptoms were assessed with self or spouse report, depending on the cohort in which they participated. However, we found no moderating effect of type of report on the results in the structural modeling analyses, suggesting results were relatively robust. A third limitation is that, besides the influence of child pathology and (the interdependence of) parental symptoms, parenting stress may also arise from family socio-demographic status (race/ ethnicity), social economic status, number of children, birth order and parental marital status (Seltzer et al., 2004; Tomeny et al., 2012). The current study was not designed to incorporate these factors and should be replicated with the inclusion of the (possibly moderating effects of) above factors to clarify the influence of these factors on parenting stress in relation to parent and child ASD/ ADHD symptoms. A fourth limitation is that we omitted gender from the analyses since overall no effect of gender on parenting stress was found and only a small number of affected girls were included in this study. Nevertheless, given the fact that other studies found an effect of gender on parenting stress (Seltzer et al., 2004; Theule et al., 2010; Tomeny et al., 2012), repeating our analyses with a larger group of affected girls is recommended. A fifth limitation is that in this study only

current self-reported symptoms of parents were used. Hypothetically, it can't be ruled out that parental self-report may be influenced by having a child with a similar diagnosis. Using more objective assessments of parental symptoms, based on diagnostic interviews and/or observations, may be recommended in future studies.

In conclusion, the results highlight the increased burden on parents rearing a child with ASD and/or ADHD. Clinicians treating children with ASD and/or ASD should be using a systems approach and be aware that (sub)threshold symptoms of ASD and ADHD of parents may act as a catalyst in increasing one's own and spouses' parenting stress and depressive feelings, which in turn results in a suboptimal family environment for the already vulnerable children. These parents may benefit from treatment targeting parenting skills (for example, coping with difficult behavior, seeking social support, reframing and understanding the behavior of the child), to enhance the resilience of parents and decrease parenting stress and depressive feelings (Walsh, 2002, 2003).

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General discussion

GENERAL DISCUSSION

Background and general aims of this study

ASD and ADHD are highly heritable disorders that often co-occur in the same child, and put a large strain on parenting skills of parents. Despite the fact that ASD and ADHD often co-occur, these disorders have been studied for the last decades in isolation from each other, leaving open questions about the influence of the combined effect of ASD and ADHD on family functioning. Moreover, because of the familial-genetic loadings of these disorders, children with ASD or ADHD are more likely to have one or two parents with subthreshold or above threshold symptoms of ASD or ADHD. These parental ASD or ADHD symptoms may affect parenting skills, and in this way create a suboptimal environment for these already vulnerable children. Although previous studies provide evidence that high levels of parental ASD or ADHD interfere with family functioning, parental symptoms and the impact on family functioning for long remained a very sensitive and neglected area of research since in the 1940's the cause of autism was attributed to a lack of maternal warmth, which resulted in blaming the parents for their children's autism. In addition, a particular combination between child and parent symptoms (for example, child ASD and parental ADHD or child ADHD and parental ADHD) may results in a more suboptimal family functioning since a poor match between child and parental characteristics may influence family functioning. However, there is a lack of studies examining the influence of the combination of parent and child symptoms on family functioning. Therefore, the main aim of this thesis was to disentangle the effects of child symptoms, parental symptoms and the reciprocal relationships between these factors on family functioning.

General discussion of the main findings

Association between child and parental ASD and ADHD symptoms

In *Chapter 2* we were interested in (cross-)assortative mating (one's tendency to [not randomly] choose a partner that is either similar [for example, father ASD and mother ASD] or dissimilar [for example father ASD and mother ADHD] from oneself) and parent-of-origin effects (whether parents differ in the relative quantity of risk factors they transmit to the offspring) regarding ASD and ADHD symptoms. It was hypothesized that the frequent co-occurrence of both disorders could be partly related to (cross-)assortative mating for ASD and ADHD in parents. Results revealed that (cross-)assortative mating is not an explanation for the frequent co-occurrence of ASD and ADHD within children and families since we found very small or no correlations between paternal and maternal ASD/ ADHD symptoms (*Chapter 2 and 6*). However, we found an association between child and parental ASD and ADHD symptoms. More specifically, we found that parental ASD and ADHD symptoms are

related to similar ASD and ADHD symptoms in their offspring. In accordance with previous studies, ASD symptoms in fathers and mothers were equally strongly transmitted to their offspring (Goos, Ezzatian, & Schachar, 2007; Kim et al., 2007). However, our results also indicate that the transmission of ADHD appears to be dependent upon the sex of the parent with girls being more susceptible for the inheritance of maternal ADHD. Although previous literature has supported the selective effect of ADHD transmission towards female offspring (Goos et al., 2007; Hawi et al., 2005), conflicting reports about the role of paternal ADHD and maternal ADHD transmission have been also reported. In other words, there is evidence that only paternal ADHD were related to ADHD symptoms in offspring, but also an equally strong transmission of both paternal and maternal ADHD symptoms towards their offspring were found (Gizer, Ficks, & Waldman, 2009; Goos et al., 2007; Hawi et al., 2010; Kent et al., 2005). A possible explanation for the mixed findings is that parent-of-origin effects were influenced by mechanisms that takes place in the utero environment such as genomic imprinting (a particular allele of a gene is only active when it originates from the father or the mother) and prenatal maternal effects (physiological or hormonal factors) (Wang, Liu, Zhang, Aragam, & Pan, 2012; Weinberg, 1999) and may influence parent-of-origin effects. This may also have influenced our results regarding the cross parent-of-origin effects (dissimilarity between parents symptoms) since only maternal, but not paternal, ADHD symptoms were predictive for offspring ASD pathology. However, it is also possible that the risk factors of ASD may overlap more with the risk factor of ADHD, than vice versa, but more research in this area is needed.

Family functioning in families with children with ASD and/or ADHD

The differential effect of ASD and ADHD child pathology on family functioning

In contrast to our expectation that ASD and ADHD in children may have a different impact on family functioning, in this study no evidence is found for differences between families of children with ASD, ADHD and ASD+ADHD pathology (*Chapter 3, 4, 5 and 6*). In accordance with a recent study (Dyches, Smith, Korth, Roper, & Mandelco, 2012), measures of family functioning (family climate, parenting styles, parent-child interaction and parenting stress) are overall comparable for ASD and ADHD children, indicating no different impact of the type of child pathology on family functioning. Interestingly, even the additive effect of ADHD symptoms on ASD seems to have no different effect on family functioning. It is possible that parents do not need to adapt their parenting behaviors when raising a child with ASD compared to a child with ADHD. For example, children with ASD or ADHD may benefit all from an environment with a large amount of organization and structure, and this highly organized and structured environment may also be sufficient for children with ASD and comorbid ADHD symptoms. Another possibility is that the clinical overlap

between the two disorders may be the reason why in this study no differences are found between the two disorders. In clinical practice it is difficult to disentangle both disorders from each other which may lead to a proportion of children that received a diagnosis of ASD, but throughout development are alternatively diagnosed with ADHD, or vice versa (Fein, Dixon, Paul, & Levin, 2005). Although, no differences were found between families of children with ASD and/ or ADHD pathology, it is possible that the individual symptom domains of the disorders such as repetitive and restricted behavior and interest (ASD symptom) do have a different effect on family functioning compared to attention problems (ADHD symptom) (Hayes & Watson, 2013). However, more research is needed to clarify this issue. In any case, it seems that families with ASD, ADHD and ASD+ADHD in this study are comparable to each other regarding family functioning implying that the type of disorder does not cause differences in family functioning in our study.

The influence of child ASD and ADHD symptoms on family functioning

In *Chapter 3, 4, 5* and *6* we examined the effect of child ASD, ADHD and ASD+ADHD pathology on family functioning. It appears that in families of children with ASD and/ or ADHD pathology, (a) parents tend to use a more permissive parenting style (high on responsiveness, low control) regarding their affected children (*Chapter 4*) and a less authoritative and authoritarian parenting style towards affected and unaffected children, (b) affected children report less parental conflict resolution skills (refers to the quality of preventing and solving problems) and acceptance than their unaffected siblings, but unaffected children report less parental conflict resolution skills than the norm (*Chapter 5*), (c) parenting stress in parents is related and both parents report more parenting stress than parents of typically developing children towards the unaffected and unaffected child (*Chapter 6*), and (d) parents report a less optimal family climate when there are multiple affected children in a family (*Chapter 3*) (see Figure 1). Above results support previous findings that parenting a child with pathology put a large strain on parenting skills of parents (Bekhet, Johnston, & Zauszniewski, 2012; Harpin, 2005; Herring et al., 2006; Rutgers et al., 2007). This is cause for concern since all of these factors separately have been associated with an increased risk for developmental problems and less well being in parents (see for example van IJzendoorn et al., 2007; Reed, Osborne, McHugh, & Saunders, 2008; Wachtel & Carter, 2008).

Despite the increased burden for parents to raise a child with pathology, mothers and fathers of children with ASD and/ or ADHD pathology report a positive family climate (cohesion, expressiveness, conflict, control and organization) in their families (*Chapter 3*). In other words, there are also positive elements in the family climate in families of ASD and/ or ADHD pathology. It is possible that what we consider as negative family functioning is just a method of parents to cope with the disorder of

their child. Parents of children with ASD/ ADHD may attribute most of the child's misbehavior to the ASD/ ADHD symptoms, rather than to their child's personality and temperament (*a positive coping strategy*) (Hastings et al., 2005; Montes & Halterman, 2007; Whittingham, Sofronoff, Sheffield, & Sanders, 2008; Wong, Shui-fong Lam, Leung, Ho, & Au-Yeung, 2013). In addition, parents of children with ASD/ADHD also seem to use *planning* as a coping strategy (Wong et al., 2013) since we find normal scores of organization and control in families of children with ASD and/ or ADHD pathology. However, coping strategies of parents of children with ASD and/ or ADHD pathology are beyond the scope of this thesis and further research is necessary to compare families with a positive family climate with families with less positive family climate to observe the possible protective mechanism in families with a positive family climate. Nevertheless, coping strategies may both act as protective mechanisms and may be incorporated into family treatment of families of children with ASD and/ or ADHD pathology.

Also beyond the scope of this thesis, but important to note, is that besides coping strategies of parents other factors may also have a positive or negative influence on family climate such as socioeconomic status (SES), the amount of social support, work and marital status (Belsky, 1984; Bradley & Corwijn, 2002; Schemerhorn et al., 2012; Williamson & Johnston, 2013). For example, previous literature provides evidence for the fact that divorced parents and/ or low SES families are at greater risk for a more suboptimal family climate (Bradley & Corwijn, 2002; Kurdek & Fine, 1993). In line with this, the finding of a positive family climate in families with ASD and/ or ADHD pathology may also be explained by the fact that our study consists of families with two biological parents and with moderate to high SES. This highlighted the fact that, beside coping strategies, other factors must be considered when treating families with ASD and/ or ADHD pathology. Since affected children are feeling less accepted than their unaffected siblings and these feelings may be a strong predictor of poorer social and emotional outcomes in children (Brown & Jenkins, 2012), family treatment should also incorporate individual feelings of each family member.

The influence of parental ASD or ADHD symptoms on family functioning

In *Chapter 3, 4, 5 and 6* we examined the influence of parental ASD and ADHD symptoms on family functioning. Our studies show that only a small proportion of the parents score above the ASD and ADHD clinical cut off, indicating that parents of children with ASD and/ or ADHD pathology overall had relatively normal levels of ASD and/ or ADHD symptoms. However, our findings are relevant in showing that, across the whole ASD and ADHD continuum (high and low levels of symptoms), a relationship between parental ASD and ADHD symptoms and family functioning is present. The results point out that both paternal and maternal ASD were negatively associated with parent-child relationships (cohesion, expressiveness and conflict [*Chapter 3*])

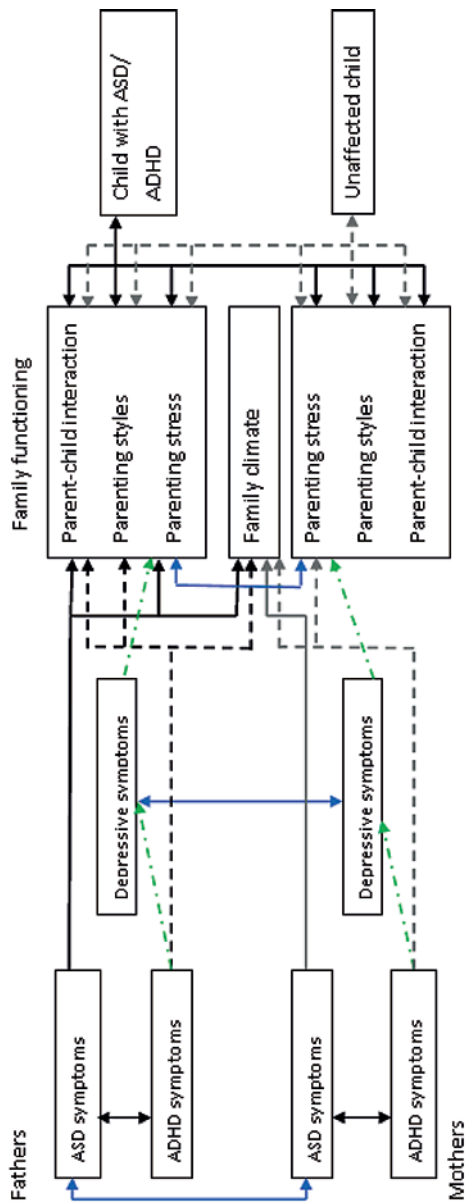


Figure 1 Model linking parental symptoms and child diagnosis with family functioning.

One way arrows represent the impact of one variable on another. Double-headed arrows represent correlations between variables. Black lines represent fathers' ASD symptoms and black dashed lines represent fathers' ADHD symptoms. Grey lines represent mothers' ASD symptoms and grey dashed lines represent mothers' ADHD symptoms. Arrows between parents in blue lines, Green arrows indicate the relation between ADHD symptoms, depressive symptoms and parenting stress.

suggesting that parents with high ASD symptoms have difficulties with the expression of affection towards their offspring and experience more conflict situations due to the fact that they may have more rigid and poorer social skills. In addition, both maternal and paternal ADHD (not ASD) symptoms on parenting stress was mediated by depressive symptoms, that is, a higher level of ADHD symptoms was related to more depressive symptoms, which in turn was related to more parenting stress. Previous literature has suggested that parents with more social awareness are more likely to develop depressive symptoms because they are more aware of their failures in parenting (Barhill & Smith Myles, 2001; Wing, 1981). It is not difficult to imagine that parents with high ADHD symptoms have more social awareness than parents with high ASD symptoms.

Also selective negative effects of paternal or maternal ASD or ADHD symptoms on family functioning were found. Paternal ASD, but not maternal ASD, symptoms were negatively related to parent- child interactions (warmth, comfort and protection [*Chapter 5*]) and parenting stress (*Chapter 6*). Paternal ADHD symptoms were negatively related to family relationships (cohesion, expressiveness and conflict [*Chapter 3*]), parenting styles (*Chapter 4*), parent- child interactions (*Chapter 5*) and depressive symptoms (*Chapter 6*) whereas maternal ADHD symptoms were negatively related to family structure (organization and control [*Chapter 3*]) parenting stress and depressive symptoms (*Chapter 6*). This selective effect of paternal and maternal ADHD on the different aspects of family functioning may be explained by the different roles that parents fulfill in the family. In other words, fathers are usually more involved in play, talking, educational and recreational activities (Craig, 2006; Parke, 2002) and ASD symptoms in fathers may influence the quality of these parent-child interactions. Moreover, since recent literature report that child ADHD symptoms have a profound influence on father- child interactions (Chang, Chiu, Wu, & Gau, 2013) it is not difficult to imagine that ADHD symptoms in fathers have also a negative influence on father- child interactions. In contrast, mothers are more involved in the more practical day-to-day care and nurturing activities (organizing the household, structuring play activities of the children, cooking meals) (Craig, 2006; Parke, 2002) and ADHD symptoms may influence the quality of these activities (Mokrova, O'Brien, Calkins, & Keane, 2011). It may be expected that maternal ASD symptoms may also have a considerable influence on these activities, but results suggest that mothers perhaps need less social skills to fulfill their roles as practical day-to-day caregiver or, mothers may have more skills to compensate the influence of ASD symptoms on family functioning (Attwood, 2007; Lai et al., 2011). It is also possible that mothers with ASD symptoms may have limited self awareness and as a consequence reported less ASD symptoms and more positive family functioning (Berthoz & Hill, 2005; Kooij et al., 2008; Mazefsky et al. 2011). However, this contrasts with the observation of moderate to substantial spouse-correlations regarding

various measures of family functioning. Given the possible negative influence of parental symptoms on family functioning it is important to identify subthreshold or above threshold symptoms of ASD or ADHD in parents and related problems in family functioning in families of children with ASD and/ or ADHD pathology.

The reciprocal relation between child and parental symptoms and the influence on family functioning

The results indicate that some of the findings of this thesis (less favorable parenting styles, conflict resolution skills, parenting stress) are found for both affected children and unaffected children. Apparently, the strategies of parents to cope with the burden of an affected child influence the family as a whole, resulting in the same overall approach of parents towards their affected and unaffected offspring. The same approach towards both affected and unaffected children may not be so negative since variation in parenting (differential parenting) towards children is associated with poorer social and emotional outcomes (Brown & Jenkins, 2012; Solmeyer, Killoren, McHale, & Updegraff, 2011). Unexpectedly, we also found some evidence for the effects of a mismatch between parents with ASD/ ADHD symptoms and their unaffected offspring. Parents with a higher degree of ASD/ ADHD symptoms tend to use a more permissive parenting style towards their unaffected children compared to their affected children and norm data (*Chapter 4*) which implies that particularly unaffected offspring seem at risk to receive a more permissive parenting style when their parents have an increased number of ASD/ADHD symptoms. Despite this, no other evidence is found for a specific match or mismatch between parent and offspring in our study. This suggests that family functioning is for the greater part not influenced by a particular combination between parent and child symptoms.

The influence of spouse symptoms on family functioning

In *Chapter 6* we explore the role of own and spouse ASD, ADHD and depressive symptoms in parenting stress. In accordance with several other studies, depressive symptoms and parenting stress in fathers are related towards similar symptoms in mothers, and vice versa (*Chapter 6*) (Hastings, 2003; Hastings et al., 2005; Luoma et al., 2013; Roach, Orsmond, & Barratt, 1999). suggesting that the well-being of one spouse depends on the well being of the other spouse. This is also supported by the interesting finding that maternal ASD symptoms are related to parenting stress in fathers and back to depressive symptoms in mothers. In other words, the symptoms of a spouse may have negative consequences for the other spouse because of the additional caretaking burden for the other spouse (Barling, MacEwen, & Kelloway, 1994) and the lack of parent support (Hastings, 2003). However, the interdependence of parental depressive symptoms and parenting stress in families of children with ASD and/ or ADHD pathology in this study was not at the expense of a positive family

climate or the amount of warmth, comfort and protection in these families. This could be explained by the fact that parents of children with ASD and/ or ADHD pathology may have a supportive relationship with their partner, which may be a protective factor against the negative effects of the relation between spouses' symptoms on family functioning (Armstrong, Birnie- Lefcovitch, & Ungar, 2005; Snowdon, Cameron, & Dunham, 1994). However, it is also possible that sample bias explains our findings since our sample consists of families with two biological parents with mainly a moderate to high SES; two protective factors regarding family climate (Bradley & Corwijn, 2002; Kurdek & Fine, 1993). It could also be that the same coping strategies that parents use to manage the burden of a child with a disability, were used to cope with the burden of spouse symptoms, or perhaps parents with high levels of symptoms use compensatory strategies to reduce the impact of their symptoms (Williamson & Johnston, 2013). Nevertheless, since increased depressive symptoms and parenting stress were found in parents of children with ASD and/ or ADHD pathology and these symptoms may be increased by spouses symptoms, it is importance to examine both paternal and maternal symptoms when examining the family functioning of families of children with ASD and/ or ADHD pathology.

Clinical implications

In the field of child and adolescent psychiatry the co-occurrence of parental and child psychiatric symptoms (specifically ASD and/or ADHD symptoms) is a common phenomenon. The case report of Benjamin (see general introduction) is an example of a family of the BOA-study recruited at the Karakter Child and Adolescent Psychiatry University Centre that illustrates the impact on family functioning of a child having an ASD and his mother ADHD. The high occurrence of ASD and/ or ADHD in parents of children with ASD (with/ without ADHD) and the influence of the combination of impairments on the family requires a life span and family perspective to assessment, diagnosis and intervention. Broadening the clinician's focus on both child behaviors and behaviors of parents and siblings probably leads to more efficient and effective assessments programs than separating children's and adult's trajectories. This requires that each family member should be routinely screened for (subthreshold) psychiatric symptoms, e.g. depression, ASD and ADHD. The proposed screening of all family members should be incorporated into the regular services (assessment and treatment) of specialized centers for child- and adolescent- as well as adult psychiatry, and calls for a close collaboration between centers (Karst & Vaughan Van Hecke, 2012). Family members being considered at risk after screening should receive further diagnostic evaluations completed by standard assessment of family functioning including parent-child interactions, parenting stress and parental coping strategies. Based on this thesis family based interventions are also recommended. These interventions should take into account the fact that, although a positive family

climate and warm, accepting and protective family environment were found in families of children with ASD and/ or ADHD pathology, affected and unaffected children may grow up in an environment characterized by a less optimal parenting style, less parental conflict resolution skills, less acceptance towards affected children and more parenting stress.

Limitations and directions for further research

This study gives important insights in the effects of child symptoms, parental symptoms, and the reciprocal relationships between these effects on family functioning, while also providing directions for further research. First, replication of our findings with more objective measurements besides parent and child reports of the family functioning (for example home observations) and the use of more informants reporting on the ASD and ADHD symptoms of parents and children is recommended.

Second, in our study we corrected for the age differences between affected children and their unaffected siblings by selecting one unaffected sibling closest in age to the affected child. The absolute age difference between siblings was included as covariate in the analyses and revealed no effect of sibling age differences on family functioning. However, it may still be the case that family functioning differs in families with younger and older sibling pairs since age has a significant effect on family functioning. There is evidence that parents with preschool children are more overwhelmed by taking care of their children and have more parenting stress, family conflict and less positive parent- child interactions than parents of older children (Scharlach, 2001). Moreover, older children may spend less time with their parents than younger children so the quality of parent- child relationships may differ in families with younger versus older children (Milkie, Bierman, & Schieman, 2008; Yeung, Sandberg, Davis-Kean, & Hofferth, 2001). Third, it is interesting to examine the possible effects of the symptom domains of parents and children on family functioning since these may have a different effect on family functioning. For example, it appears that parental inattentive symptoms are more strongly associated with parenting impairments than hyperactive/ impulsive symptoms (Johnston, Mash, Miller, & Ninowski, 2012). Other studies have found that the inattentive (not the hyperactive/ impulsive) symptoms of mothers are strongly related to more inconsistent discipline and less positive involvement (Chen & C., 2007), whereas hyperactive/ impulsive (and not inattentive) symptoms are associated with greater over-reactivity and lax parenting (Griggs & Mikami, 2011). Moreover, since the literature also provides evidence for the differential effect of the various ASD and ADHD symptom domains of children on family functioning (Hayes & Watson, 2013), further research in this area is needed. Fourth, a longitudinal study can capture the dynamic process of the family functioning over time. For example, it could provide important insights into the

possible outcomes of a suboptimal family functioning regarding affected and unaffected children of ASD and/ or ADHD families. Fifth, given evidence that the level of parental warmth and control differs across cultures (Deater-Deckard et al., 2011), it will be important to examine whether the outcomes of this study are only attributable to families of Caucasian descent or also to other cultures. In line with this, it is also unclear to what extent the results are equally applicable to low SES families or to families with only one biological parent.

In the case of Benjamin's family...

To have better control over her life, the ADHD symptoms of mother were treated with medication. In addition, father was encouraged to participate actively in household tasks and in care activities to protect mother from becoming overwhelmed. Both father and mother received specific guidelines to cope with the behavior of Benjamin. Although there are still situations that are difficult, they now feel that they have more techniques to cope with the rigid behavior of their son. Because they communicate more about their approach towards Benjamin, both parents are satisfied by the role of their partner in handling the difficult behavior of Benjamin. Both father and mother are encouraged to give special attention to Amy and spent individual time with her. As results of above interventions, both father and mother reported that the situation is much improved but they still feel that they must overcome many barriers regarding the behavior of Benjamin, where they need help with.

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NEDERLANDSE SAMENVATTING

Inleiding

Dit proefschrift richt zich op het functioneren van gezinnen met kinderen met een Autisme Spectrum Stoornis (ASS) en/of een Attention Deficit Hyperactivity Disorder (ADHD). ASS wordt gekenmerkt door beperkingen op het gebied van de sociale interactie en communicatie, alsmede door beperkte repetitieve en stereotiepe gedragingen en interesses.

ADHD wordt gekenmerkt door problemen op het gebied van aandacht, impuls-beheersing en hyperactiviteit. Zowel ASS en ADHD zijn erfelijke stoornissen die vaak tegelijkertijd voorkomen bij een kind en/of gezin. Deze stoornissen kunnen het gezinsfunctioneren negatief beïnvloeden. Het gezinsfunctioneren is een overkoepelende term voor aspecten die belangrijk zijn in het met elkaar omgaan in gezinnen. Deze aspecten omvatten gezinsstructuur, organisatie, communicatie, rollen, affectieve responsiviteit en controle van gedrag. Belangrijk is dat gezinsfunctioneren vanuit een systeemtheoretisch kader wordt gezien. Hierbij wordt van het gegeven uitgegaan dat leden van een gezin niet begrepen kunnen worden in isolatie van elkaar. Wederzijdse communicatie in het gezin vormt een belangrijk element in de ontwikkeling van het gedrag van individuele gezinsleden. Dit betekent dat de aanwezigheid van ASS en/of ADHD symptomen bij kinderen van invloed kan zijn op de kwaliteit van het gezinsfunctioneren. Te denken valt dan aan problematische ouder- en kindrelaties, opvoedstress en gezinsconflicten. Ondanks het feit dat ASS en ADHD vaak samen voorkomen bij kinderen en/of families, zijn ze in voorgaande studies voornamelijk los van elkaar onderzocht. Hierdoor bestaat onduidelijkheid over de gecombineerde effecten van ASS en ADHD op het gezinsfunctioneren.

Naast de invloed van ASS en ADHD symptomen bij het kind op het gezinsfunctioneren, is het belangrijk om rekening te houden met het gegeven dat ouders van kinderen met ASS en/of ADHD ook zelf last kunnen hebben van symptomen van ASS en/of ADHD, en dat die symptomen op hun beurt van invloed kunnen zijn op het gezinsfunctioneren. Hoewel er in de literatuur aanwijzingen zijn dat ouderlijke ASS of ADHD symptomen kunnen interfereren met een effectieve opvoeding, ontbreekt hiervoor het sluitend bewijs. Een negatief gezinsfunctioneren kan verder ook het gevolg zijn van een interactie tussen ouder en kind symptomen. Dit betekent dat het effect van de symptomen van een kind op het gezinsfunctioneren, afhangt van het gegeven of één of beide ouders ook symptomen heeft, en omgekeerd. Ouder en kind symptomen zijn echter vaak apart van elkaar onderzocht. Hierdoor is het nog onduidelijk wat de gecombineerde effecten van ouder en kind symptomen zijn op het gezinsfunctioneren.

Tot slot kan het gezinsfunctioneren verder gecompliceerd worden doordat de mentale gezondheid en/of de symptomen van één van de ouders, die van de andere

ouder kan beïnvloeden. Het kan zijn dat een ouder met ASS symptomen een partner aantrekt met ADHD symptomen of omgekeerd. Het is eveneens mogelijk dat een ouder met ADHD symptomen een partner aantrekt met ook ADHD symptomen (selectieve partnerkeuze). Een andere mogelijkheid is dat – door bijvoorbeeld gebrek aan steun van de ouder met symptomen - depressieve symptomen en/of opvoedstress van de ene ouder dezelfde symptomen van depressie of opvoedstress teweegbrengen bij de andere ouder.

Uit bovenstaande blijkt dat er nog veel onduidelijk is over de (wederkerige) invloed van kind- en oudersymptomen op het gezinsfunctioneren. De doelstelling van dit proefschrift is om te onderzoeken wat de afzonderlijke en gecombineerde effecten zijn van kindsymptomen, ouderlijke symptomen en de wederkerige relatie tussen deze factoren op het gezinsfunctioneren. Ook is onderzocht of de effecten van ADHD en van ASS symptomen bij kind en/of ouder op het gezinsfunctioneren van elkaar verschillen, of juist gelijksoortig zijn.

Dataverzameling

Gezinnen werden gerekruteerd uit twee genetica projecten (Biologische Oorzaken van Autisme [BOA] en de Internationale Multicentra ADHD Genen studie [IMAGE]. De BOA en IMAGE projecten hadden beide als doel om de genetische, biochemische en cognitieve oorzaken van ASS en ADHD te onderzoeken, alsmede om de overlap tussen ASS en ADHD op deze niveaus te bestuderen. Voorts werd het functioneren van gezinnen met kinderen met ASS en ADHD symptomen onderzocht. Bij het bepalen van de geschiktheid van een gezin werden de volgende criteria gehanteerd:

- a. Het gezin bestond uit tenminste één kind (tussen 2 en 20 jaar oud) met een klinische diagnose van ASS (met/zonder ADHD) (BOA), of tenminste één kind (tussen de 5-19 jaar oud) met een klinische diagnose van ADHD (gecombineerde subtype: inattentieve en hyperactieve/ impulsieve symptomen) (IMAGE).
- b. Het gezin bestond uit tenminste één biologisch broertje of zusje (ongeacht mogelijke ASS of ADHD status).
- c. Het gezin bestond uit tenminste één biologische ouder.

Voor het huidige onderzoek werden alleen gezinnen geïncludeerd waarin twee biologische ouders samenleven. Alle gezinnen moesten van Kaukasische afkomst zijn. Gezinnen werden geëxcludeerd als bij het kind sprake was van een $IQ \leq 60$, specifieke leer- of taalstoornissen, een diagnose van epilepsie, een diagnose van een bepaalde genetische of niet-genetische oorzaak van ASS (Rett's syndroom, fragile-X-syndroom) of ADHD, of een genetische ziekte zoals het Down syndroom. Comorbide DSM-IV aandoeningen werden niet uitgesloten, met uitzondering van een autistische stoornis in de IMAGE studie (kinderen met Asperger syndroom en PDD-NOS mochten wel meedoen).

Overzicht van de belangrijkste bevindingen

De associatie tussen ouder en kind symptomen van ASS en ADHD

In *hoofdstuk 2* waren we geïnteresseerd in selectieve partnerkeuze (iemand's neiging om [niet willekeurig] een partner te kiezen die hetzelfde of juist anders is). Ook hebben we ons gericht op de vraag of het uitmaakt of de vader of de moeder degene is met de ADHD en/of ASS symptomen, en het risico op ADHD en/of ASS bij de kinderen (zogenoemde *parent-of- origin effects*). De mogelijkheid werd onderzocht of het frequent samen voorkomen van beide stoornissen -naast de genetische overlap tussen ASD en ADHD- deels te wijten is aan selectieve partnerkeuze van ASS en ADHD bij ouders (een vader/moeder met veel ASS symptomen zoekt een partner uit met veel ADHD symptomen of andersom).

Uit de resultaten bleek echter dat selectieve partnerkeuze geen verklaring is voor het frequent voorkomen van ASS en ADHD bij kinderen en gezinnen. Voorts bleek wel dat ASS en ADHD symptomen van ouders voorspellend zijn voor soortgelijke symptomen in hun kinderen. We hebben ook gevonden dat het uitmaakt of vader of moeder degene is met de ADHD en/of ASS symptomen: hyperactieve- impulsieve symptomen van moeder (niet vader) waren voorspellend voor soortgelijke symptomen in dochters, maar niet bij zonen. Bij dit selectieve effect spelen mogelijk genomische imprinting (een bepaald allel van een gen is alleen actief als het afkomstig is van vader of moeder) en fysiologische of hormonale factoren een rol.

Het gezinsfunctioneren in gezinnen met kinderen met ASS en/ of ADHD

De impact van type symptomen op het gezinsfunctioneren

In tegenstelling tot onze verwachting bleken ASS en ADHD symptomen bij kinderen geen verschillende impact te hebben op het gezinsfunctioneren (*hoofdstuk 3, 4, 5 en 6*). Dit geeft aan dat het gezinsfunctioneren vergelijkbaar is voor ASS en ADHD kinderen. Interessant is echter ook dat het samengaan van ADHD symptomen bij kinderen met een diagnose ASS geen effect heeft op het gezinsfunctioneren. Het is mogelijk dat ouders hun gedrag niet hoeven aan te passen wanneer ze een kind opvoeden met ASS in vergelijking met een kind met ADHD. Met andere woorden, kinderen met ASS en ADHD kunnen beiden profiteren van een gestructureerde en georganiseerde opvoedomgeving. Deze opvoedomgeving kan ook voldoende zijn voor kinderen met ASS en comorbide ADHD problematiek. Het is tevens mogelijk dat de overlap tussen ASS en ADHD symptomen kan leiden tot deze bevindingen aangezien het in de klinische praktijk al erg lastig is om deze stoornissen uit elkaar te trekken.

De invloed van ASS en ADHD symptomen van kinderen op het gezinsfunctioneren

In *hoofdstuk 3, 4, 5 en 6* is het effect onderzocht van ASS symptomen bij het kind (met/zonder ADHD symptomen) op het gezinsfunctioneren. Hieruit blijkt dat ouders (a) de neiging hebben een suboptimale opvoedstijl te hanteren naar hun aangedane

en niet aangedane kinderen; (b) minder acceptatie tonen volgens hun aangedane kinderen; (c) minder conflictoplossende vaardigheden hebben volgens hun aangedane en niet aangedane kinderen; (d) meer opvoedstress rapporteren over hun aangedane en niet aangedane kinderen.

Omdat de individuele gezinsfactoren al worden geassocieerd met een verhoogd risico op ontwikkelingsproblemen bij het kind en mentale problemen bij ouders, is dit reden tot bezorgdheid. Ondanks het feit dat het opvoeden van een kind met symptomen veel vraagt van ouders, lijkt dit niet ten koste te gaan van een positief gezinsklimaat (de mate van samenhang tussen gezinsleden, expressiviteit, conflict, controle en organisatie). Met andere woorden, er lijken ook positieve aspecten te zijn in het gezinsfunctioneren van gezinnen met kinderen met ASS en/of ADHD symptomen. Het is mogelijk dat hetgeen wij als een negatief gezinsfunctioneren definiëren (permissieve opvoedstijl/ minder conflict oplossende vaardigheden), juist een methode is van ouders om met een kind met symptomen om te gaan. Ouders van kinderen met ASS en/of ADHD symptomen schrijven mogelijk het probleemgedrag van hun kind toe aan de ASS en/of ADHD symptomen in plaats aan de persoonlijkheid of temperament van het kind.

De invloed van ASS en ADHD symptomen van ouders op het gezinsfunctioneren

In hoofdstuk 3, 4, 5 en 6 is de invloed van ASS en ADHD symptomen van de ouders op het gezinsfunctioneren onderzocht. Resultaten geven aan dat zowel ASS symptomen van vader als moeder negatief gerelateerd waren aan ouder-kind relaties (de mate van samenhang, expressiviteit en conflicten [hoofdstuk 3]). Dit suggereert dat ouders die wat meer rigide zijn en minder sociale vaardigheden hebben, meer moeite hebben met de expressie van affectie naar hun kinderen, en meer conflictsituaties ervaren. Voorts zijn er verschillende effecten gevonden van ASS en ADHD symptomen bij ouders op het gezinsfunctioneren. Zo waren ASS symptomen bij vaders negatief gerelateerd aan ouder-kind interacties (de mate van warmte, comfort en bescherming [hoofdstuk 5]) en opvoedstress (hoofdstuk 6). ADHD symptomen van vaders waren echter negatief gerelateerd waren aan ouder-kind relaties (hoofdstuk 3), opvoedstijlen (hoofdstuk 4), ouder-kind interacties (hoofdstuk 5) en aan depressieve symptomen (hoofdstuk 6). ADHD symptomen bij moeders waren negatief gerelateerd aan de mate van structuur in gezinnen (organisatie en controle [hoofdstuk 3]), opvoedstress en depressieve symptomen (hoofdstuk 6). Dit verschillende effect van ASS en ADHD symptomen van vaders en moeders op het gezinsfunctioneren kan verklaard worden door de verschillende rollen die ouders innemen in het gezin. Met andere woorden, vaders zijn meestal meer betrokken bij activiteiten zoals spel, praten, onderwijs en recreatie. ASS symptomen bij vaders kunnen de kwaliteit van deze activiteiten beïnvloeden. Het is tevens mogelijk dat

ADHD symptomen bij vaders ook een negatieve invloed kunnen hebben op deze activiteiten, zeker gezien het feit dat ADHD symptomen van kinderen al worden geassocieerd met een verminderde vader-kind interactie. Daarentegen zijn moeders vaak meer betrokken bij de dagelijkse zorg voor kinderen (organiseren van het huishouden, het structureren van spelsituaties en het koken van maaltijden). ADHD symptomen van moeders kunnen de kwaliteit van deze dagelijkse zorg beïnvloeden. We vinden echter geen soortgelijk effect van ASS symptomen bij moeders op deze activiteiten. Dit impliceert mogelijk dat moeders beter in staat zijn om hun ASS symptomen te compenseren of dat de rol van moeders in het gezin minder van de sociale vaardigheden van moeders vraagt. Het is ook mogelijk dat moeders met ASS symptomen zich minder bewust zijn van hun ASS symptomen. Dit is echter in tegenspraak met de observatie dat we een duidelijk verband vinden tussen rapportages van vaders en moeders over het gezinsfunctioneren. Dit zou namelijk kunnen betekenen dat vaders en moeders vrijwel hetzelfde rapporteren en dat het niet zo is dat moeders zich minder bewust zijn van hun ASS symptomen. Vanwege het feit dat ASS en ADHD symptomen van ouders een negatieve invloed hebben op het gezinsfunctioneren is het belangrijk om deze symptomen en gerelateerde problemen in gezinnen van kinderen met ASS en/of ADHD symptomen in het gezinsfunctioneren te identificeren.

De combinatie tussen kind en oudersymptomen en de invloed op het gezinsfunctioneren

De resultaten van dit proefschrift geven aan dat bepaalde bevindingen (suboptimale opvoedstijlen, minder vaardigheden op het gebied van het voorkomen en oplossen van conflicten bij ouders en opvoedstress) gelden voor zowel aangedane als niet aangedane kinderen van gezinnen met ASS en/of ADHD symptomen. Hieruit blijkt dat copingstrategieën van ouders om met een aangedaan kind om te gaan, het gezinsfunctioneren als geheel beïnvloeden. Dit resulteert in dezelfde aanpak van ouders naar hun aangedane en niet aangedane kinderen. Dit hoeft niet per definitie ongunstig of ongewenst te zijn, gezien het feit dat minder variatie (en dus grotere voorspelbaarheid) in de opvoeding van kinderen leidt tot betere sociale en emotionele uitkomsten voor kinderen, in vergelijking met de uitkomsten bij kinderen die op een telkens verschillende wijze worden benaderd door hun ouders. Verrassend waren echter de bevindingen voor een mismatch tussen ouders met ASS/ADHD symptomen en hun niet aangedane kinderen. Ouders met een hoge mate van ASS en ADHD symptomen bleken de neiging te hebben om een meer permissieve opvoedstijl (hoog op responsiviteit, maar laag op controle) te gebruiken naar hun niet aangedane kinderen, in vergelijking met aangedane kinderen, en in vergelijking met ouders van zich normaal ontwikkelde kinderen (*hoofdstuk 4*). Dit impliceert dat niet aangedane kinderen een verhoogd risico lopen om een suboptimale opvoedstijl te ontvangen. Er

werd echter geen ander bewijs gevonden voor een specifieke match of mismatch tussen kind en ouder symptomen. Dit kan betekenen dat het gezinsfunctioneren voor een groot deel niet wordt beïnvloed door een specifieke combinatie van ouder en kind symptomen.

De invloed van de symptomen van een partner op het gezinsfunctioneren

In *hoofdstuk 6* werd onderzocht of de depressieve symptomen en/of opvoedstress bij de ene ouder dezelfde symptomen teweegbrengen als bij de andere ouder. Uit de resultaten blijkt dat depressieve symptomen en opvoedstress van vaders gerelateerd zijn aan depressieve symptomen en opvoedstress van moeders en omgekeerd. ASS symptomen bij/van moeders zijn gerelateerd aan opvoedstress bij/van vaders, en beide zijn weer gerelateerd aan depressieve symptomen bij moeders. Deze resultaten suggereren dat de mentale gezondheid van de ene ouder afhankelijk is van de mentale gezondheid van de andere ouder. Ondanks deze afhankelijkheid van ouder symptomen ging dit niet ten koste van een positief gezinsklimaat in gezinnen van kinderen met ASS en/of ADHD symptomen. Het is mogelijk dat ouders van deze kinderen een steunende relatie hebben. Dit kan een beschermende factor zijn tegen de negatieve effecten van de afhankelijkheid van ouder symptomen. Het is ook mogelijk dat dezelfde copingstrategieën die ouders gebruiken om met hun kind met hun symptomen om te gaan, gebruikt worden om met de symptomen van de partner om te gaan. Ondanks bovenstaande worden er wel verhoogde depressieve symptomen en opvoedstress gevonden bij ouders, en deze symptomen kunnen versterkt worden door symptomen van de andere partner. Hierdoor is het belangrijk om symptomen van beide ouders te analyseren wanneer het gezinsfunctioneren van gezinnen van kinderen met ASS en/of ADHD symptomen wordt onderzocht.

Klinische implicaties

In de kinder- en jeugdpsychiatrie is het gelijktijdig voorkomen van ouder- en kind-psychiatrische symptomen (in het bijzonder ASS en/of ADHD symptomen) een veel voorkomend verschijnsel. Het frequent voorkomen van ASS en/of ADHD bij ouders van kinderen met ASS (met/zonder ADHD), en de invloed van de combinatie van deze problemen op het gezinsfunctioneren, vereist een gezinsperspectief van diagnostiek en interventie. Het verbreden van het gezichtsveld van de professional op zowel het gedrag van het kind als het gedrag van ouders en broers en zussen, leidt tot een efficiënter en effectiever beoordeling dan wanneer er aparte trajecten voor diagnostiek en behandeling voor ouders en kinderen worden gehanteerd. Dit vereist dat elk gezinslid moet worden gescreend op (subklinische) psychiatrische symptomen, zoals depressie, ASS en ADHD. De voorgestelde screening van alle gezinsleden dient te worden opgenomen in de reguliere zorg (diagnostiek en behandeling) van gespecialiseerde centra voor kind en volwassen psychiatrie en

vraagt om een nauwe samenwerking tussen de twee centra. Gezinsleden die na screening een verhoogd risico lopen op een diagnose ASS en/of ADHD moeten verder diagnostisch onderzocht worden. Tevens is het wenselijk dat het gezinsfunctioneren, waaronder de ouder-kind interacties, opvoedstress en ouderlijke coping-strategieën, in kaart worden gebracht. Gezien de resultaten van dit onderzoek worden gezinsinterventies aanbevolen. Hierbij moet rekening gehouden worden met het feit dat aangedane en niet aangedane kinderen kunnen opgroeien in een omgeving die wordt gekenmerkt door een negatief gezinsfunctioneren. Met andere woorden, ouders van gezinnen van kinderen met ASS en/of ADHD symptomen kunnen

- (a) een minder optimale opvoedstijl hanteren;
- (b) minder ouderlijke vaardigheden hebben voor het oplossen en voorkomen van conflicten;
- (c) minder in staat zijn om acceptatie naar aangedane kinderen te laten zien;
- (d) meer last hebben van opvoedstress.

Deze aspecten zullen in de behandeling mee moeten worden genomen. Organisatorisch kan een en ander het best gerealiseerd worden in zogenaamde gezinspoliklinieken waarin kinder- en jeugdpsychiatrie en volwassenpsychiatrie samenwerken.

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*You raise me up, so I can stand on mountains
You raise me up, to walk on stormy seas
I am strong, when I am on your shoulders
You raise me up... to more than I can be.
Bron: Brendan Graham, Secret garden*

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'Cause you'll be in my heart

Yes, you'll be in my heart

From this day on

Now and forever more

Bron: You'll Be In My Heart, Phil Collins

Kusje op je neus...x

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Margo Schrieken, Janne Visser, Iris Oosterling, **Daphne J van Steijn**, Danielle Bons, Jos Draaisma, Rutger-Jan van der Gaag, Jan K Buitelaar, R Donders, & Nanda NJ Rommelse, (2012). Head circumference and height abnormalities in autism revisited: The role of pre- and perinatal risk factors. *European Child & Adolescent Psychiatry*, *22(1)*:35-43.

CURRICULUM VITAE- NEDERLANDS

Daphne Johanna van Steijn werd op 12 juli 1979 geboren te Nijkerk. Het VBO diploma verzorging werd behaald in 1995 en de MBO diploma Sociaal Pedagogisch Werk (SPW) in 1998. Vervolgens studeerde zij Sociaal Pedagogische Hulpverlening aan de Hogeschool van Utrecht, waar ze stage liep als pedagogisch medewerkster in het voormalig Lorentz Ziekenhuis Zeist. In 2001 startte ze met de opleiding Pedagogiek aan de Universiteit van Utrecht. Haar wetenschappelijke scriptie getiteld 'Temperament, hechting en risicofactoren: factoren die samenhangen met externaliserend probleemgedrag bij kinderen van 21 maanden?' voerde ze uit bij de afdeling Kinder- en jeugdpsychiatrie van het UMC Utrecht. Tijdens haar studie werkte ze bij een logeershuis voor verstandelijk gehandicapten als gediplomeerd begeleidster. Haar stage heeft ze uitgevoerd op Vosseveld, een kinderpsychiatrische buitenkliniek van het UMC Utrecht voor kinderen met oppositionele gedragsproblemen en/of anti sociale gedragstoornis. In 2004 behaalde ze haar master diploma pedagogiek. Hierna begon ze bij MEE, een organisatie voor mensen met een beperking, als psychodiagnostisch medewerkster en verrichtte ze tevens projectwerkzaamheden bij Karakter kinder- en jeugdpsychiatrie. Ze coördineerde onder andere de uitgave van de ESAT, een screeningsinstrument voor het detecteren van ASS op jonge leeftijd, waar ze nog steeds trainingen voor geeft. In december 2008 startte ze bij Karakter Kinder- en Jeugdpsychiatrie, onder leiding van prof. dr. J. K. Buitelaar, prof. dr. M.A.G. van Aken en dr. N.N.J. Lambregts-Rommelse aan het promotieonderzoek dat leidde tot dit proefschrift. Dit promotieonderzoek is een onderdeel van het BOA-project, een familie-genetisch onderzoek naar de Biologische Oorzaken van Autisme.

CURRICULUM VITAE- ENGLISH

Daphne Johanna van Steijn was born on 12th July 1979 in Nijkerk. She finished secondary school in 1995, and passed the Social Work exams in 1998 at the community college in Amersfoort. Thereafter, she studied Social science at the HU University of Applied Sciences Utrecht, where she work as an intern in Lorentz Hospital in Zeist. In 2001 she began studying Educational and Behavioral Development at the University of Applied Science Utrecht. Her thesis was titled 'Temperament, attachment, and risk factors: factors associated with externalizing behavior in children at the age of 21 months?', and was carried out at the department of child and adolescent psychiatry at the University Medical Centre Utrecht. In the meantime, she also worked at a home for mentally handicapped children. She did her internship at Vosseveld, a psychiatric clinic for children who suffer from oppositional defiant disorder and/ or conduct disorders. After graduation in 2004, she did clinical work at MEE, an organization that aims to support people with disabilities, and at Karakter child- and adolescent psychiatry in Nijmegen. Furthermore, she co-coordinated the coordination of a screenings instrument 'Early Screening of Autistic Traits Questionnaire (ESAT)' for detecting ASD at an early age. In December 2008, she began her PhD-project at Karakter child- and adolescent psychiatry, under the supervision of prof. dr. J.K. Buitelaar, prof. dr. M.A.G. van Aken en dr. N.N.J. Lambregts-Rommelse. This thesis is a part of the BOA-project, a family-genetic study into the Biological Origins of Autism.

kinder- en jeugdpsychiatrie

karakter