Social functioning and mental health in children: the influence of chronic illness and intellectual function

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Abstract

Chronic illness, and in particular neurodevelopmental disorders, are associated with an increased risk of mental health problems and social difficulties in children. Across the neurodevelopmental disorders, the presence of cognitive impairment, such as intellectual disability, is one factor which has been related to this increased risk.

The overall aim of the present thesis was to extend our knowledge about the influence of chronic illness and intellectual function on mental health and social functioning in children. More specifically, we wanted to explore how chronic illness and intellectual function was related to mental disorders in children, to explore if children with chronic illnesses in which intellectual function tends to be compromised are prone to show more social difficulties than children with other chronic illnesses, and finally, we explored the relation between intellectual and social functioning in a sample of children representing a wide range of social functioning.

Data stem from the first two waves of a longitudinal population-based study, the Bergen Child Study (BCS). The first wave was conducted when the children were 7-9 years old, in which an extensive screening questionnaire was administered to the parents and teachers. As part of this wave, 329 children were invited to take part in a comprehensive clinical examination. The second wave was conducted when the children were 11-13 years old, in which the parents, teachers, and the children themselves responded to a questionnaire similar to the one administered in the first wave. Intellectual function (IQ) and mental health were assessed as part of the clinical examination, which included a standardized IQ test (WISC-III) and a semi-structured clinical interview (Kiddie-SADS-PL) eliciting DSM-IV child psychiatric diagnoses and a general level of functioning score. Chronic illness was assessed by parent report in the questionnaires in the first and second wave, while social functioning was assessed by the Autism Spectrum Screening Questionnaire (ASSQ), which was part of the parent and teacher questionnaires in both waves.

The present thesis showed that chronic illness was associated with a twofold increased risk of having a mental disorder. While having an IQ below the normal range and having a mental disorder was more frequent in children with chronic illness, IQ within the normal range or higher was associated with better mental health regardless of having a chronic illness. Having a neurodevelopmental disorder was associated with more social difficulties, represented by higher scores on the ASSQ, compared to groups of children with other chronic illnesses and without chronic illness. In a sample representing a wide range of scores on the ASSQ, IQ had a main effect on social functioning, with the ASSQ scores showing a gradual decline with higher IQ. Having an uneven IQ profile (discrepantly higher verbal- or performance IQ) was mainly unrelated to social functioning.

The findings of the present thesis suggest that chronic illness and neurodevelopmental disorders in children are associated with an increased risk of mental disorders and social difficulties. IQ is closely related to mental health and social functioning in children, as the rate of mental disorders and social difficulties gradually decline with higher IQ, and vice versa. The present thesis emphasizes the importance of taking intellectual function into consideration when assessing mental health and social functioning in children, and calls for broad assessments of children with neurodevelopmental problems before reaching clinical conclusions. Future studies should include other measures of cognitive functioning, to further extend our knowledge about the influence of cognitive functions on mental health and social functioning in children.

List of publications

- I. Ryland, H. K., Lundervold, A. J., Elgen, I., & Hysing, M. (2010). Is there a protective effect of normal to high intellectual function on mental health in children with chronic illness? *Child Adolesc Psychiatry Ment Health*, 4, 3. doi: 10.1186/1753-2000-4-3
- II. Ryland, H. K., Hysing, M., Posserud, M. B., Gillberg, C., & Lundervold, A. J. (2012). Autism spectrum symptoms in children with neurological disorders. *Child Adolesc Psychiatry Ment Health*, 6(1), 34. doi: 1753-2000-6-34
- III. Ryland, H. K., Hysing, M., Posserud, M. B., Gillberg, C., & Lundervold, A. J. (2014). Autistic features in school age children: IQ and gender effects in a population-based cohort. *Research in Autism Spectrum Disorders*, 8(3), 266-274. doi: http://dx.doi.org/10.1016/j.rasd.2013.12.001

List of Abbreviations

ADHD – Attention Deficit Hyperactivity Disorder

ANCOVA – Analyses of Covariance

ANOVA – Analyses of Variance

ASD – Autism Spectrum Disorder

ASSQ - The Autism Spectrum Screening Questionnaire

BCS – The Bergen Child Study

CGAS - Children's Global Assessment Scale

CNS – The Central Nervous System

CP – Cerebral Palsy

DAWBA – The Development and Well-Being Assessment

DSM-IV – The Diagnostic and Statistical Manual of Mental Disorders, 4th edition

ESSENCE - Early Symptomatic Syndromes Eliciting Neurodevelopmental Clinical Examinations

FSIQ – Full Scale IQ

ICD-10 – The International Classification of Diseases, 10th edition

IQ - Intellectual function

K-SADS-PL - The Schedule for Affective Disorders and Schizophrenia for School Aged Children: Present and Lifetime Version

NF1 – Neurofibromatosis type 1

PIQ - Performance IQ

 $RKBU \ (West) \ \hbox{-} \ Regional \ Centre \ for \ Child \ and \ Youth \ Mental \ Health \ and \ Child \ Welfare$

SDQ – The Strengths and Difficulties Questionnaire

VIQ – Verbal IQ

WISC-III - Wechsler's Intelligence Scale for Children, 3rd edition

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1. Introduction

Mental disorders are prevalent in childhood, with rates ranging from 7 % to 15 % (Goodman, Slobodskaya, & Knyazev, 2005; Heiervang et al., 2007). Social difficulties are part of the diagnostic criteria of several mental disorders (American Psychiatric Association, 2013). Furthermore, many children may be severely socially impaired by their mental health problems without meeting formal diagnostic criteria for a mental disorder (Angold, Costello, Farmer, Burns, & Erkanli, 1999; Goodman & Scott, 2005).

A range of factors may be related to social functioning and mental health in children, and the presence of a chronic, physical illness is known to represent one such risk factor in childhood (Blackman & Conaway, 2013; Hysing, Elgen, Gillberg, Lie, & Lundervold, 2007; Martinez, Carter, & Legato, 2011; Pinquart & Shen, 2011; Pinquart & Teubert, 2012). This risk is shown to be particularly high in the presence of an illness that directly affects the central nervous system (CNS) (Blackman & Conaway, 2013; Hysing, Elgen, Gillberg, & Lundervold, 2009; Martinez et al., 2011), commonly referred to as neurodevelopmental disorders. It has been known for a long time that neurodevelopmental disorders represent a powerful risk factor for mental health problems and social difficulties in children, as demonstrated by the Isle of Wight Neuropsychiatric study in the nineteen sixties. Neurodevelopmental disorders that co-exist with cognitive impairment, such as intellectual disability, is known to further increase the risk (Rutter, Yule, & Graham, 1970).

The overall aim of the present thesis was to extend our knowledge about the influence of chronic illness and intellectual function on mental health and social functioning in children. To that end, we first examined if a normal to high level of intellectual function protects children with a chronic physical illness from having a mental disorder. Based on findings showing that difficulties related to social functioning are essential in most mental disorders in childhood, and that intellectual function tends to be compromised in children with an illness affecting the CNS, a second paper investigated the influence of having a neurodevelopmental disorder on social

functioning in children. Finally, we asked if the influence of intellectual function could be found even in a sample representing a wide range of scores on a measure of social functioning.

1.1 Social functioning and mental health in children

Social functioning is a broad construct, capturing children's peer relations, social competence, and social-emotional adjustment (Adams, Streisand, Zawacki, & Joseph, 2002). Social functioning may be measured according to several aspects, including quantitative (e.g. how many friends does a child have), qualitative (e.g. how does a child interact with other children), positive (e.g. prosocial behavior) and negative (e.g. social anxiety) aspects. Within the broad area of social functioning, social interaction with peers is considered to be important for children's social development, because peer relations provide a significant source of emotional support (Hartup, 1996) and the opportunity to learn appropriate social rules and social behaviors (Parker & Asher, 1987). The impact of social functioning on children's development has gained increased research attention over the past decades (Bukowski & Adams, 2005). Not only are close peer relationships regarded as important for healthy psychological functioning and development in children in general (Bagwell, Newcomb, & Bukowski, 1998; La Greca & Harrison, 2005); peer relations can also predict later maladjustment and psychopathology (Parker & Asher, 1987; Ten Have, de Graaf, van Weeghel, & van Dorsselaer, 2013), as well as moderate the relation between risk factors and the development of psychopathology in children (Bukowski & Adams, 2005).

Although most children have good mental health, many individuals may experience mental disorders in childhood, with rates ranging from 7 % to 15 % in epidemiological studies (Goodman et al., 2005; Heiervang et al., 2007). Mental disorders may be viewed as distinct diagnostic categories, and/or as dimensions of symptoms that are normally distributed (Goodman & Scott, 2005). Social difficulties are part of the diagnostic criteria of several mental disorders, such as Autism Spectrum Disorder (ASD). ASD is a condition characterized by persistent deficits in

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social communication and social interaction, as well as restricted, repetitive patterns of behavior, interests, or activities, and may cause considerable social impairment (American Psychiatric Association, 2013). Symptoms of ASD are shown to be widely distributed in the population, where children with an ASD diagnosis represent a subgroup with a high number of symptoms (Constantino & Todd, 2003; Kamio et al., 2013; Posserud, Lundervold, & Gillberg, 2006). ASD and autistic features in the general population may have a common etiology, supported by twin studies showing an etiological, primarily genetic, similarity (Lundstrom et al., 2012). It is assumed that even mild variations of autistic features may give considerable social impairment (Constantino & Todd, 2003).

1.2 Factors affecting social functioning and mental health

A range of factors may influence the development of mental health problems and social difficulties in children. One may separate between predisposing risk factors, maintaining factors, and protective factors, which in turn may be either personal or contextual. Personal factors refer to biological or psychological characteristics of the child, while contextual factors refer to characteristics of the child's environment, such as the family and the social network (Carr, 1999).

One example of a personal, psychological protective factor associated with healthy functioning is the presence of an easy temperament. Having an easy temperament has been shown to have a protective effect against the development of youth violence (Losel & Farrington, 2012), and to differentiate children with resilient versus stress-affected outcomes (Cowen, Wyman, & Work, 1996). High self-esteem constitutes another personal, psychological protective factor, as high levels of self-esteem have been found to moderate the association between depressive symptoms and suicidal risk in adolescents (Brausch & Decker, 2013). The same study examined the protective effect of peer support, a contextual protective factor, and found a direct as well as an indirect effect on suicidal risk: perceived peer support predicted suicidal ideation and moderated the association between disordered eating and suicidal ideation in adolescents (Brausch & Decker, 2013). Warm family relationships and a

positive family environment represent other contextual protective factors, and are shown to buffer children from the negative outcomes of being bullied (Bowes, Maughan, Caspi, Moffitt, & Arseneault, 2010).

Gender and age are personal, biological factors, with male gender and young age (before puberty) representing an increased risk of developing behavioral problems, while female gender and older age (after puberty) represents an increased risk of developing emotional problems (Canino et al., 2004; Costello, Mustillo, Erkanli, Keeler, & Angold, 2003; Ford, Goodman, & Meltzer, 2003). Family, twin, and adoption studies indicate that genes (personal, biological factors) and environment (contextual factor) contribute to all child and adolescent mental disorders, and that genetic factors appear particularly important to the development of attention deficit hyperactivity disorder (ADHD) and ASD (Thapar & Stergiakouli, 2008). In the case of ASD, recent twin studies indicate that the genetic risk is different for boys and girls, as girls seem to require a greater familial etiologic load in order to exhibit the autistic phenotype, suggesting a female protective effect against autistic behavior (Robinson, Lichtenstein, Anckarsater, Happe, & Ronald, 2013). Findings from the Bergen Child Study has shown that poor family economy is a consistent predictor of overall mental health problems, including peer problems, while lower parental education level is primarily a strong predictor of behavioral problems (Boe, Overland, Lundervold, & Hysing, 2012). Improvements in household income have, on the other hand, been associated with reductions in child mental health problems (Strohschein, 2005). Number of stressful life events experienced by unaccompanied asylum-seeking children in Norway has been found to be associated with posttraumatic stress disorder, depression, and symptoms of anxiety (Jensen, Fjermestad, Granly, & Wilhelmsen, 2013). Investigating the association between adverse life events and changes in mental health problem load in Danish children, parental divorce was found to significantly raise the risk of an increase in mental health problems. A consistently high level of behavioral problems was further associated with a higher number of adverse life events (Rasmussen, Nielsen, Petersen, Christiansen, & Bilenberg, 2014).

1.3 The influence of chronic illness on social functioning and mental health

A chronic physical illness is an important risk factor for social difficulties and mental disorders in children, as documented in several epidemiologic and meta-analytic studies (Blackman & Conaway, 2013; Cadman, Boyle, Szatmari, & Offord, 1987; Hysing et al., 2007; Lavigne & Faier-Routman, 1992; Martinez et al., 2011; Pinquart & Shen, 2011; Pinquart & Teubert, 2012). Not all chronic illnesses are associated with the same risk, however. Findings from a recent US national survey of child health showed that children with asthma and diabetes had increased rates of ADHD, social difficulties, emotional and behavioral problems compared to children without chronic illness. The rates were even higher in children with vision and hearing problems and musculoskeletal conditions, but the highest rates were found in children with disorders affecting the CNS, including epilepsy and brain injury (Blackman & Conaway, 2013). High rates of behavioral problems and social difficulties in children with CNS-disorders were also reported in a recent meta-analysis conducted by Pinquart & Shen (2011). Youth with epilepsy and migraine were found to have the most elevated levels of externalizing problems, but with low effect sizes, while attention problems and social difficulties were most elevated in youth with epilepsy and spina bifida, with large effect sizes. The authors suggested that the high levels of social difficulties observed in children with epilepsy could in part be explained by changes in the brain and the associated externalizing problems. In children with spina bifida, they proposed that the peer problems could be affected by concurrent high levels of social withdrawal (Pinquart & Shen, 2011). Living with a chronic illness may unquestionably have several negative consequences that could limit social interaction with peers, including restrictions of physical activity due to physical limitations, interruption of daily activities such as school and social activities, concerns about physical appearance as a result of the illness or treatment, and lifestyle modifications due to intensive treatment protocols, which in turn may inhibit the development of social competence and peer relations (La Greca, 1990). Children

with CNS-disorders appear to have particular problems developing age-appropriate peer relations (La Greca, Bearman, & Moore, 2002).

1.4 The influence of cognitive/intellectual function on social functioning and mental health

Many CNS-, or neurodevelopmental, disorders are characterized by cognitive impairments, which may affect social functioning and mental health. In children with cerebral palsy (CP), communication problem has been shown to be a significant predictor of mental disorders (Bjorgaas, Hysing, & Elgen, 2012). Furthermore, impairments in executive functions, which are involved in social information processing skills, may in turn have a negative impact on the social functioning of children with CP (Bottcher, 2010). Executive functions have also been found to explain the relationship between spina bifida status and internalizing and depressive symptoms (Kelly et al., 2012), as well as associations between spina bifida status and social difficulties (Rose & Holmbeck, 2007). In children with neurofibromatosis type 1 (NF1), measures of cognitive control, information processing speed, and social information processing were in various ways significantly related to parent reported emotional and behavioral problems and social functioning (Huijbregts & de Sonneville, 2011). In another study of children with NF1, the authors concluded that extent of neurological involvement, such as the presence of ADHD and learning difficulties, was indicative of social and emotional functioning (Noll et al., 2007). In relation to autistic features, associations between executive functions and stereotypic behaviors and interests have been reported in high-functioning boys with ASD (Bolte, Duketis, Poustka, & Holtmann, 2011). Cognitive functions, such as speech before 5 years of age, have also been shown to be important predictors of adult outcome in ASD (Billstedt, Gillberg, & Gillberg, 2007).

Intellectual function (IQ) is consistently shown to have an impact on social functioning and mental health in children with neurodevelopmental disorders. First of all, several studies have shown that general intellectual function is related to mental health problems and social difficulties. Lower IQ-levels have been shown to account

for peer problems, including peer rejection, lack of friends, and victimization (Yude & Goodman, 1999), as well as general mental health problems (Goodman & Graham, 1996) in children with CP. Moderate to mild intellectual disability, as well as mild to borderline intellectual disability, has been associated with emotional, behavioral, and social difficulties (Dekker, Koot, van der Ende, & Verhulst, 2002; Emerson, Einfeld, & Stancliffe, 2010), as well as anxiety and disruptive disorders (such as ADHD and ODD) (Dekker & Koot, 2003). Intellectual disability in neurodevelopmental disorders such as epilepsy (Clarke et al., 2005), hydrocephalus (Lindquist, Carlsson, Persson, & Uvebrant, 2006), myotonic dystrophy (Ekstrom, Hakenas-Plate, Samuelsson, Tulinius, & Wentz, 2008), and CP (Kilincaslan & Mukaddes, 2009) is associated with an increased risk of ASD. In a recent study of children with CP, intellectual disability was significantly associated with high rates of autism spectrum symptoms, which in turn frequently co-occurred with ADHD (Bjorgaas, Elgen, Ryland, & Hysing, 2014). Several studies have indicated that childhood IO-level is an important predictor of adult outcome in ASD (Billstedt, Gillberg, & Gillberg, 2005; Billstedt et al., 2007; Howlin, Goode, Hutton, & Rutter, 2004), as well as schizophrenia (Schulz, Sundin, Leask, & Done, 2012) and other mental disorders in adulthood, including comorbidity and persistence of disorders (Koenen et al., 2009).

Conversely, above-average IQ is shown to have both a direct and a buffering or moderating (i.e., in the presence of risk factors) protective effect against antisocial behavior. This protective effect has been related to better executive functioning, as manifested in social information processing or self-regulation skills, which in turn is associated with social competence (Losel & Farrington, 2012; Masten & Coatsworth, 1998). IQ has also been shown to moderate outcome of mental health treatment, as demonstrated in a recent Norwegian study, in which children with higher IQ showed better improvement than children with lower IQ (Mathiassen et al., 2012).

Finally, discrepancies between verbal IQ (VIQ) and performance IQ (PIQ) (IQ discrepancy) have been related to mental health and social functioning in neurodevelopmental disorders. Discrepantly lower VIQ scores have been found to be associated with more behavioral problems and poorer social and adaptive skills in

children with NF1 (Martin et al., 2012), whereas a study of high-functioning children with ASD found that both discrepantly lower VIQ and PIQ were associated with more social difficulties (Black, Wallace, Sokoloff, & Kenworthy, 2009). Another study could not find support for any association between IQ discrepancy and level of social impairment in ASD (Charman et al., 2011).

1.5 Co-occurrence of symptoms

Based on the presented literature, there is mounting evidence of overlap of symptoms between different disorders. This may be especially true in neurodevelopmental disorders, in which mental health problems, social difficulties, as well as cognitive impairments, frequently co-exist. This has been acknowledged in a recent theoretical framework under the acronym ESSENCE (Early Symptomatic Syndromes Eliciting Neurodevelopmental Clinical Examinations). It refers to all neurodevelopmental disorders that are characterized by impairing symptoms early in life (before age 3-5 years), including ASD, intellectual disability, non-verbal learning disability, behavioral phenotype syndromes, as well as a range of neurological and seizure disorders. Symptoms indicative of ESSENCE include problems with general development, communication, social interaction, and motor coordination, among others (Gillberg, 2010, 2013). Although frequently conceptualized as discrete disorders, many neurodevelopmental disorders are found to have a shared genetic etiology, which contributes to explain the common symptom overlap and co-existence of disorders (Posthuma & Polderman, 2013).

The co-occurrence of neurodevelopmental disorders, IQ below the normal range, mental health problems and social difficulties, is becoming well-documented. However, the association between a normal to high level of intellectual function and mental health in children with chronic illness, and the influence of intellectual function on social functioning in children representing a wide range of scores on a measure of social functioning, is not as clear.

2. Aims

In the present thesis, including three papers using data from the Bergen Child Study (BCS), the overall aim was to contribute to extend our knowledge about the influence of chronic illness and intellectual function on mental health and social functioning in children. More specifically, the aim was to assess how chronic illness and intellectual function are related to mental disorders in children, to assess if children with disorders in which intellectual function tends to be compromised show more social difficulties than children with other chronic illnesses, and to assess how intellectual and social functioning are related in a sample representing a wide range of scores on a measure of social functioning.

3. Methods

3.1 The Bergen Child Study (BCS)

The BCS is a longitudinal population-based study of mental health and development in children living in the second largest city of Norway. The study was launched in 2002 with an aim to follow all children in the 1993 through 1995 birth cohorts in the municipality of Bergen and Sund from early school age to late adolescence. Main aims of the study were to establish prevalence data for mental health problems, including comorbidity, risk and protective factors, as well as the use of health- and educational services.

The BCS had a four wave design: the first wave of the BCS included three phases, the second wave included two phases, and the third and fourth wave each included one phase (See Figure 1). The fourth wave encompassed all youth in upper secondary school in the Hordaland County, and since the participants were now aged 16-18, the study was renamed "youth@hordaland". More information about the BCS/youth@hordaland can be found at www.uib.no/bib. The study was approved by the Regional Committee for Medical and Health Research Ethics Western Norway, and by the Norwegian Data Inspectorate.

In the current thesis, data from wave one, phases one and three, and wave two, phase one, were used.

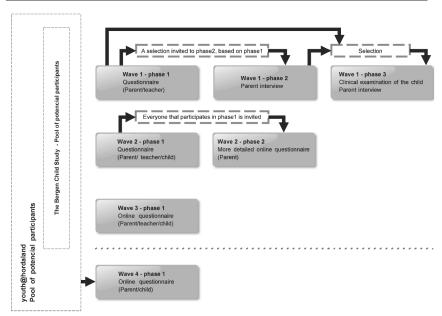


Figure 1. Flow chart visualizing the BCS/youth@hordaland study design. Retreived from www.uib.no/bib.

3.1.1 Wave 1 Phase 1

Wave 1 Phase 1 was conducted in the fall of 2002, in which an extensive *screening* questionnaire was distributed through the schools to parents and teachers of all second to fourth graders (7 – 9 years) in Bergen (n = 9430) and Sund (n = 222) (for details, see Heiervang et al., 2007). All primary schools in Bergen participated, including four special education public schools and seven private schools. The questionnaire included the Autism Spectrum Screening Questionnaire (ASSQ) (Ehlers & Gillberg, 1993; Ehlers, Gillberg, & Wing, 1999), the Strengths and Difficulties Questionnaire (SDQ) (Goodman, 1999), the Swanson, Nolan and Pelham-IV rating scale (Swanson et al., 2001), and items related to learning disabilities, obsessive compulsive behavior, tics, eating and sleep, selective mutism, hypoactivity, physical health problems, and the use of health and educational services. Informed consent to participate was provided by parents of 74 % of the

children (n = 7007). A child was defined as screen positive if: (1) the SDQ total difficulties score exceeded the 90^{th} percentile for parents and/or teachers, and/or (2) there was a severe impairment on the SDQ impact section according to parents and/or teachers, and/or (3) the score on one of the other scales included in the questionnaire was equal to or above the 98^{th} percentile.

3.1.2 Wave 1 Phase 2

Data from Wave 1 Phase 2 was not used in the present thesis, but a brief description will be given to ease the comprehension of the recruitment of participants to Phase 3.

Phase 2 was conducted during the spring of 2003 and included the parents of all children defined as screen positive in Phase 1 and a random sample of parents of screen negative children. The parents were interviewed with the Development and Well-Being Assessment (DAWBA) (Goodman, Ford, Richards, Gatward, & Meltzer, 2000), designed to assign psychiatric diagnoses according to the Diagnostic and Statistical Manual of Mental Disorders, 4th edition (DSM-IV) (American Psychiatric Association, 1994) and the International Classification of Diseases, 10th edition (ICD-10) (World Health Organization, 2004). A total of 2393 parents were invited to participate in Phase 2, with a participation rate of 44 % (n = 1047).

3.1.3 Wave 1 Phase 3

Wave 1 Phase 3 took place in 2003/2004, in which a sample of 329 children was selected to participate in an extensive clinical assessment. The sample included 97 children who received a psychiatric diagnosis according to the DAWBA, 207 children without any DAWBA diagnosis (a random sample of screen positive and screen negative in Phase 1), and 25 children invited directly from Phase 1. The 25 children invited directly from Phase 1 were children with a chronic physical illness. The reason they were invited directly from Phase 1 was to increase the participation of children with chronic illness in Phase 3. The Phase 3 clinical assessment included a physical examination of the child (blood pressure, weight, height), a motoric assessment with the Movement Assessment Battery for Children (Henderson &

Sugden, 1992), a semi-structured diagnostic interview of parent(s) and child (The Schedule for Affective Disorders and Schizophrenia for School Aged Children: Present and Lifetime Version [K-SADS-PL]) (Kaufman et al., 1997; Løkke & Sund, 2000), and a neuropsychological assessment of the child. The neuropsychological assessment included Wechsler's Intelligence Scale for Children, 3rd edition (WISC-III) (Ellertsen & Johnsen, 2003; Wechsler, 1991), Stroop Color Word Interference Test (Lund-Johansen, Hugdahl, & Wester, 1996), Conner's Continuous Performance Test II (Conners, 2000), Attention Network Test (Fan, 2001; Rueda et al., 2004), d2 test of attention (Brickenkamp & Zilmer, 1998), Developmental Test of Visual Motor Integration (Beery & Beery, 2004), Children's Auditory Verbal Learning Test-2 (Talley, 1993), Children's Color Trails Test (Llorente, Williams, Satz, & D'Elia, 2003), and the parent Behavior Rating Inventory of Executive Function (Gioia, Isquith, Guy, & Kenworthy, 2000). The Diagnostic Interview for Social and Communication Disorders (Wing, Leekam, Libby, Gould, & Larcombe, 2002) was included in order to identify children with autism spectrum disorders (see Posserud, Lundervold, & Gillberg, 2009, for details).

3.1.4 Wave 2 Phase 1

Wave 2 Phase 1 was conducted in 2006. Parents, teachers and the children themselves, now in the fifth to seventh grade (11–13 years), participated by completing a questionnaire similar to the one used in Wave 1 Phase 1, including the ASSQ. In this wave, the target population was children in all public and four private schools in Bergen (n = 9218). A few private schools refrained from participating and the municipality of Sund did not take part in Wave 2. The participation rate in Wave 2 Phase 1 was 63 % (n = 5781).

3.2 Assessment

3.2.1 Social functioning

The Autism Spectrum Screening Questionnaire (ASSQ)

The ASSQ (Ehlers & Gillberg, 1993; Ehlers et al., 1999) is an instrument designed to identify school age children who may need a more comprehensive evaluation due to suspected ASD. It was designed for completion by lay informants, and identical versions exist for parents and teachers. The ASSQ covers a wide range of symptoms predictive of a diagnosis within the autism spectrum, including difficulties with social interaction, verbal and non-verbal communication, restricted and repetitive behavior, motor clumsiness, and tics. It consists of 27 items scored on a three-point scale: "not true" (0), "somewhat true" (1), or "certainly true" (2). Possible scores range from 0-54, with higher scores indicating a greater symptom load. The ASSQ has been used in several international studies during the last decade, with topics ranging from the population prevalence of ASD (Mattila et al., 2012; Petersen, Bilenberg, Hoerder, & Gillberg, 2006; Posserud et al., 2006; Webb et al., 2003), to comparison of symptoms of inattention and autism in children with ADHD and pervasive developmental disorder (Fujibayashi, Kitayama, & Matsuo, 2010; Hattori et al., 2006), behavioral problems in children with epilepsy (Kobayashi et al., 2013), and behavior and emotional well-being of extremely low birth weight teenagers (Georgsdottir, Haraldsson, & Dagbjartsson, 2013). The ASSQ is shown to have good screening properties both in clinical (Ehlers et al., 1999; Guo et al., 2011; Mattila et al., 2012) and populations settings (Mattila et al., 2012; Posserud et al., 2009), although optimal cut-off scores differs between countries. A study from the BCS has shown that the ASSQ has good internal consistency (Cronbach's alpha = 0.86) and a stable three factor structure with factors labeled social difficulties, motor/tics/OCD, and autistic style (Posserud et al., 2008). The ASSQ is available in the publications by Ehlers & Gillberg (1993) and Ehlers et al. (1999).

Depending on the context, the characteristics of ASD may be regarded as symptoms or as features. In the present thesis, the terms autism spectrum symptoms, or

problems associated with ASD, were used in paper II because the aim was to assess the frequency of autism spectrum symptoms and to identify children with an ASSQ score associated with ASD in a clinical high-risk group, i.e. children with neurodevelopmental disorders. In paper II, the term autistic features was used since the aim was to assess the distribution of autistic features in a population-based cohort. Posserud and collaborators (2006) also used this term when assessing the distribution of autistic features in the BCS total population.

3.2.2 Mental health

The Schedule for Affective Disorders and Schizophrenia for School Aged Children (6-18 years): Present and Lifetime Version (K-SADS-PL)

The K-SADS-PL is a semi-structured interview designed to evaluate present and past episodes of psychopathology in children and adolescents (6-18 years old) (Kaufman et al., 1997) according to the DSM-III R (American Psychiatric Association, 1987) and DSM-IV criteria (American Psychiatric Association, 1994). It includes an introductory interview, a diagnostic screening interview with 5 diagnostic supplements, as well as impairment ratings for each diagnosis. Each item is rated on a three-point scale, in which a score of 0 indicates that no information is available; a score of 1 indicates that the symptom is not present; a score of 2 indicates a subthreshold level of the symptom; and a score of 3 indicates clinical threshold. In the initial study assessing the psychometric properties of this version of the K-SADS-PL, interrater reliability for present and lifetime diagnoses were high, ranging from 93 % -100 %, and test-retest reliability for present and lifetime diagnoses ranged from moderate to excellent ($\kappa = 0.55-1.00$) (Kaufman et al., 1997). The study by Kaufman et al. did not validate the K-SADS-PL against clinical diagnoses, but this was done in a Korean study assessing the psychometric properties of the Korean version of the K-SADS-PL (K-SADS-PL-K). In this study of 91 clinical cases, concordance rates between clinical diagnoses and K-SADS-PL-K threshold diagnoses were statistically significant. Agreement ranged from fair for emotional disorders ($\kappa = 0.24-0.29$), to moderate for oppositional defiant disorder and tic disorders ($\kappa = 0.41-0.43$), and good

for ADHD (κ = 0.70) (Kim et al., 2004). The K-SADS-PL is a widely used instrument in research and in the clinic (Posserud et al., 2013).

The K-SADS-PL also includes the *Children's Global Assessment Scale (CGAS)*, a 100-point rating scale assessing the child's general level of functioning. Scores below 60 indicate definite case, scores of 60-70 indicate possible/probable case, and scores above 70 indicate normal function. Depending on the current and prior psychiatric status of the child, one may assign one or two of totally three CGAS scores (current, most severe prior psychiatric episode, and/or previous highest level of functioning) (Shaffer et al., 1983). The CGAS has been widely used as an outcome measure in research and in clinical settings (Rey, Starling, Wever, Dossetor, & Plapp, 1995; Shaffer et al., 1983; Winters, Collett, & Myers, 2005). It has been used most extensively as a measure of psychosocial functioning in different clinical groups, including children with chronic illness (Vandvik, 1990), but is also sensitive to change in mental health symptoms (Weissman, Warner, & Fendrich, 1990) and to treatment effects (Winters et al., 2005). In Norway, it is currently used as a global assessment of functioning according to the ICD-10 Axis VI (World Health Organization, 1999) in children referred to Child and Adolescent Mental Health Outpatient Clinics. In a cross-national comparison study rating 20 written vignettes, the interrater reliability for the CGAS was moderate, with an intraclass correlation coefficient of 0.61 (Hanssen-Bauer et al., 2007); similar to the intraclass correlation coefficients (0.53-0.63) reported by Rey et al. (1995) in a clinical setting, but lower than the agreement reported in earlier studies of the CGAS (Bird, Canino, Rubio-Stipec, & Ribera, 1987; Shaffer et al., 1983).

In the BCS, clinical psychologists and MDs trained by an experienced child psychiatrist in using the K-SADS-PL conducted the interview, first with the parent and later on the same day with the child. Immediately after the assessment of both informants, the interviewer scored the diagnoses as definite, probable, in remission, or not present according to the K-SADS-PL schedule, and scored the CGAS. When in doubt, cases were discussed with a clinical psychologist who had the main responsibility for the diagnostic conclusions. In paper I of the present thesis, a

psychiatric disorder was defined as *any definite diagnosis*, and the CGAS score indicating the *current* general level of functioning was used.

3.2.3 Chronic illness

Information about chronic illness was included in paper I and paper II in the present thesis, and defined as reported by parents on the screening questionnaires in Wave 1 and Wave 2 of the BCS. In paper I, chronic illness was also confirmed by parents in the clinical interview in Wave 1 Phase 3. On the screening questionnaires, parents replied to a question that was identically phrased in the two waves regarding whether or not their child had a chronic illness or disability. Parents who reported such an illness or disability as present were asked to categorize it as either a) asthma, b) epilepsy, c) diabetes, or d) other illness. In Wave 2, the parents could also endorse "intellectual disability". The parents were asked to specify if selecting the "other illness" category. An experienced pediatrician categorized the reported illnesses into subgroups, and only physical conditions were included. Reported psychiatric disorders and specific learning disabilities were disregarded as chronic illnesses and were included in the non-chronic illness group for analyses. In Wave 1 Phase 3, 106 of the 329 participating children (32.2 %) were confirmed to have at least one chronic illness. In Wave 2, 496 of the 5781 participating children (8.6 %) were reported to have at least one chronic illness.

Paper 2 examined social functioning in children with a chronic illness affecting the CNS, referred to as "neurological disorders" in the current paper. In the introduction and discussion of this thesis, such disorders have been termed "neurodevelopmental disorders" in order to encompass a wider range of CNS-disorders that are characterized by impairing symptoms early in life and that frequently co-exist and share symptoms.

3.2.4 Intellectual function

Wechsler Intelligence Scale for Children, 3rd ed. (WISC-III)

The WISC-III was used in paper I and paper III to assess intellectual function. The WISC-III is a widely used instrument for assessing general intellectual abilities in children and adolescents aged 6-16 years. It contains 13 subtests that generate three IQ scores (Verbal, Performance and Full Scale), of which five subtests comprise the VIQ score and another five subtests comprise the PIQ score. The Full scale IQ (FSIQ) is a composite of the VIQ and PIQ scores. In addition, the WISC-III yields four indexes generated from a factor analysis: the Verbal Comprehension Index, the Perceptual Organization Index, the Freedom from Distractibility Index, and the Processing Speed Index. The IQ and indexes are represented by standard scores with a mean of 100 and a standard deviation of 15 (Wechsler, 1991).

In the BCS, the Norwegian version of the WISC-III was used (Ellertsen & Johnsen, 2003) with Swedish norms (Sonnander, Ramund, & Smedler, 1998), and the test was administered and scored by trained and experienced test-technicians employed at a Neuropsychological Outpatient Clinic. The WISC-III has been considered a valid and reliable tool for assessing general intellectual abilities in children (Sonnander et al., 1998).

In the current thesis, the FSIQ score was analyzed at a continuous as well as a categorical level, for which it was divided into three levels: FSIQ below 70, FSIQ ranging from 70-84, and FSIQ equal to or above 85. A discrepancy score was also calculated according to the IQ discrepancy that reaches statistical significance (p < .05) in the Swedish norms (Sonnander et al., 1998), in which a significant IQ discrepancy was defined as a difference between VIQ and PIQ of at least 14 IQ points.

Table 1. Summary of the BCS waves and phases, core variables and instruments included in the three papers of the current thesis. Paper I Paper II Paper III Wave 1 Phase 1 X X Wave 1 Phase 3 X Χ Wave 2 Phase 1 X **ASSQ** Χ Χ K-SADS-PL X **CGAS** X Chronic illness X X WISC-III X X

3.3 Statistical analyses

Researchers responsible for the Bergen Child Study at the Centre for Child and Adolescent Mental Health and Child Welfare, including co-authors of the papers in the thesis, have prepared the data files for the statistical analyses computed in the present studies. SPSS (version 15, 17 and 20, respectively) was used for statistical analyses. Hilde Katrin Ryland conducted the statistical analyses, supervised by the co-authors of the separate papers.

In paper 1, descriptive statistics and chi square tests were used to explore the rate of mental disorders in children with chronic illness compared to children without chronic illness, as well as the rate of mental disorders according to FSIQ level.

Logistic regression analyses were conducted to further explore the influence of chronic illness and FSIQ level on mental disorders. Analyses of variance (ANOVA) were conducted to explore the influence of chronic illness and FSIQ level on the general level of functioning.

In paper 2, analyses of covariance (ANCOVAS) were conducted to explore parent and teacher reported ASSQ scores in children with neurological disorders compared to children with other chronic illnesses and children without chronic illness, with intellectual disability and gender as covariates. Post hoc tests and effect sizes (Cohen's *d*) were used to evaluate the results of the ANCOVAS. Cross-tabs and chi-squares were conducted to explore the rate of children with a parent and/or teacher reported ASSQ score equal to or above the 80th, 90th, 95th, and 98th percentile. Bivariate correlation analyses (Pearson's *r*) were conducted to explore parent-teacher agreement in ASSQ scores, and McNemar chi-square tests were conducted to explore parent-teacher agreement on single items in children with neurological disorders.

In paper 3, independent samples t-tests were conducted to explore gender differences in ASSQ scores. Bivariate correlation analyses (Pearson's r) were conducted to explore associations between the FSIQ and ASSQ scores in the total sample and for boys and girls separately. Univariate ANOVAs were conducted to further explore the influence of FSIQ, IQ discrepancy and gender on ASSQ scores. Effect sizes (Cohen's d and np^2) were used to evaluate the results of the t-tests and ANOVAS.

4. Results

The following section provides a summary of the results presented in the three papers of the current thesis

4.1 Paper 1

Paper 1 examined if a normal to high level of intellectual function had a protective effect on mental health in children with chronic illness, and if this effect was stronger in this group than in a group of peers without such an illness.

The results showed that the rate of children with chronic illness with a mental disorder was significantly higher than in their peers without chronic illness (OR = 2.04, 95% CI: 1.11-3.77, p = .02), but this rate decreased as a function of higher FSIQ level. The lowest rate with mental disorders was found in children with a FSIQ level at or above 85 (i.e., within the normal range or higher), followed by those with a FISQ level between 70 and 84, with the highest rate of mental disorders found in children with a FSIQ level below 70. FSIQ level also had a corresponding significant main effect on the general level of functioning (CGAS) score, where the children with chronic illness showed a higher CGAS score as a function of a higher FSIQ score. These relations between the FSIQ score and the two indicators of mental health were also found in the group of peers, suggesting that the protective effect of a normal to high intellectual function was not restricted to children with chronic illness, but rather had a general effect on mental health in children.

4.2 Paper 2

Paper 2 examined social functioning in children with a chronic illness affecting the CNS, referred to as neurological disorders in the current paper. Social functioning was assessed by parent- and teacher reported scores on the Autism Spectrum Screening Questionnaire (ASSQ).

When compared to children with other chronic illnesses and peers without chronic illness and adjusting for intellectual disability and gender, children with neurological disorders showed significantly higher ASSQ scores (p < .01, d = 0.50-1.01). This effect seemed to be specific to this group of children, because the two other groups were not significantly different from each other. Compared to these two other groups, significantly more children with a neurological disorder were rated by their parents and teachers with an ASSQ score associated with ASD (equal to or above the 98th percentile) ($x^2(2) = 338.79$, p < .001), and a higher frequency also obtained an ASSQ score equal to or above the 80^{th} , 90^{th} , and 95^{th} percentile. Parent-teacher agreement over ASSQ scores was higher for children with neurological disorders than for the two other groups, but agreement over single items in children with neurological disorders was generally poor.

4.3 Paper 3

Paper 3 examined the association between intellectual function (FSIQ and VIQ-PIQ discrepancies), gender, and social functioning in children representing a wide range of parent reported scores on the ASSQ. The ASSQ total score and the three factor scores were analyzed.

The results showed that boys obtained significantly higher scores than girls on most of the ASSQ variables (p < .001, d = 0.37-0.45). Moderate, negative correlations were found between the FSIQ score and the majority of ASSQ scores in the total sample and when the scores of boys and girls were analyzed separately (r = 0.30-0.43, p < .01, 2-tailed), with the ASSQ scores showing a gradual decline with higher FSIQ for both genders. Further explorations of these associations revealed that gender and FSIQ had main effects on most ASSQ scores (with mainly moderate effect sizes), indicating that being male or scoring at the lower end of the IQ scale was associated with more autistic features. The autistic style factor score showed the weakest or no association with gender and FSIQ. Having an uneven IQ profile (discrepantly higher verbal- or performance IQ) only had an impact on the motor/tics/OCD factor score and interacted with gender, F = 3.9, p = 0.22, $np^2 = 0.024$.

5. Discussion

5.1 Summary of findings

In the present thesis, chronic illness was associated with an increased rate of mental disorders. While having an IQ below the normal range and having a mental disorder was more frequent in children with chronic illness, IQ within the normal range or higher had a general protective effect on mental health in children. Having a neurodevelopmental disorder was associated with more social difficulties, as represented by higher scores on the ASSQ and a symptom load associated with ASD, compared to groups of children with other chronic illnesses and without chronic illness. The association between IQ and social functioning was mainly explained by an IQ level below 70, while uneven IQ profiles (discrepantly higher verbal- or performance IQ) were mainly unrelated to social functioning. Thus, level of intellectual function not only had an influence on mental health and social functioning in children with chronic illness and neurodevelopmental disorders, but also in a sample representing a wide range of scores on the ASSQ.

5.2 General discussion

The present thesis showed that mental disorders were frequent in children with chronic illness. These findings are in line with results from several meta-analyses and epidemiological studies examining the association between chronic illness and mental health in children (Blackman & Conaway, 2013; Cadman et al., 1987; Hysing et al., 2007; Lavigne & Faier-Routman, 1992; Pinquart & Shen, 2011). The high rates of social difficulties shown in children with neurodevelopmental disorders are further in line with previous studies (Blackman & Conaway, 2013; Hysing et al., 2009; Martinez et al., 2011; Pinquart & Shen, 2011).

By separating between children with neurodevelopmental disorders and children with other chronic illnesses, it was evident that social difficulties were much more common in children with a disorder affecting the central nervous system (CNS). Not

only were they more frequently rated with a score on the ASSQ associated with ASD – a higher frequency also scored above the 80th percentile cutoff point on the ASD symptom dimension. It is therefore likely that these children affect the percentile cutoff scores for ASD for the total population, by being overrepresented in the highest quartile. In contrast, children with non-CNS related chronic illnesses did not have significantly more social difficulties than their peers without chronic illness. Similar findings have been reported in studies of social functioning comparing children and/or adolescents with juvenile rheumatoid arthritis (Feldmann, Weglage, Roth, Foell, & Frosch, 2005; Huygen, Kuis, & Sinnema, 2000; Noll et al., 2000), cancer (Noll et al., 1999), or hemophilia (Trzepacz, Vannatta, Davies, Stehbens, & Noll, 2003) with non-chronic ill peers.

The consistent finding of an increased risk of social difficulties and mental health problems in children with neurodevelopmental disorders has been related to the cognitive impairments that are frequently found in this group of children, such as in children with CP (Biorgaas et al., 2012; Bottcher, 2010), spina bifida (Kelly et al., 2012; Rose & Holmbeck, 2007), NF1 (Huijbregts & de Sonneville, 2011; Noll et al., 2007), and ASD (Bolte et al., 2011). In the present thesis, and in line with previous studies (e.g. Bjorgaas et al., 2014; Dekker & Koot, 2003; Dekker et al., 2002; Emerson et al., 2010), IQ below the normal range, and IQ below 70/intellectual disability in particular, was shown to be significantly related to mental disorders and social difficulties. In accordance with the concept of ESSENCE which takes into account the common symptom overlap and co-occurrence of disorders (Gillberg, 2010), low IQ is more frequent in children with chronic illness and in neurodevelopmental disorders specifically, and is of importance to understand the high rate of mental health problems and social difficulties in these groups. The present study does not give us answer regarding pathways relating IQ to mental health or social functioning. One possibility is that low IQ, no matter its cause, predisposes a child to mental health problems/social difficulties. Another possibility is that intellectual disability and mental health problems/social difficulties are independently caused by the same biological factors, and that low IQ primarily acts as a marker for the severity of the underlying neurological abnormalities, which, in

turn, makes a child susceptible to develop mental health problems/social difficulties. The latter may seem more likely in this case, as the risk of social difficulties associated with ASD differs according to the type or severity of the neurodevelopmental disorder (Goodman & Scott, 2005).

Apart from the effect of low IQ in neurodevelopmental disorders, other mechanisms involved in chronic illness, such as restrictions of physical activity or increased school absence, may also have an impact on social functioning through limited social interaction with peers (La Greca, 1990). However, as discussed in several reviews (La Greca et al., 2002; Nassau & Drotar, 1997; Reiter-Purtill, Waller, & Noll, 2009), and as the results of this thesis show, the CNS-disorders that are associated with cognitive impairments, such as low IQ, seem to represent a particular challenge for children's social functioning, while children with chronic illnesses not affecting the CNS do not differ much from their peers, despite the negative consequences their illness or its treatment might have for social interaction.

The rate of mental disorders in children with IQ in the range 70-84 in paper 1 was nearly as high as in the children with IQ below 70, irrespective of having a chronic illness. Several studies have shown that children with IQ below the normal range, or what is sometimes referred to as borderline intellectual functioning or borderline intellectual disability, have more mental health problems than those with higher IQs (Emerson et al., 2010), or similar rates as those with moderate to mild intellectual disability (Dekker et al., 2002). However, it is argued that less attention has been paid to the associated cognitive limitations, academic challenges and the mental health of this higher proportion of the population with borderline IQ, as compared to the problems of the smaller proportion of people with intellectual disability (Ferrari, 2009; Gillberg & Soderstrom, 2003; Snell et al., 2009).

In contrast, children with intellectual disability and borderline IQ differed more with respect to social difficulties, as the results showed a gradual reduction in autistic features with higher IQ levels. This finding seems to be supported by studies showing that the rate of ASD or autistic features varies with the level of intellectual function

(e.g. Dekker & Koot, 2003; DiGuiseppi et al., 2010; Kamio et al., 2013). The inclusion of a dimensional measure in paper 1 revealed a similar trend, by showing that the general level of functioning increased significantly with higher IQ levels. This suggests that dimensional measures may give a more distinct picture of children's mental health problems and social difficulties, and supports the inclusion of dimensional measures as a supplement to categorical measures (Shaffer et al., 1983).

A normal to high level of intellectual function was shown to have a protective effect on mental health and social functioning in children included in the present thesis. Although the rate of mental disorders was higher than what would be expected in a general child population, children with IQ within the normal range or higher had significantly lower rates of mental disorders and social difficulties than children with IQ levels below the normal range. These findings are in line with the conception of higher IQ as a protective factor for children's outcome and development (Losel & Farrington, 2012; Masten & Coatsworth, 1998; Mathiassen et al., 2012). However, research has shown that intellectually gifted (defined as having at least a FSIQ score, a VIQ score, or a PIQ score of 120 or more) children and adolescents with ASD can have substantial psychosocial difficulties (Foley Nicpon, Doobay, & Assouline, 2010), suggesting that high IQ may not contribute to better outcomes once a severely impairing neurodevelopmental disorder is present.

Discrepant verbal- versus performance IQ was not found to be closely related to social functioning. As the direction of such a discrepancy and the relation with social functioning has been inconsistent across studies (Black et al., 2009; Charman et al., 2011; Martin et al., 2012), the influence of IQ discrepancy on social functioning in children remains unclear with this thesis. Still, uneven abilities may matter in the longer term, as persistence of significantly lower PIQ than VIQ, or nonverbal learning disability, has been shown to be associated with poor cognitive and social adaptive outcome in young adults with ASD (Hagberg, Nyden, Cederlund, & Gillberg, 2013).

Not surprisingly, gender was significantly associated with social functioning, with boys being more prone to show social difficulties than girls. This corresponds with findings from population studies, showing that boys display more autistic features than girls (Constantino & Todd, 2003; Kamio et al., 2013; Posserud et al., 2006). It also supports findings from recent twin studies showing that boys and girls have a different genetic risk of ASD, with girls appearing to require a greater familial etiologic load in order to exhibit the autistic phenotype (Robinson et al., 2013).

5.3 Methodological issues

5.3.1 Strengths

The main strengths of the current thesis are the population-based study samples and the use of validated instruments to assess social functioning, mental health, and intellectual function in children.

The use of the ASSQ allowed us to examine several facets of social functioning in children, including overall social difficulties, clusters of symptoms, as well as isolated symptoms. Examinations of the influence of intellectual function on clusters of symptoms (ASSQ factors) in paper 3 revealed a differentiated association between these variables. Furthermore, the use of multiple informants has been encouraged in reports of social functioning and child mental health problems, as several studies have reported low to moderate agreement between different raters (Achenbach, McConaughy, & Howell, 1987; De Los Reyes & Kazdin, 2005; Kumpulainen et al., 1999; Munkvold, Lundervold, Lie, & Manger, 2009; Renk & Phares, 2004; Verhulst, Koot, & Van der Ende, 1994). The use of parent and teacher reports in paper 2 provided interesting findings regarding parent-teacher agreement of autism spectrum symptoms in children with neurodevelopmental disorders, as compared to children with other chronic illnesses and children without chronic illness.

Using the K-SADS-PL allows for clinical decisions based on responses from the parent(s) and child, as well as the clinician's own observations. This may enhance the ability to identify true cases (increase the sensitivity of the instrument). A BCS study

assessing the influence of instrument on ADHD diagnosis showed only fair agreement between the K-SADS-PL and the DAWBA (κ = 0.31). The K-SADS-PL identified more children with an ADHD diagnosis than the DAWBA, which seemed to underestimate the rate of children with ADHD (Posserud et al., 2013). Furthermore, research has shown that even experienced clinicians are inclined to ignore important information (e.g. information required to diagnose coexisting disorders) when not using (semi-)structured instruments, such as the K-SADS-PL (Ambrosini, 2000). The inclusion of a global assessment of functioning (CGAS) could be considered an additional strength, as a recent study showed that psychosocial impairment (as assessed by the CGAS) in childhood uniquely predicted future disability pension in adults with ADHD, even when controlling for the presence of an ICD-10 disorder (Mordre, Groholt, Sandstad, & Myhre, 2012). This highlights the importance of assessing both symptoms and functional impairment as part of a diagnostic evaluation.

5.3.2 Limitations

Assessment of social functioning

The ASSQ was used to assess social functioning in the present thesis. As this instrument only includes negatively worded items, there was a focus on difficulties rather than strengths of social functioning. Choosing a problem focus without considering strengths may be considered a limitation. On the other hand, it has been suggested that the internal consistency of a scale may increase when all items are phrased in the same way (Ronning, Handegaard, Sourander, & Morch, 2004), and the ASSQ has been shown to have good internal consistency (Posserud et al., 2008).

Furthermore, teacher and/or parent reports on the ASSQ were used to assess social functioning. Teachers' perspective may prove useful when assessing social functioning, because teachers have the opportunity to compare children's functioning within a larger group of peers (La Greca & Lemanek, 1996; Macintosh & Dissanayake, 2006; Parker & Asher, 1987). They may, however, be biased by other knowledge about the child, such as academic performance (Newcomb, Bukowski, &

Pattee, 1993; Parker & Asher, 1987). Parents may also be useful informants of social functioning, because they have knowledge about their children's social behavior across multiple contexts (Macintosh & Dissanayake, 2006), although they may observe their children mostly at home and not in direct interactions with peers (Reiter-Purtill & Noll, 2003). However, the child and particularly the child's peers may be considered the best source of information of social functioning, because peers have the most daily interactions with the child (Reiter-Purtill et al., 2009). Peer report was not obtained in the BCS, and there is no self-report version of the ASSO. It has been argued that children and adolescents may be less reliable as informants in the context of ASD or autistic features, because these problems may impair the ability of children and adolescents to judge their own social behavior (Barnhill et al., 2000; Foley Nicpon et al., 2010). Moreover, although the results of paper 2 showed that the parent-teacher agreement over single items in children with neurodevelopmental disorders was generally poor, the agreement over ASSQ scores was higher for children with neurodevelopmental disorders than for the two other groups, indicating that information from either parents or teachers could be sufficient when assessing these children

Assessment of mental health

The Wave 1 Phase 3 sample of the BCS was oversampled for children with physical and developmental disabilities. The appropriateness of using the K-SADS-PL with children who are severely affected by physical and intellectual disability was recently questioned in a study of mental disorders in children with CP (Bjorgaas et al., 2012), as the interviewer found it impossible to distinguish between symptoms of physical discomfort and symptoms of discomfort due to mental health problems in children with a severe degree of CP combined with intellectual disability. However, this did not seem to represent a major problem in the BCS Wave 1 Phase 3 sample, as the K-SADS-PL was incomplete only for three of the 329 children participating in this phase of the study (which may or may not have been due to these children having a severely disabling condition).

The K-SADS-PL may generate 32 DSM-IV childhood mental disorders. However, we did not differentiate between disorders or report the coexistence of disorders. A mental disorder was defined as any mental disorder that was definitely present at the time of the data collection. The reason for using such a crude definition was due to the sample size. As the sample was split between children with and without chronic illness as well as between three IQ levels, exposing the numbers of children with specific disorders, or even less crude categories of mental disorders (such as internalizing versus externalizing disorders), would pose a threat to confidentiality. Still, information about type of disorder is of interest, as research shows that outcome and prognosis in the short or in the long term varies with different disorders and with the coexistence of disorders (Mordre, Groholt, Kjelsberg, Sandstad, & Myhre, 2011; Mordre et al., 2012; Pardini & Fite, 2010; Sourander et al., 2007).

Assessment of chronic illness

Some issues pertaining to the definition of chronic illness needs to be mentioned. First, chronic illness was measured as reported by parents, without medical verification of the reported illnesses or their severity. Assessment of chronic illness differs between clinical and population studies. Clinical studies usually allow for collecting more detailed information about the specific diagnosis or diagnoses that are being studied, while population studies, such as the BCS, are usually aimed at covering several areas of children's health, limiting the amount of information that may be collected about each area of interest. However, the parent reported chronic illnesses were easily recognizable by the pediatrician in charge of the categorization.

Intellectual disability and syndromes involving intellectual disability was categorized as neurodevelopmental disorders in the studies included in the current thesis. In relation to this, one may ask why the group without chronic illness in paper 1 consisted of children with a FSIQ level below 70, which is part of the definition of intellectual disability according to the diagnostic manuals (American Psychiatric Association, 2013; World Health Organization, 1999). The reason for this is that

many children with mental health and/or cognitive problems were identified through their participation in the BCS.

Assessment of intellectual function

The Norwegian translation of the WISC-III was not appropriately validated and standardized, questioning the appropriateness of using the Swedish norms to evaluate the results of the Norwegian version (Lundervold, Posserud, Sorensen, & Gillberg, 2008; Sundberg, Egeland, Andreassen, & Stensli, 2006). The WISC-III did not differentiate between children scoring two standard deviations or more from the population mean (Nilsen, 2005)¹, and compared to other versions of the WISC, more children obtained IQ scores below 70 (Kjenseth, 2010; Sundberg et al., 2006)^{2,3}. This may contribute to explain the skewed distribution of IQ scores towards the lower end of the IQ scale shown in paper 1 and paper 3 of the current thesis. However, it may also be due to the recruitment of participants to the Wave 1 Phase 3 of the BCS.

Chronic illness and intellectual function as risk factors

Apart from chronic illness and intellectual function, a range of other risk and protective factors not considered in the present thesis, such as genes (Robinson et al., 2013; Thapar & Stergiakouli, 2008), socioeconomic status (Boe et al., 2012; Stroschein, 2005), life events (Jensen et al., 2013; Rasmussen et al., 2014), temperament (Cowen et al., 1996; Losel & Farrington, 2012), social support (Brausch & Decker, 2013), and family environment (Bowes et al., 2010), may affect children's mental health and social functioning. The association between chronic illness and mental health may also be explained by other cognitive factors than intellectual function, such as executive (Bottcher, 2010; Huijbregts & de Sonneville, 2011; Kelly et al., 2012; Rose & Holmbeck, 2007). In a study using the Kiddie-SADS-PL to assess mental health in children with CP, communication problem was shown to be a

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¹ Available in Norwegian only

^{2,3} Summaries of the articles in English are available online at http://www.psykologtidsskriftet.no/index.php?seks_id=111969&a=2 and http://www.psykologtidsskriftet.no/index.php?seks_id=250270&a=2, respectively.

significant predictor of mental disorders, while intellectual disability was not (Bjorgaas et al., 2012). However, in a more recent study of the same CP-population, intellectual disability, but not communication problem, was significantly associated with autism spectrum symptoms. Future studies should include standardized measures of several cognitive functions, in order to evaluate their individual contribution to social functioning and mental health in children.

5.3.3 Representativeness

Certain issues regarding the representativeness of the samples included in the three papers needs to be mentioned. Nonresponse is a general challenge in epidemiological research and may affect the generalizability of the research findings. Population surveys of mental health problems in children, such as the BCS, may be specifically susceptible to nonresponse bias because the children's parents, who are the ones who consent to participate, might be unwilling to report such problems (Owens et al., 2002).

Based on the teacher ratings of 2544 children for whom parent ratings were not obtained in Wave 1 Phase 1 of the BCS, the impact of nonresponses on estimates of mental health problems was examined. Children rated to have mental health problems by their teachers were less likely to participate, but this mainly concerned children with moderate levels of symptoms (Stormark, Heiervang, Heimann, Lundervold, & Gillberg, 2008).

In Wave 1 Phase 2, 645 (44.6 % of invited) screen positive and 364 (49.7 % of invited) screen negative children participated. The nonparticipation from Phase 1 to Phase 2 in Wave 1 did not seem to be related to the children's level of mental health problems, as indicated by the parent and teacher questionnaires in Phase 1. Age and sex differences between participants and nonparticipants, screen positive and screen negative children, were also non-significant (Heiervang et al., 2007).

The Wave 1 Phase 3 sample included a large group of high-risk children (screen positive in Phase 1 and/or with a DAWBA diagnosis from Phase 2). Due to the

recruitment of participants to this phase, the frequency of mental health problems in children both with and without chronic illness was expected to be higher than in the total BCS population. The recruitment of participants also influenced the distribution of FSIQ scores, which were skewed towards the lower end of the FSIQ scale. These issues affected the representativeness and generalizability of the paper 1 (Ryland, Lundervold, Elgen, & Hysing, 2010) and paper 3 findings (Ryland, Hysing, Posserud, Gillberg, & Lundervold, 2014).

In Wave 2 Phase 1, a total of 5781 children from a target population of 9281 children participated. The impact of nonresponse on estimates of mental health has not been assessed in Wave 2. However, analyses conducted in paper 2 showed that the participants in Wave 2 had somewhat lower parent and teacher reported ASSQ total scores compared to the Wave 1 sample, but the effect sizes were small (Ryland, Hysing, Posserud, Gillberg, & Lundervold, 2012).

5.3.4 Ethical considerations

Disseminating knowledge about the risk of mental health problems and social difficulties in relation to chronic illness/neurodevelopmental disorders and cognitive impairment is important, but also raises ethical challenges. Ideally, it will motivate policy- and decision makers to provide increased resources to improve health services for children. On the other hand, awareness of additional problems in already vulnerable groups of children could feel stigmatizing to affected families. When disseminating such knowledge, it is therefore important to emphasize that although some children are at increased risk of co-existing mental health problems and social difficulties, this does not account for every child with a chronic illness, a neurodevelopmental disorder, or a cognitive deficit.

Asking people about mental health problems and social difficulties is also of ethical concern. Participants may provide such information in an attempt to get proper help. In the BCS, all participants were given information about how to contact the researchers if they needed further assistance after completing the questionnaire. Furthermore, all children with a DAWBA diagnosis from Wave 1 Phase 2 were

invited to participate in Phase 3, which included a diagnostic interview and a neuropsychological assessment. When mental health problems and/or cognitive deficits (such as IQ below 70) were detected, the families who needed further assistance were helped to get in touch with the proper school or health services.

5.4 Clinical implications

The results of the present thesis highlight the importance of taking intellectual function into account when assessing social functioning and mental health in children. Not only intellectual disability, but also borderline intellectual functioning (IQ 70-84) may have a considerable influence on mental health that warrants attention. Given that mental health problems tend to persist across childhood and into early adult life in people with intellectual disability (Einfeld et al., 2006), the need for preventive interventions at an early age for children with borderline IQ seems warranted (Emerson et al., 2010).

Altogether, the associations between chronic illness, intellectual function, mental health and social functioning reported in the studies of the present thesis call for a broad perspective when assessing children. Children presenting with impairing neurodevelopmental problems are frequently seen by only one specialist, making cooccurring problems often go unrecognized. It is argued that some of these problems could have been avoided if clinicians were more aware of the common symptom overlap and co-existence of disorders (Gillberg, 2010, 2013). In the case of ASD, research indicate that it is the co-existing problems, such as nonverbal learning disability (Hagberg et al., 2013), low childhood IQ (Billstedt et al., 2005, 2007; Gray et al., 2012; Howlin et al., 2004), and delayed speech (Billstedt et al., 2007), that predict poor adult outcomes, and not the autism in itself. This further calls for the need for a broad and multidisciplinary perspective when assessing and treating children presenting with impairing symptoms early in life, taking all co-occurring problems into account (Carlsson et al., 2013; Gillberg, 2010; Hedvall et al., 2013; Kantzer, Fernell, Gillberg, & Miniscalco, 2013; Klein-Tasman, Phillips, Lord, Mervis, & Gallo, 2009; Levy et al., 2010; Lindblad, Gillberg, & Fernell, 2011).

Applying such an approach could perhaps contribute to early identification, better prediction of outcome, and individually adapted interventions (Gillberg, 2010, 2013).

As presented in the introduction of this thesis, social interaction with peers is considered to be of great importance for the social development of all children. Peer relations provide a significant source of emotional support (Hartup, 1996) and the opportunity to learn appropriate social rules and social behaviors (Parker & Asher, 1987). They can predict later psychopathology (Parker & Asher, 1987; Ten Have et al., 2013) and moderate the relation between risk factors and the development of psychopathology in children (Bukowski & Adams, 2005). Peer relations may be particularly important for children with chronic illness, as support from close friends can buffer the impact of illness related stressors, such as adapting to a chronic illness or coping with a complex medical treatment (La Greca et al., 1995; La Greca et al., 2002). In light of the present and previous findings (Blackman & Conaway, 2013; Hysing et al., 2009; Martinez et al., 2011; Pinquart & Shen, 2011) showing that children with neurodevelopmental disorders are at particular risk of social difficulties, assistance to engage in social interaction with peers seem especially vital to this group of children.

Some researchers recommend social skills interventions for children with chronic illness (Martinez et al., 2011), but others are cautious about recommending this, even for children with CNS-disorders (Noll & Bukowski, 2012). If the primary reason for the intervention is based upon parent and/or teacher reported social difficulties, providing social skills training to children with chronic illness may meet the concerns of parents and/or teachers. If child- or peer reports of such difficulties are absent, however, the justification for the intervention is weaker and it could be potentially harmful, i.e. make the children doubt their own social competence (Lilienfeld, 2007; Noll & Bukowski, 2012). Social skills training programs can also be implemented in the schools and be directed towards all children as part of the education (La Greca, 1983). A different strategy showing promising results is the use of peers as the target of the intervention. A recent peer-mediated intervention designed for children with ASD, teaching peers strategies to help classmates who have trouble making friends,

resulted in significant improvements on several measures, including friendship nominations and teacher ratings. Most importantly, these improvements seemed to sustain from one school year to the next. Given that children with CNS-disorders frequently show social difficulties associated with ASD, it is possible that this peer intervention could be effective for this group of children (Kasari, Rotheram-Fuller, Locke, & Gulsrud, 2012)

5.5 Future research

The influence of intellectual function on mental health and social functioning in children with and without chronic illness has been emphasized in the current thesis. However, as presented in the introduction, other cognitive functions have also been shown to be related to these areas of child functioning. Future studies should include other measures of cognitive functioning, in order to evaluate their individual contribution to social functioning and mental health in children. Furthermore, in the case of ASD, cognitive abilities have recently been associated with adaptive functioning in preschool children (Hedvall et al., 2013) and young adults (Hagberg et al., 2013). Measures of adaptive functioning should therefore be included in future studies assessing the influence of cognitive functions on mental health and social functioning in children.

Wave 4 of the BCS (youth@hordaland) may provide further opportunities to study the relationship between chronic illness and mental health and social functioning. High school dropout is increasing in Norway, and has become a public health concern (De Ridder et al., 2012). It may have detrimental effects to the individual youth, as well as severe socio-economic consequences, with more and more youth receiving disability pension (De Ridder, Pape, Cuypers, et al., 2013). High school dropout has been associated with chronic illness, but there is a need for more research on this important topic, including the mechanisms involved, as well as studies taking a life course perspective (De Ridder, Pape, Johnsen, et al., 2013). Wave 4 of the BCS may contribute to extend this knowledge. In this wave, self-reports about physical and mental health, information about school absence and the reasons for such absence,

among other variables, were obtained from around 10 000 youth, and data on academic grades and school attendance were obtained from the school registry. The majority of the participants also consented to linkage to registry data, allowing researchers to obtain information about future academic attainments and school dropout. By this, we could study how the associations between chronic illness, cognitive abilities, and mental health and social functioning in childhood influence academic attainments/school dropout and health and well-being in late adolescence and young adulthood. Extending this knowledge could hopefully contribute to improve the education of youth with chronic health challenges, to prevent further high school dropout.

5.6 Conclusions

In this thesis, data from the Bergen Child Study were used to extend our knowledge about how chronic illness and intellectual function is related to mental health and social functioning in children. The results show that chronic illness is associated with a twofold increased risk of having a mental disorder, and that neurodevelopmental disorders in particular are associated with an increased risk of social difficulties. IQ is shown to be closely related to mental health and social functioning in children, as the rate of mental disorders and social difficulties gradually decline with higher IQ, and vice versa. The present thesis emphasizes the importance of taking intellectual function into account when assessing mental health and social functioning in children, and calls for broad assessments of children with neurodevelopmental problems before reaching clinical conclusions. Future studies should assess other aspects of cognitive functioning and include measures of adaptive functioning, to further extend our knowledge about the association between cognitive functions and outcome in children.

Source of data

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