KATI RANTANEN

Neurocognitive Functioning and Social Competence in Preschool Children with Epilepsy

ACADEMIC DISSERTATION
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Tampere, August 2012 Kati Rantanen

Abstract

Epilepsy is one of the most common neurologic conditions in children. Earlier studies have demonstrated both neurocognitive impairment and behavioral problems in school-aged children with epilepsy. The aim of this dissertation was to investigate neurocognitive functions and social competence in preschool-aged children with epilepsy to find out whether these problems were already present at younger ages.

This dissertation is a population based cohort study of neurocognitive functions and social competence in preschool-aged (i.e. three to six years old) children with epilepsy ($N = 64$). The results indicated neurocognitive impairments, mental retardation or severe learning disabilities in half of the cohort. These impairments were typically seen in children with complicated epilepsy, i.e. those with underlying central nervous system pathology or additional neurologic conditions. Specific neurocognitive problems in language, verbal-short-term memory, and attention were also found in children with uncomplicated epilepsy. In addition to neurocognitive problems, preschool-aged children with epilepsy had weaker social competence compared to their healthy peers. Poorer social competence reported by parents was demonstrated in poorer social skills and more frequent behavior problems (especially internalizing problems).

A review of earlier studies on social competence indicated that social competence was not usually defined or problematized. The studies reviewed mostly focused on social adjustment and demonstrated problems in this area in school-aged children with epilepsy. However, not all aspects of social competence have been studied. Therefore, more studies on social skills and performance are needed to increase our understanding of social competence among children with epilepsy. Also, future studies should address the role of epilepsy-related factors and neurocognitive functions as mediating factors for social competence.

Tiivistelmä

Epilepsia on yleisimpiä lastenneurologisia sairauksia. Epilepsian ja kognitiivisten toimintojen suhdetta on aikaisemmin tutkittu etenkin kouluikäisillä lapsilla. Myös epilepsiaan liittyviä käyttäytymishäiriöitä on tutkittu paljon kouluikäisillä lapsilla. Tutkimuksissa on todettu, että epilepsia, samoin kuin muutkin neurologiset sairaudet lisäävät sekä kognitiivisten että käyttäytymisen ongelmien todennäköisyyttä. Riski on erityisesti suurentunut niillä lapsilla, joiden epilepsian syy on rakenteellinen tai aineenvaihdunnallinen. Kuitenkin myös niillä lapsilla, joilla on geneettinen (tai idiopaattinen) epilepsia on todettu kapea-alaisempia neurokognitiivisia erityisvaikeuksia, esimerkiksi tarkkaavuudessa ja lyhytkestoisessa työmuistissa.

Tässä väitöskirjatyössä selvitettiin sekä neurokognitiivisia toimintoja että sosiaalista toimintakykyä eli kompetenssia alle kouluikäisillä epilepsiaa sairastavilla lapsilla. Tutkittavat lapset olivat Pirkanmaan sairaanhoitopiirin seurannassa olevia lapsia, joista oli poimittu väestöpohjainen kohortti (N = 64). Noin puolella tutkittavissa oli kehitysvamma tai siihen verrattavissa oleva älyllinen suorituskyky. Myös niillä lapsilla, joiden kognitiivinen suoriutuminen oli yhdenmukainen ikäodotusten kanssa, todettiin ryhmätasolla vaikeuksia kielellisissä toiminnoissa, lyhytkestoisessa kielellisessä muistissa ja tarkkaavuudessa. Myös vanhemmat raportoivat kyselylomakkeissa enemmän tarkkaavuuden ja käyttäytymisen vaikeuksia kuin terveiden ikätovereiden vanhemmat.

Väitöskirjatyöhön sisältää systemaattisen katsauksen aikaisempiin epilepsiaa sairastavien lasten sosiaalista toimintakykyä käsitteleviin tutkimuksiin. Katsauksen tulokset osoittavat, että aikaisemmissa tutkimuksissa sosiaalisen kompetenssin käsitettä ei ollut määritelty. Lisäksi tutkimukset keskittyivät lähes yksinomaan sosiaalisen sopeutumisen ongelmiin eli käyttäytymishäiriöihin. Tutkimukset epilepsiaa sairastavien lasten sosiaalisista taidoista tai sosiaalisesta suoriutumisesta olivat merkittävästi vähäisempiä. Tulevaisuudessa näihin keskeisiin sosiaalisen kompetenssin osa-alueisiin on syytä keskittyä enemmän, jotta saadaan kokonaiskuvaa epilepsiaa sairastavien lasten sosiaalisesta toimintakyvystä. Lisäksi jatkotutkimusten on hyvä selvittää epilepsiaan ja neurokognitiivisiin toimintoihin liittyvien tekijöiden merkitystä sosiaalista kompetenssia välittävinä tekijöinä.

Kliinisessä työssä on suositeltavaa tehdä neuropsykologinen kartoitus varhaisvaiheessa kaikille epilepsiaan sairastuville lapsille. Kognitiivisten tekijöiden ohella enemmän huomiota on syytä kiinnittää myös käyttäytymisvaikeuksiin ja iänmukaisten sosiaalisten taitojen tukemiseen.

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Abbreviations

AED	Antiepileptic medication
BSID-II	Bayley Scales of Infant Development-II
CBCL	Child Behavior Checklist
CE	Complicated epilepsy
CNS	Central nervous system
CPRS-R	Conners' Parent Rating Scale - Revised
DQ	Developmental Quotient
EEG	Electroencephalogram
FE	Focal (i.e. partial) epilepsy
FSIQ	Full Scale Intelligence Quotient
GE	Generalized epilepsy
ILAE	International League Against Epilepsy
IQ	Intelligence Quotient
MRI	Magnetic resonance imaging
NEPSY	The Developmental Neuropsychological Assessment, NEPSY-test
PIQ	Performance Intelligence Quotient
TCI	Transient cognitive impairment
UCE	Uncomplicated epilepsy
VIQ	Verbal Intelligence Quotient
VSMS	Vineland Social Maturity Scales
WISC-III	Wechsler's Intelligence Scale for Children – III edition
WPPSI-R	Wechsler's Preschool and Primary Scale of Intelligence - Revised

1. Introduction

Epilepsy is one of the most common neurological disorders in childhood. However, historically, epilepsy has been related to magic and religious beliefs about the divine or demonic origin of the disease (Diamantis, Sidiropoulou & Magiorkinis, 2010). A scientific conception of epilepsy as a disease and symptom was formulated in the past two centuries from a sacred or contagious disease to a more neutral view, where people with epilepsy were seen as patients rather than being possessed (Sidiropoulou, Diamantis & Magiorkinis, 2010).

Epilepsy is a heterogeneous condition, characterized as recurrent seizures (Aicardi, 1999), and including a variety of seizure, epilepsy and epilepsy syndrome types. The International League Against Epilepsy (ILAE; Fisher, Boas, Blume, Elger, Genton, Lee, et al., 2005) defines epilepsy as *"a disorder of the brain characterized by an enduring predisposition to generate epileptic seizures and by the neurobiologic, cognitive, psychological, and social consequences of this condition"*. During the last 50 years, significant advances in understanding the etiology of epilepsy have taken place; genetic factors and neuroimaging especially have been a focus of intense interest (Shorvon, 2011). Similarly, antiepileptic medication has improved: the older antiepileptic drugs (AEDs) developed before the 1940s were replaced with newer ones in the 1990s (Bourgeois, 1998, 2002, 2004; Kwan & Brodie, 2001). Along with these advances, the perspective in understanding epilepsy and its association with cognitive and social functions has changed over the decades. From the beginning of the 20th century systematic research has been conducted on the impact of epilepsy on cognition.

The first studies on cognitive functions in children with epilepsy focused on intellectual functions, and epilepsy was mostly regarded as a degenerative disease, but the focus has shifted to the study of the neurocognitive profile specific to various epilepsy and seizure types (see Dodrill, 2004; Seidenberg, Pulsifer & Hermann, 2007). Also, epilepsy related factors contributing to or associated with cognitive functions have been of interest. There was a period when the severity or benignity of epilepsy was

judged exclusively by the frequency of seizures and the likelihood of remission (Deonna & Roulet-Perez, 2005). Deonna and Roulet-Perez (2005) called this time *'an era of optimism'*, when epilepsy was regarded as benign condition with recovery before adolescence in children with uncomplicated epilepsy. Then, learning and behavioral problems in intellectually normal children were mostly explained by a psychological reaction to the neurologic condition.

A change in perspective took place during the 1990's. Overt seizures were more frequently seen as the tip of the iceberg (Aicardi, 1999), and nowadays cognitive and social impairments are recognized as an elementary part of the epilepsy itself rather than as secondary deficits due to the adjustment problems of a chronic condition (Berg, 2011; Elger, Helmstaedter & Kurthen, 2004). There is also growing agreement that although in some childhood onset epilepsies the long-term seizure outcome is regarded as favorable (Ben-Ari & Holmes, 2006), the later cognitive and psychosocial outcome e.g. on school achievement, employment, and marriage may be poor (Jalava, Sillanpää, C. Camfield & Camfield et al., 1997; Sillanpää, Jalava, Kaleva & Shinnar, 1998; Wakamoto, Nagao, Hayashi & Morimoto, 2000). Studies have mostly been conducted on infants or school-aged children, but studies on toddlers and preschool-aged children are still rare. In this dissertation, both aspects, neurocognitive functioning and social competence, were investigated in a cohort of preschool-aged (i.e. three to six years old) children with epilepsy.

1.1 Epilepsy in children

1.1.1 Diagnosis and classification

Epilepsy is defined as recurring unprovoked seizures (Aicardi, 1999). Epilepsies are classified according to the ILAE criteria that have been published as classifications of seizures and epilepsies since 1960 (Commission on Classification and Terminology of the International League Against Epilepsy, 1981, 1985, 1989; Merlis, 1970). Recently, the ILAE classification was re-evaluated to update the terminology and concepts for the classification of seizures and epilepsies reflecting advances in clinical neuroscience and genetics (Berg, Berkovic, Brodie, Buchhalter, Cross, van Emde Boas, et al., 2010).

Epilepsies were previously classified according to their etiology as idiopathic, symptomatic and cryptogenic epilepsy (ILAE; Engel, 2001). These have now been replaced with the terms genetic, structural-metabolic, and unknown epilepsy (Berg et al., 2010). Idiopathic (or genetic) epilepsy refers to epilepsies resulting directly from a known or presumed genetic deficit and without any underlying structural brain lesion (Berg et al., 2010). These epilepsies often have age-dependent clinical manifestation (Engel, 2001; 2006; Hommet, Sauerwein, De Toffol & Lassonde, 2006). Symptomatic (or structural/metabolic) epilepsy refers to epileptic seizures resulting from an identifiable structural or metabolic condition or disease of the brain (Berg et al., 2010; Engel, 2001). Cryptogenic (i.e. unknown) epilepsy refers to epilepsies with underlying as cause yet unknown (Berg et al., 2010). Earlier, cryptogenic epilepsy was seen as synonymous with probably symptomatic i.e. it was assumed to be symptomatic, but no etiology had been identified (Engel, 2001). In addition to etiology, epileptic seizures are classified into generalized (GE) and focal (FE) seizures (Engel, 2001). The ILAE (Berg et al., 2010) defines generalized seizures as originating within, and rapidly engaging, bilaterally distributed neural networks within the central nervous system. The focal seizures originate within networks limited to one hemisphere and are either discretely localized or more widely distributed.

Most genetic epilepsies have been regarded as uncomplicated which implies that there are no other neurological signs or symptoms and cognition is within normal range or only slightly impaired (Elger et al., 2004; Hommet et al., 2006; Mandelbaum & Burack, 1997; Motamedi & Meador, 2003). Although children with uncomplicated epilepsy (UCE) have epilepsy, their neurological and social development is apparently age appropriate (Berg, Langfitt, Testa, Levy, DiMario, Westerveld, et al., 2008). Sillanpää (1992) referred to these children with epilepsy but without any associated neurological disorder or other chronic illnesses as ‘epilepsy only’. The term complicated epilepsy (CE) (or ‘epilepsy plus’; Sillanpää, 1992) has been used to refer to epilepsies of remote symptomatic / structural or metabolic origin or epileptic encephalopathy (Berg et al., 2008). The neurologic and cognitive development of these children is often more compromised than that of children with UCE.

1.1.2 Epilepsy in the developing brain

Early childhood is a critical period for central nervous system (CNS) development, during which the normal maturation of the CNS and the expected developmental course of cognitive functions may be disrupted or interfered with (Elger et al., 2004; Hommet et al., 2006; Motamedi & Meador, 2003). Epileptic activity (e.g. the presence of an active electrophysiological epileptic focus or repetitive epileptiform generalized discharges) affecting brain function is discontinuous and potentially reversible in nature, and therefore the effects are often differentiated from static congenital or acquired brain disorder (Deonna & Roulet-Perez, 2005).

The developing, immature brain is more epileptogenic than the mature brain (Moshé, 1987, 1993), which partly explains the higher prevalence of epilepsy during childhood. The risk for epilepsy is highest during the first year of life (C. Camfield, Camfield, Gordon, Wirrell & Dooley, 1996), and the median age at onset of seizures is between 5 and 6 years (Berg, Shinnar, Levy & Testa, 1999). In developed western countries the prevalence of active epilepsy in children is 3–11 per 1,000 children (Larsson & Eeg-Olofsson, 2006). In Finland, the prevalence is 2–4 per 1,000 in children less than 16 years of age (Eriksson & Koivikko, 1997; Sillanpää et al., 1998). Increased seizure susceptibility in children is suggested to be due to e.g. functional immaturity of a substantia nigra, GABA-sensitive output system (Moshé, 1987; Veliskova, Velisek, Sperber, Haas & Moshé, 1994). Animal studies have shown that epilepsy can directly interfere with brain structure, e.g. alter the development of cortical networks, create abnormal local synaptic circuits, or enhance later epileptogenicity (Ben-Ari & Holmes, 2006; Holmes, 2004). Early seizures may also increase the later vulnerability of the mature brain to the effects of seizures (Holmes, 2004; Squier, Salisbury & Sisodiya, 2003).

In addition to the maturation of the CNS, childhood, including the preschool years, is a phase of rapid cognitive and psychosocial development. There is a relationship between CNS maturation and the development of cortical functions (Aylward, 1997; Kagan & Herschkowitz, 2005; Luria, 1981). The development of psychological functions and abilities is partially dependent on specific changes in brain anatomy, physiology and biochemistry. During childhood (i.e. between 2 and 8 yrs), some of the most important features of cognitive development are increasing semantic

representations, integration of past and present, and child's ability to inhibit inappropriate behavior (Kagan & Herschkowitz, 2005). These developmental changes are facilitated with myelination of long cortical tracts, synaptic densities (especially in prefrontal cortex), concentrations of neurotransmitters, pruning and shift of predominant blood flow from the right hemisphere to the left hemisphere (Anderson, Northam, Hendy & Wrennall, 2001; Kagan & Herschkowitz, 2005). For example, the linear increase of memory performance seen is greatest between 4 and 5 years (Gathercole, Pickering, Ambridge & Wearing, 2004) may partly be explained by the achievement of hippocampal integrity due to proximal dendrites reaching adult size and form (see Kagan & Herschkowitz, 2005).

The development of primary and secondary functions forms a foundation for the subsequent development of more complex and associative cortical functions, skills and competencies (e.g. academic skills and social competence) (Luria, 1981). Due to different critical and sensitive periods, specific functions (e.g. language) mature separately (Anderson et al., 2001). Therefore the child's age at the time of a CNS disruption is important. Although, a CNS related condition may often compromise the expected developmental course, parallel or alternative routes for the development of skills may also exist (see Anderson et al., 2001).

1.1.3 Epilepsy-related factors and development

A number of studies (e.g. Battaglia, Rando, Deodato, Bruccini, Baglio, Frisone, et al., 1999; Berg et al., 2008; Chaix, Daquin, Monteiro, Villeneuve, Laguitton & Genton, 2003; Cormack, Cross, Isaacs, Harkness, Wright, Vargha-Khadem, et al., 2007; Høie, Mykletyn, Sommerfelt, Bjørnæs, Skeidsvoll & Waaler, 2005; Kobayashi, Ohtsuka, Ohno, Tanaka, Hiraki & Oka, 2001; Mangano, Fontana & Cusumano, 2005; Vasconcellos, Wyllie, Sullivan, Stanford, Bulacio, Kotagal, et al., 2001) have shown that the etiology and early age at onset of epilepsy are two of the most important factors associated with cognitive and social functioning in children with epilepsy. The most consistently reported factor related to cognitive and social impairment is etiology (Nolan, Redoblado, Lah, Sabaz, Lawson, Cunningham, et al., 2003). In the 19th century, scientific interest focused on 'genuine epilepsy' i.e. idiopathic epilepsy (Shorvon, 2011). Since there are no confounding variables due to the absence of other neurologic

disease or lesion in idiopathic epilepsy, it has been regarded as a good model to study the independent effects of epilepsy on cognitive and social functions (Elger et al., 2004). Symptomatic or organic epilepsy was considered a manifestation or symptom of the lesion rather than epilepsy per se (Shorvon, 2011). Both cognitive impairments (including mental retardation) and behavior problems are reported more frequently in children with symptomatic epilepsy than in children with idiopathic or cryptogenic epilepsy (Rodin, 1989; Svoboda, 2004).

As demonstrated in several studies, early age at onset of seizures is another significant risk factor contributing to both cognitive impairment (Battaglia et al., 1999; Bourgeois, Prensky, Palkes, Talent & Busch, 1983; Bulteau, Jambaque, Viguier, Kieffer, Dellatolas & Dulac, 2000; Cormack et al., 2007; Freitag & Tuxhorn, 2005; Mangano et al., 2005; Smith, Elliott & Lach, 2002) and behavior problems (Dunn, Austin & Huster, 1997; Freilinger, Reisel, Reiter, Zelenko, Hauser & Seidl, 2006; Keene, Manion, Whiting, Belanger, Brennan, Jacob, et al., 2005). Studies conducted on candidates for epilepsy surgery (Vasconcellos et al., 2001) and on infants with epilepsy (Vendrame, Alexopoulos, Boyer, Gregas, Haut, Lineweaver, et al., 2009) have shown that early age at seizure onset may be a risk factor for cognitive impairment independent of etiology. Children with seizure onset during the first year of life are especially likely to have poorer cognitive outcome (Cormack et al., 2007; Mangano et al., 2005; Vanderlinden & Lagae, 2004).

There is some controversy concerning the role of duration of epilepsy in impairments associated with childhood epilepsy. Rather than being an independent factor contributing to cognitive or social functions, duration is regarded as a composite factor reflecting several other variables, e.g. lifetime number of seizures, age at onset, and number of AEDs (Dodrill, 2004; Vingerhoets, 2006). On the one hand, duration of epilepsy has been found to be associated with cognitive (Elger et al., 2004; Smith et al., 2002) and adverse long-term psychosocial outcomes, even in patients attaining remission (Shinnar & Pellock, 2002). On the other hand, several studies (Austin, Harezlak, Dunn, Huster, Rose & Ambrosius, 2001; Dunn et al., 1997; Fastenau, Johnson, Perkins, Byars, deGrauw, Austin, et al., 2009; Kolk, Beilmann, Tomberg, Napa & Talvik, 2001; Oostrom, Smeets-Schouten, Kruitwagen, Peters, Jennekens-Schinkel & Dutch Study Group of Epilepsy in Children, 2003) have shown that cognitive and social impairment may already be present at the time of seizure onset in

children with idiopathic or cryptogenic epilepsy. Thus, the conclusion that cognitive deficits should be understood as the initial symptoms of epilepsy rather than the long-term effects due to chronic epilepsy (Berg et al., 2010; Elger et al., 2004) is supported.

Other epilepsy related factors that may have an impact on child's development include seizure type, frequency, and AEDs. When compared to the possible impact of etiology or age at onset on developmental factors, less is known about the effects of epileptic seizures on neurocognitive and social functioning (Baker & Taylor, 2008; Dodrill, 2004; Vingerhoets, 2006). Children with focal seizure types have been found to perform cognitively better than children with generalized seizures (Dodrill, 2004; Høie et al., 2005; Mandelbaum & Burack, 1997). The association between seizure frequency and cognitive function has also been addressed (Aldenkamp & Bodde, 2005; Elger et al., 2004). Seizure frequency has been found to coincide with both symptomatic etiology and additional neuroimpairments (Eriksson & Koivikko, 1997; Ramos-Lizana, Aguilera-López, Aquirre-Rodríguez & Cassinello-García, 2009). With respect to behavioral problems, there is also some evidence that seizure frequency or recurrent seizures, especially during the past year, is a more significant predictor of problems than age at seizure onset (Caplan, Sagun, Siddarth, Gurbani, Koh, Gowrinathan, et al., 2005; Keene et al., 2005; see also, Ott, Siddarth, Gurbani, Koh, Tournay, Shields, et al., 2003).

AEDs may affect both cognitive functions and behavior, but in the majority of children these effects are regarded as slight. Studies conducted on adults show more cognitive effects to be related to older rather than newer AEDs (Bourgeois, 2004). Studies conducted on children reveal that especially polytherapy (i.e. several AEDs) often related to refractory seizures is associated with neurocognitive problems, lower intellectual performance (Bulteau et al., 2000; Rejnö-Habte Selassie, Viggedal, Olsson & Jennische et al., 2008), and behavioral problems (Freilinger et al., 2006). However, the effect of AEDs on development may also be positive. For example, Sirén, Kylliäinen, Tenhunen, Hirvonen, Riita and Koivikko (2007) demonstrated that AEDs improved neurocognitive functions (e.g. attention, fine-motor fluency and visual memory) in children with absence epilepsy. Similarly, Kölfen, Edrich, König and Formanski (2001) demonstrated the AEDs improved behavior and after their withdrawal the children without relapse did not have any behavioral or psychiatric disturbances and their performance was comparable to healthy peers, but those children

with occasional seizures exhibited behavioral problems. Reviews (Bourgeois, 1998, 2002, 2004; Kwan & Brodie, 2001) show inconclusive and contradictory results on the effects of antiepileptic medication on cognitive functions and behavior. Criticism of the methodology in AEDs studies has also been addressed; most importantly, studies focusing on children are mostly lacking (e.g. Bourgeois, 2002; Kwan & Brodie, 2001).

When compared to healthy children or children with other chronic condition, cognitive and behavioral problems are more often found in children with epilepsy. In summary, there are myriad factors, e.g. etiology, age at onset of seizures, seizure frequency and antiepileptic medication possibly affecting neurocognitive or social impairments in childhood epilepsy (Bourgeois, 2004). Due to the multifactorial origin of impairments and complex association between epilepsy and development, no direct causality has been demonstrated (Noeker, Haverkamp-Krois & Haverkamp, 2005; Tromp, Weber, Aldenkamp, Arends, Linden & Diepman, 2003). In addition to pathophysiological (i.e. CNS dysfunction or underlying lesions) and epilepsy related factors, environmental, including family related factors (Rodenburg, Meijer, Decovic & *Aldenkamp,* 2005) may affect the child's development. This effect may be direct or mediated through epilepsy related or / and neurocognitive factors which, in turn, may also have an independent effect on a child's development.

1.2 Neurocognitive functioning in childhood epilepsy

Neurocognitive functioning childhood epilepsy may be impaired globally indicating overall intellectual impairment (including mental retardation). Alternatively, despite normal intellectual functions, deficits may be limited to specific neurocognitive functions (e.g. attention, language).

1.2.1 Intellectual functioning

Intellectual functioning refers to overall cognitive abilities measured with intellectual tests and reported as intellectual quotient (IQ, e.g. Wechsler, 1999) or developmental

quotient (DQ, e.g. Bayley, 1994). As with mainstream population, intellectual functioning varies from normal to severely impaired or mentally retarded in children with epilepsy. It has been estimated (Berg et al., 2008; C. Camfield & Camfield, 2007; Sillanpää, 1992) that about 70-80% of all children with epilepsy have normal intellectual functioning. However, in population based studies, the proportion of mental retardation (i.e. learning disability defined as IQ <70) varies between 20% and 57% in children with epilepsy (C. Camfield & Camfield, 2007; Sidenvall, Forsgren & Heijbel, 1996; Sillanpää, 1992; Waaler, Blom, Skeidsvoll & Mykletun, 2000). Borderline cognitive function or mild mental retardation was reported in 8% and more severe mental retardation or devastating impairments were found in about 16% of children (C. Camfield & Camfield, 2007). In Finland, Sillanpää (1992) reported mental retardation in 31% of children with epilepsy.

Intellectual impairment is more obvious in certain subgroups of childhood epilepsy. Mental retardation is more frequently related to symptomatic cause and epileptic encephalopathy with typically high seizure frequency (Shields, 2000; Vasconcellos et al., 2001). In contrast, intellectual function is usually on the normal end of the continuum in children with idiopathic epilepsy (Elger et al., 2004; Hommet et al., 2006; Motamedi & Meador, 2003). Despite cognitive performance within normal range, differences between children with epilepsy and healthy controls have been often reported (e.g. Cormack et al., 2007; Høie et al., 2005). However, strongly intercorrelated, younger age at onset (<5 years), symptomatic cause, epileptic encephalopathy, and continued AED treatment were independently associated with outcome. Developmental quotient is reported to rise with increasing age at epilepsy onset, and decrease in proportion to life with epilepsy (Vendrame et al., 2009). One of the subgroups in which mental retardation is reported to be overrepresented is surgical candidates with severe refractory epilepsy (Freitag & Tuxhorn, 2005; Vasconcellos et al., 2001). Freitag and Tuxhorn (2005) reported percentage of mental retardation over 70 in preschool-aged candidates for epilepsy surgery. This emphasizes the importance of etiology, and the impact of high seizure frequency on intellectual function.

In the course of epilepsy, there is also a possibility of cognitive decline in some children with epilepsy (for a review see Dodrill, 2004). This has been demonstrated in follow-up studies conducted on children with early onset epilepsy and longer duration (e.g. Mangano et al., 2005; Vendrame et al., 2009). Others (e.g. Rodin, 1989), however,

have reported early cognitive impairment with little subsequent deterioration. Meinardi, Aldenkamp and Nunes (1992) have proposed a cognitive deterioration in epilepsy characterized by a discontinued, cascading process, i.e. a sudden and irreversible cognitive decline immediately after the onset of the seizures and a later plateau of cognitive function without further decline.

1.2.2 Specific neurocognitive functions

Despite intellectual function within normal range, especially in children with uncomplicated epilepsy, the specific neurocognitive functions may be affected. The association between epilepsy and neurocognitive function is complex and no specific neuropsychological pattern can be identified. Rather, a diffuse and generalized cognitive dysfunction has been described (Hermann, Jones, Dabbs, Allen, Sheth, Fine, et al., 2007; Schoenfeld, Seidenberg, Woodard, Hecox, Inglese, Mack, et al., 1999). This may be due in part to multifactorial etiology and the heterogeneous nature of the condition with a variety of epilepsy-related factors possibly interfering with or contributing to the development and maturation of neurocognitive functions. Impairments reported associated with epilepsy include problems in attention and executive functions, language, memory, visuomotor function, and information processing.

Attention problems are regarded as specific to epilepsy (Plioplys, Dunn & Caplan, 2005; Rodenburg, Stams, Meijer, Aldenkamp & Dekovic, 2005). Problems have been reported in overall attention (Gülgönen, Demirbilek, Korkmaz, Dervent, & Townes, 2000; Oostrom, Teeseling, Smeets-Schouten, Peters, & Jennekens-Schinkel, 2005), and specific deficits in visual and verbal attention (Henkin, Sadeh, Kivity, Shabtai, Kishon-Rabin & Gadoth, 2005; Williams, Griebel, & Dykman, 1998). Attention problems include both inattentive (Dunn & Kronenberger, 2005), and impulsive type (Leonard & George, 1999; Williams, Schulz, & Griebel, 2001). In addition, problems in executive functions have been reported in recent onset epilepsy (Parrish, Geary, Jones, Seth, Hermann & Seidernberg, 2007).

Language impairments are quite frequently reported in children with epilepsy. Sillanpää (1992) reported the proportion of speech disorders to be about 28% in children with childhood onset epilepsy. In their longitudinal study, Cohen and Le

Normand (1998) investigated language function in children with epileptogenic foci localized in the left frontal lobe. They demonstrated dissociation in linguistic performance between comprehension and production in 3 to 8 year-old children. Linguistic comprehension gradually improved to normal range by the age of seven, but impairments in linguistic production persisted. When studying children with idiopathic generalized epilepsy, Henkin et al. (2005) found deficits in word fluency and phonological awareness in children with absence seizures. Impairments in verbal fluency (Lindgren, Kihlgren, Melin, Croona, Lundberg & Eeg-Olofsson, 2004), in receptive language ability, and phonological processing skills (Northcott, Connolly, Berroya, McIntyre, Christie, Taylor, et al., 2007; Northcott, Connolly, Berroya, Sabaz, McIntyre, Christie, et al., 2005) have been demonstrated in school-aged children with benign rolandic epilepsy.

As seen in adults with epilepsy, various memory problems have been associated with childhood epilepsy. This close relationship between epilepsy and impaired memory function is because the most epileptogenic areas of the brain are the temporal lobe and the underlying hippocampus. These same areas and structures are closely involved in memory function, e.g. memory encoding (Anderson et al., 2001). In addition to memory dysfunction in children with temporal lobe epilepsy (e.g. Jambaque, Dellatolas, Dulact, Ponsot & Signoret, 1993), impairments have also been demonstrated in other epilepsy types, e.g. those with frontal lobe epilepsy and absence epilepsy (Nolan, Redoblado, Lah, Sabaz, Lawson, Cunningham, et al., 2004). Material-specific memory impairments have been reported in school-aged children with uncomplicated epilepsy. Both verbal memory problems (Gülgönen et al., 2000; Henkin et al., 2005; Jambagué, et al., 1993; Lindgren et al., 2004; Northcott et al., 2005) and visual memory problems (Gülgönen et al., 2000; Jambagué, et al., 1993; Lindgren et al., 2004; Northcott et al., 2007; Northcott et al., 2005; Pavone, Bianchini, Trifiletti, Incorpora, Pavone & Parano, 2001) have been demonstrated. Memory impairments may include problems in short-term memory (Bailet & Turk, 2000; Bhise, Burack & Mandelbaum, 2010; Oostrom et al., 2005), or in delayed recall (Henkin et al., 2005; Pavone et al., 2001).

In addition to the attention, language and memory problems occuring in childhood epilepsy, impairments in visual and visual-spatial functions have been reported. Visual problems have been reported e.g. in children with rolandic epilepsy (Danielsson & Petermann, 2009) and in children with idiopathic occipital lobe epilepsy

(Chilosi, Brovedani, Moscatelli, Bonanni & Guerrini, 2006). However, some (e.g. Høie et al. 2005) have argued that non-verbal problems seem to be more typical in children with symptomatic etiology than with idiopathic epilepsy. Moreover, problems in information processing have been reported in children with idiopathic or uncomplicated epilepsy. Particularly, slower reaction times and psychomotor speed (Aldenkamp & Arends, 2004; Bailet & Turk, 2000; Boelen, Nieuwenhuis, Steenbeek, Veldwijk, Ven-Verest, Tan, et al., 2005; Leonard & George, 1999) have been reported. This partly supports the model of a transient cognitive impairment (TCI), i.e. cognitive impairment in direct relation to episodes of epileptiform EEG discharges without other clinical manifestation (Aldenkamp & Arends, 2004). Rather than producing permanent cognitive impairments, TCI results more likely in variable cognitive performance. Thus the TCI model refers to impairments that should be distinguished from the effects caused by the clinical syndrome or the underlying etiology (e.g. from post-ictal or long-term stable interictal effects) (Aldenkamp & Arends, 2004).

Although benefits have been reported in earlier studies on neurocognitive functions in childhood epilepsy, some limitations may be addressed. First, various and sometimes contradictory neurocognitive impairments have been reported. The cross-sectional study designs used in most of the studies may partly explain these discrepant findings. In addition to contradictory findings, an absence of population-based cohort studies limits the generalizability of the findings. Second, and perhaps a more important limitation is the age of participants in earlier studies. Although early onset of seizures has been found to be an important predictor of later neurocognitive functioning, the vast majority of studies have focused on school-aged children, and ignoring young and preschool-aged children. Most of the studies on younger children have concentrated on seizures in infancy or before three years (e.g. Battaglia et al., 1999; Chaix et al., 2003; Datta & Wirrell, 2000; Loddenkemper, Holland, Stanford, Kotagal, Bingaman & Wyllie, 2007; Mangano et al., 2005; Vanderlinden & Lagae, 2004; Vendrame et al., 2009). Consequently only few of the studies (e.g. Danielsson & Petermann, 2009; Freitag & Tuxhorn, 2005; Rejnö-Habte Selassie et al., 2008) have focused on the neurocognitive functions of preschool aged children with epilepsy.

1.3 Social competence in childhood epilepsy

Social competence is regarded as one of the best predictors of later social and academic success, and also for current and future behavioral and emotional problems (John, 2001). In addition to neurocognitive function, social competence may be impaired in childhood epilepsy. Studies of social competence in childhood epilepsy have increased significantly in the past two decades. Several studies have addressed behavioral problems in children with epilepsy (see e.g. Dunn, 2003; Dunn & Austin, 1999; Rodenburg, Stams, et al., 2005). Similarly to neurocognitive impairments, behavioral problems are now seen as elementary parts of epilepsy rather than a consequence of neurologic condition (Plioplys et al., 2007). As in cognitive functions, the effect of epilepsy related variables on social competence may be indirect rather than direct (Austin, Dunn, Caffrey, Perkins, Harezlak & Rose, 2002; Noeker et al., 2005; Ott et al., 2003).

1.3.1 Definition of social competence

Definitions of social competence vary, but there is an agreement that social competence refers to a global judgment and is based on behavioral performance (Gresham, 1986). At a general level, Doll (1977) defined social competence as the individual's ability to function equivalent to age-appropriate and cognitive abilities. A more precise definition is provided by Cavell (1990). His model defines social competence as a multilevel construct comprising subcomponents of social adjustment, social performance and social skills. This three-component model of social competence is considered to be sensitive to the effects of CNS conditions (like epilepsy or cerebral palsy) (Cavell, 1990). The key subcomponents of and factors associated with social competence in childhood epilepsy may be summarized in a conceptual framework, as seen in Figure 1. The associations between epilepsy and social competence are complex and no direct causality has been demonstrated**.** The proposed conceptual framework hypothesizes that both pathophysiological (i.e. CNS dysfunction or lesions) and environmental factors (including family related factors) may affect the social competence. This effect may be direct or mediated through epilepsy related or / and neurocognitive factors which, in turn, may also have an independent effect on the development of social competence (see Noeker et al., 2005).

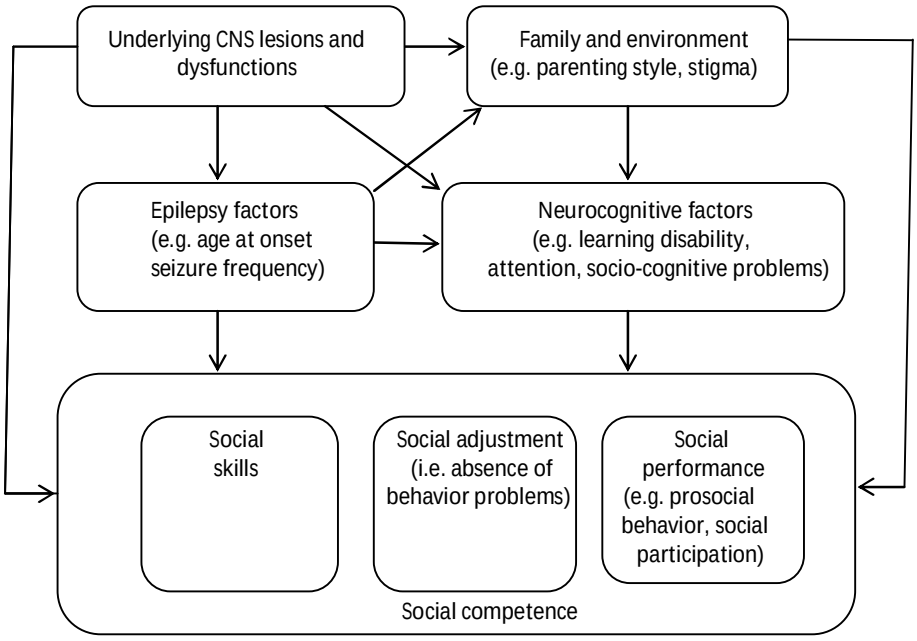


Figure 1. Conceptual framework of social competence, its subcomponents, and hypothetical connections in childhood epilepsy (modified from Rantanen, Eriksson & Nieminen, 2011).

1.3.2 Problems of social competence

Earlier reviews have reported behavioral problems and psychopathology in children with epilepsy (Caplan & Austin, 2000; Dunn, 2003; Leonard & George, 1999; Plioplys et al., 2007; Rodenburg, Stams, et al., 2005). Also, associations between family problems and psychopathology have been addressed (Rodenburg, Meijer, et al., 2005). Behavioral problems may be evident early in course of epilepsy i.e. precede the first recognized seizure (e.g. Austin et al., 2002), or they may be more related to recurrent seizures (Dunn, et al., 2003). Children in remission or with good seizure control are

reported to have fewer behavioral problems. Further, behavioral problems related to different seizure types (e.g. complex partial seizures, childhood absence epilepsy) have been addressed (e.g. Caplan et al., 2005; Ott, Caplan, Guthrie, Siddarth, Komo, Shields, et al., 2001).

Reviews have shown increased risk for psychopathology, including internalizing (e.g. anxiety) and externalizing (e.g. aggression) problems (Rodenburg, Stams, et al., 2005) in children with epilepsy. Between studies, estimates of the proportion of psychiatric disorders have been varied considerably (from 37% to 77%) in children with epilepsy (Davies, Heyman & Goodman, 2003; Plioplys et al., 2007). Behavioral or emotional problems have been were evident in 22% of children with epilepsy (Freilinger et al., 2006). Attention, thought and social problems have been regarded as specific to epilepsy (Plioplys et al., 2007; Rodenburg, Stams, et al., 2005). When compared to siblings, higher levels of behavioral problems (e.g. internalizing problems) have been reported (Austin et al., 2002; Austin et al., 2001; Dunn, Austin, Caffrey & Perkins, 2003). Problems reported also include higher frequency of depressive symptoms than the general population of healthy children (Baki, Erdogan, Kantarci, Akisik, Kayaalp & Yalcinkaya, 2004). Few studies have addressed social skills in children with epilepsy. Lower adaptive skills (Berg, Smith, Frobish, Beckerman, Levy, Testa, et al., 2004), and poorer social skills (Tse, Hamiwka, Sherman & Wirrell, 2007) have been reported in children with epilepsy. In addition, children with epilepsy have been found to be less assertive than e.g. their siblings (Tse, et al., 2007).

There are some limitations in earlier studies. As with neurocognitive functions, most studies on behavioral issues in childhood epilepsy have been conducted on school-aged children. Despite the fact that early onset epilepsy is regarded as an important predictor of later development and social competence, only little attention has been paid to these issues in preschool-aged children with epilepsy. Secondly, most of the earlier studies have focused on behavioral problems and psychopathology rather than other aspects social competence.

2. Aims of the study

The purpose of this study was to investigate neurocognitive functioning and social competence in preschool-aged children with epilepsy. The specific aims were:

1) to describe the medical characteristics of a population based cohort of preschool-aged children with epilepsy (Study I);
2) to evaluate neurocognitive functioning in children with epilepsy (Studies I-II);
3) to review studies on definitions and assessment methods of social competence, to evaluate the study designs, and to provide an overview of the main empirical findings of social competence in childhood epilepsy (Study III);
4) to assess social competence in children with uncomplicated and complicated epilepsy compared to healthy controls (Study IV).

According to earlier studies on school-aged children with epilepsy, the intellectual functioning was expected to be within normal range in children with uncomplicated epilepsy and impaired in those with complicated epilepsy (Studies I and II). Neurocognitive deficits were anticipated to be diffuse in children with uncomplicated epilepsy (Study II). Cognitive impairment was expected to be associated with underlying etiology, age at onset of seizures, duration of epilepsy and seizure frequency (Study I). Finally, no differences were anticipated between children with uncomplicated epilepsy and healthy children in social competence, but behavioral problems would be more likely observed among children with complicated epilepsy (Study IV).

3. Methods

3.1 Original studies

This research was conducted in collaboration with the Department of Psychology at the University of Tampere, the Pediatric Neurology Unit of Tampere University Hospital and the Pediatric Research Centre of the Medical School at the University of Tampere. The ethical committee of Tampere University Hospital approved the study protocol.

3.1.1 Participants

A population-based cohort of preschool-aged children with active epilepsy ($N = 64$) was identified through the medical records of the Pediatric Neurology Unit, Tampere University Hospital, Finland, which is the only centre for pediatric neurology services in the hospital district. On the point prevalence day, September 30th, 2004, the total population of the hospital district was 464,976, of whom 19,821 were children aged 3 years to 6 years 11 months. The study cohort consisted of all children aged 3 to 6 years 11 months with diagnosed epilepsy.

3.1.2 Medical and background data

All medical and psychological records, neurophysiological recordings and available clinical data were reviewed retrospectively. Medical data including demographic factors, duration of epilepsy (at the time of psychological assessment), seizure and epilepsy type, seizure control during the period of the study, electroencephalogram (EEG), imaging of the brain with 1.5T magnetic resonance imaging (MRI), current AEDs and most recent AED levels were analyzed retrospectively from children's medical records.

3.1.3 Neurocognitive assessment

In studies I and II, cognitive functioning was assessed with standardized tests of the Bayley Scales of Infant Development, BSID-II (Bayley, 1994) or with the Finnish versions of Wechsler's Primary and Preschool Scale of Intelligence – Revised, WPPSI-R (Wechsler, 1995) or the Wechsler Scale of Intelligence for Children –III, WISC-III (Wechsler, 1999) (see Table 1). In Study II, neurocognitive functions were assessed with the Developmental Neuropsychological Assessment, the NEPSY test (Korkman, Kirk & Kemp, 1997). The Finnish version of the NEPSY test was selected because it has been standardized on a single sample of children (Korkman, 2000), and is widely used in clinical practice. The specific neurocognitive functions assessed with the NEPSY were Attention and Executive Function, Language, Sensomotor Function, Visuospatial Function, and Memory and Learning. Ten subtests (two per function) were selected to obtain the core assessment of neurocognitive development, i.e. a brief overview of the five complex, neurocognitive functions above mentioned. From the subtests available for core assessment the 10 recommended by Korkman et al. (1997) for both ages 3–4 and ages 5–6 were chosen.

3.1.4 Assessment of social competence

A wider range of assessments was used in Study IV for the assessment of social competence in children with epilepsy (see Table 1). For the assessment of social skills and adaptive behavior the Vineland Social Maturity Scales (VSMS) (Doll, 1977) was selected. The VSMS measures social competence, self-help skills, and adaptive behavior required to function in an age-appropriate manner. The VSMS provides an overall composite score for an objective and uniform index for acquired social skills. In this study, the VSMS raw scores were converted to an age equivalent score, expressed as social age. Secondly, the most commonly used assessment methods in both clinical and research practice; the Conners' Parent Rating Scale–Revised (Conners, 1997) and the Child Behavior Checklist by Achenbach (1991; 1992) were used to assess behavior and behavioral problems (including attention problems). These behavioral assessments have also proven to have good reliability. Social competence was assessed with questionnaires on behavior and social skills completed by parents. The reliability (Cronbach's alpha) for the VSMS was .90, for the CPRS-R .96, and for the CBCL

scales .71-.87 (different rating scales for 2–3 year-old and 4–6 year-old children) respectively.

Table 1. *Assessment methods used in Studies I, II and IV.*

Function	Assessment method: Subtest or subscale
Intellectual functions	BSID-II[1], WPPSI-R[2], WISC-III[3]
Neurocognitive Functions	
Attention	NEPSY[4]: Statue, Visual attention
	CPRS-R[5]: Hyperactivity, AHDH Index, Restless-Impulsive, Emotional Lability, Total Index
Language	NEPSY[4]: Comprehension of Instructions, Phonological
Visuospatial	Processing
Sensorimotor	NEPSY[4]: Copying, Blocks
Memory	NEPSY[4]: Imitating Hand Position, Visuomotor Precision
	NEPSY[4]: Repetition of Sentences, Narrative Memory
Social Competence	
Social age	Vineland Social Maturity Scale
Social adjustment	CBCL[6]: Internalizing Problems, Externalizing Problems, Total Behavior Problems
	CPRS-R[5]: Oppositional, Cognitive problems / Inattention, Anxious / Shy, Perfectionism, Social Problems, Psychosomatic

Note. [1]Bayley Scales of Infant Development, [2]Wechsler's Primary and Preschool Scale of Intelligence – Revised, [3]Wechsler Scale of Intelligence for Children –III; [4]Developmental Neuropsychological Assessment , [5]Conners' Parent Rating Scale –Revised; [6]Child Behavior Checklist

3.1.5 Statistical analysis

In Studies I-II and IV the statistical analyses were carried out with the Statistical Package for Social Sciences (SPSS, versions 15.0 and 16.0). In Study I, continuous and normally distributed variables were compared with Student's *t*-test and categorical variables with χ^2-test and Fisher's exact test. The Bonferroni correction procedure was used in Study II. The association between epilepsy related factors and neurocognitive variables were explored with Spearman's rho. *P* values <.05 were considered as statistically significant. A logistic regression analysis was used to predict cognitive

impairment (Study I). Clinically significant neurocognitive impairment was considered to exist when a child scored two standard deviations below the neuropsychological test mean (i.e. standard score < 4) (Korkman, 2000; Lezak, 1995).

In Study IV social composite score and social age obtained from the VSMS was used in the analysis of the group differences. T-scores of the CPRS-R subscales and the broadband scales of the CBCL (i.e. Total Behavior Problems, Internalizing and Externalizing Problems) were used for the comparisons between children with epilepsy and healthy children. The non-parametric tests of Mann-Whitney and Kruskall-Wallis were used. *P*-values less than .05 were considered statistically significant.

3.2 Review of studies

In Study III a systematic literature search was conducted. Data were identified in January 2011 by searches in Medline and PsycINFO (January 1988 – December 2010). In addition, cross-references from relevant articles were inspected. For Medline and PsycINFO, the search terms were: epilepsy, behavior, behav* and social competence or social function*, social adjustment, social performance, social skills or socio-cognit*, psychosocial or peers and their combinations. The inclusion criteria for the original studies were 1) 0–18 year-old children with diagnosed epilepsy, 2) all types of seizures, epilepsies, and epilepsy syndromes, 3) empirical studies with behavioral or social assessments either questionnaires or structured interviews, and 4) articles in English or articles with a detailed abstract in English. Since the purpose was to get an overview of studies on social competence in childhood epilepsy, both children with both normal cognitive function and those with cognitive impairment or mental retardation were included. Also, observational studies would have been included but none were found. Qualitative studies and review articles were excluded from the search, and intervention studies were also beyond the scope of the review.

The original search yielded 4,509 articles, of which 105 articles remained after removing duplicates and studies not meeting the selection criteria. Additional 21 articles were included after reviewing reference lists. Thus abstracts of these 126 articles were reviewed resulting in the removal of 70 articles meeting the exclusion criteria. Finally, 56 articles were fully reviewed, of these 45 met the eligibility criteria.

4. Results

4.1 Characteristics of the cohort

The study cohort consisted of 64 children (33 girls and 31 boys) with epilepsy. Prevalence of epilepsy was 3.2 per 1,000 children. The mean age of the cohort was 65.2 months (*SD* 13.4, range 36–83), and the mean age at the onset of seizures was 27.0 months (*SD* 21.1, range 0–75). About 52% (*n* = 33) of the cohort had been diagnosed with epilepsy before two years of age. The study cohort comprised of variety of etiologies: epilepsy was classified as idiopathic for six children, symptomatic for 27 and cryptogenic for 31 children. Neuroimaging (with MRI) was normal in 35 children and abnormal in 29 children. Seizure control was good in 40% of the cohort and partial or poor for 60% of the participants. For descriptive purposes the cohort was divided into two subgroups: children with uncomplicated (UCE, *n* = 26) and complicated (CE, *n* = 38) epilepsy. The clinical characteristics are presented in detail in Table 2.

Table 2. *Clinical and Demographic Characteristics of the Study Cohort.*

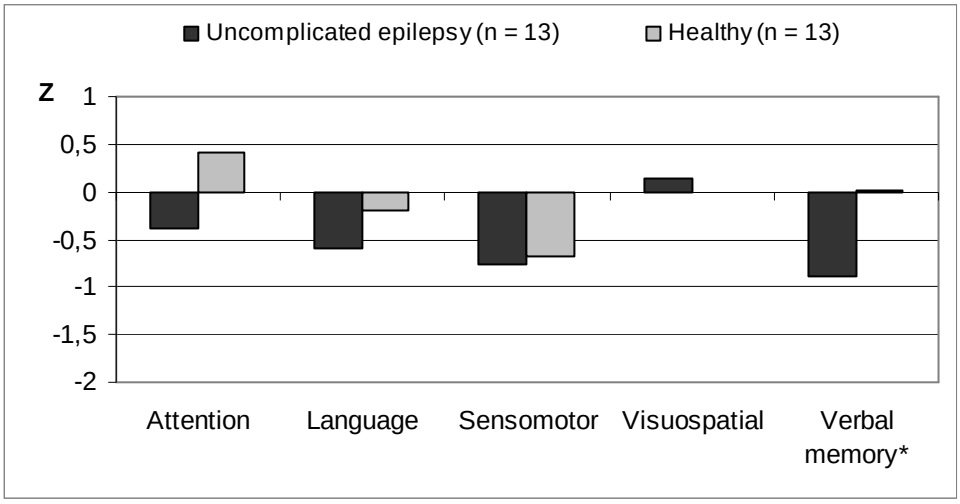
	Study I	Study II	Study IV
Participants (*n*)	64	13	26
Gender (*n*)			
Female	33	7	15
Male	31	6	11
Age (months)			
Mean (*SD*)	65.2 (13.4)	58.7 (10.8)	60.9 (15.0)
Range	36–83	43–75	39–82
Age at onset of seizures (months)			
Mean (*SD*)	27.0 (21.1)	27.9 (17.4)	24.7
Range	0–75	6–64	2–64
Duration (months)			
Mean (*SD*)	37.9 (24.0)	30.2 (20.7)	40.7 (22.2)
Range	2–83	2–69	9–77
Etiology			
Idiopathic	6 (9%)	4	4
Symptomatic	27 (42%)	0	5
Cryptogenic	31 (48%)	9	17
MRI*			
Normal	35 (55%)	13	20
Abnormal	29 (45%)	-	6
Epilepsy type			
Focal	27 (42%)	6	14
Generalized	31 (48%)	7	12
Unclassified	6 (9%)	-	-
Seizure control**			
Poor	19 (30%)	3	9
Partial	19 (30%)	6	10
Good	26 (40%)	4	7
Status epilepticus			
No	50 (78%)	9	17
Yes	14 (22%)	4	9
AED***			
No AED	6 (9%)	1	2
Monotherapy	41 (64%)	9	14
Polytherapy	17 (27%)	3	10
Controls (n)	-	13	26

Note. *MRI: magnetic resonance imaging; **Seizure control: Good: >1 year remission, Partial: Monthly-Yearly seizures, Poor: Daily-Weekly seizures; ***AED: antiepileptic medication.

4.2 Neurocognitive functions in preschool-aged children with epilepsy

The first aim of this dissertation was to determine the frequency and the level of cognitive impairment in a population-based cohort of preschool children with epilepsy (Study I). The results showed that intellectual functioning was within normal or borderline range for 50% of the cohort; mildly retarded for 22%, and moderately to severely retarded for 28%. The mean IQ of the cohort was 76.0, which was statistically significantly lower than the normative mean. Intellectual impairment was more frequent in children with CE, i.e. epilepsies with associated neurologic diseases or underlying brain abnormalities. The overall mean IQ in children with CE was significantly lower than in children with UCE (91 vs. 63). The performance of the uncomplicated group was within normal distribution.

The second aim of this dissertation was to study neurocognitive functioning of the subgroup of children with uncomplicated epilepsy (Study II). The results showed that despite the UCE children's intellectual functioning within normal range, the participants had significantly more neurocognitive problems than their healthy age and gender matched peers. This was contrary to expectations. Statistically significant differences were found in Verbal IQ (VIQ) and Full Scale IQ (FSIQ). When compared to the healthy controls, there was a trend for VIQ to differ more than Performance IQ (PIQ), i.e. VIQ scores lower than 1 *SD* from PIQ in the study group. As seen in Figure 2, despite diffuse impairments found in several neurocognitive domains, e.g. attention and language, statistically significant problems were found in verbal short-term memory in children with uncomplicated epilepsy. A similar trend for the study group to perform less well was found in Comprehension of Instructions. In clinical practice, the neurocognitive impairments found would be considered as mild problems.



Note. Bonferroni correction was used. **p* >.01.

Figure 2. Mean *z* scores for the uncomplicated epilepsy group and the control group for the neurocognitive functions assessed with the NEPSY test.

The third aim was to study the associations between neurocognitive functions and epilepsy related factors (Study I). Intellectual impairment was related to complicated epilepsy, additional neurological problems, age at onset of epilepsy, and abnormal MRI. Age at the onset of seizures was the only significant predictor of intellectual impairment. In the final logistic regression model, age at onset of seizures, etiology, MRI (normal vs. abnormal), additional neurological diagnosis, and seizure frequency were entered as predictors of intellectual impairment. The overall model predicted about 32% of the cognitive impairment with age at onset of seizures being the only significant predictor. Age at onset (r = .306, p < .05), but not duration was related to cognitive impairment. As seen in Table 3, about 64% of the children with the seizure onset before the age of two years were mildly to severely retarded vs. 35% in those with later onset of epilepsy.

Table 3. *Cognitive Impairment (N, %) and Age at Onset of Epilepsy.*

Intellectual level (IQ)	Age at onset (months)			
	1-24	25-48	49-60	Total
	N (%)	*N* (%)	*N* (%)	*N* (%)
Normal (>80)	9 (27)	8 (40)	6 (55)	23 (36)
Borderline (70–79)	2 (6)	4 (20)	0 (0)	6 (9)
Mildly to moderately retarded (35–69)	16 (49)	4 (20)	2 (18)	22 (34)
Severe/profound, -not testable (<34)	5 (15)	4 (20)	1 (9)	10 (16)
Unknown*	1 (3)	0 (0)	2 (18)	3 (5)
Total *N* (%)	33 (100)	20 (100)	11 (100)	64 (100)

Note. *No consent obtained for the psychological assessment.

4.3 Social competence in preschool-aged children with epilepsy

4.3.1 Review of studies on children with epilepsy

The aim of Study III was to summarize studies of social competence in children with epilepsy over the past twelve years. The specific aims of the study were 1) to describe how social competence has been defined and which aspects of social competence have been studied in childhood epilepsy, 2) to evaluate the study designs (e.g. representativeness of age) for the assessment of social competence, 3) to describe what assessment methods have been used, and 4) to provide an overview of the main empirical findings of social competence on children with epilepsy. The review included a total of 45 studies drawn from MEDLINE and PsycINFO (1998–2010) and their reference lists. A review of the earlier studies indicated that social competence had not been fully studied. With one exception social competence was not defined in the studies reviewed. The majority of the studies (76%) focused on social adjustment (i.e. psychopathology and behavior problems), and a quarter of the studies investigated other aspects of social competence; 10 studies focused on social performance and only three studies on social skills. Most of the studies reviewed (85%) were cross-sectional, and seven follow-up studies. Either population based or community based cohorts were used. Mean age of subjects varied from 4.9 to 15.0 years (median 10.9 years), and there was only one study with subject's mean age under 6 years. Achenbach's CBCL (1991; 1992), which includes problem scales and social competence scales, was utilized in the

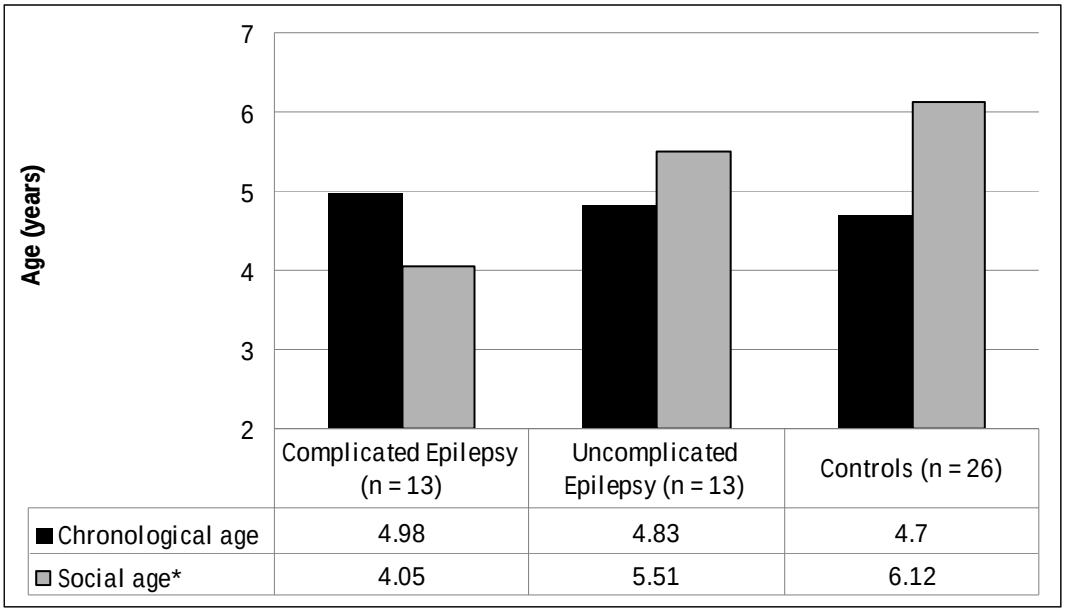
majority of studies. Developmental disability or mental retardation usually excluded from the study samples (71%). Healthy children (e.g. classmates, or siblings) or children with some other chronic disease (e.g. asthma) were used as controls in 64% of the studies reviewed. Age and gender matched children were used in nine studies. Of the assessment methods, the CBCL was most often used (in 76% of studies).

The overview of the empirical findings demonstrated that the majority of studies reviewed focused on social adjustment, and reported problems in this area. Rates of behavior problem scores were higher than for siblings or children with other chronic illness. Percentages for problems in social adjustment varied considerably, for example, the estimates for psychiatric problems or diagnosis (26–61%), for internalizing problems (13–70%), for externalizing problems (11–43%), and for total behavior problems (16–68%). Social adjustment problems were related to children with low IQ, recurrent seizures, and younger age at onset. Most consistently problems were reported related to attention (8–67%), depression (8–40 %) and anxiety (4–49%). When compared to the healthy children and siblings, two studies reported poorer social skills in both preschool and school-aged children with epilepsy. In school-aged children, social skills impairment was reported in 13% of children with epilepsy, but no difference in the proportion of clinically significant deficits was found between these groups (Tse et al., 2007). One of the articles reviewed (Golouboff, Fiori, Delalande, Fohlen, Dellatolas & Jambaqué, 2008) investigated underlying socio-cognitive skills and their relation to behavioral problems in early-onset temporal lobe epilepsy, and reported a possibility of compromised development in recognizing facial expressions of emotion.

The social competence scales of the CBCL comprise items related to social performance, (e.g. sports, other recreational activities, group activities and social relationships). Although the overall scores on the CBCL Social Competence scale were within the normal range in children with epilepsy, the proportion of clinical or borderline scores in children with epilepsy was greater than in healthy children or siblings. More problems were evident in School Competence scale than in healthy children or siblings. A significantly higher proportion of impairment on the CBCL Social Competence scales was related to intractable epilepsy with recurrent seizures.

4.3.2 Empirical findings of social competence in preschool-aged children with epilepsy

The aim of Study IV was to evaluate social competence in preschool children with epilepsy in a subgroup of the study cohort. A total of 26 children with epilepsy and age- and gender-matched controls participated in the study. As seen in Figure 3, both groups of children with epilepsy (UCE and CE) had lower scores on the VSMS than the healthy children, indicating a significant difference in social age. Both groups of children with epilepsy had fewer age-appropriate social skills than healthy children. Further, the social age of the uncomplicated epilepsy group differed significantly from that of the complicated epilepsy group.

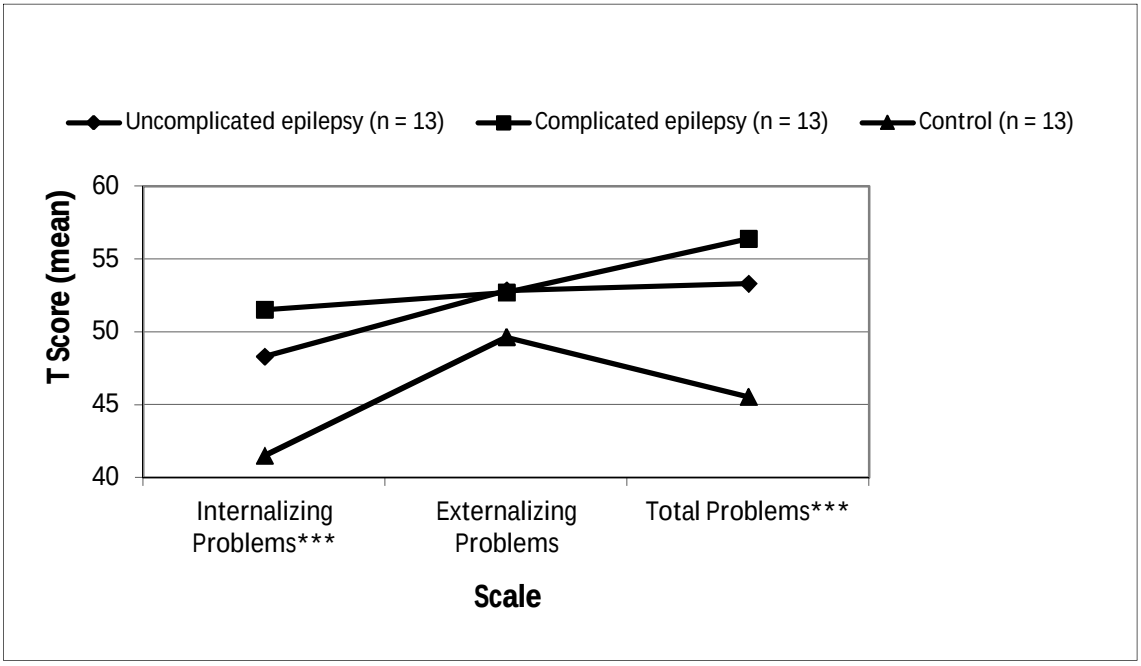


Note. *Between groups $p < .01$

Figure 3. Mean chronological and social ages for the complicated epilepsy group, uncomplicated epilepsy group and controls.

The parents of children with epilepsy reported more attention and behavioral problems in the CPRS-R and the CBCL than did the parents of healthy children. Children with epilepsy had higher scores than healthy controls on Conner's Global Index (CGI), CGI-Restless-Impulsive, and ADHD Index. In addition, differences were found between the CE group and the controls in Social Problems, Psychosomatic, and ADHD Index, but no differences were found between the UCE group and the controls.

CGI-Restless-Impulsive was the only scale where a difference between the UCE group and the healthy controls was found. As shown in Figure 4, the children with epilepsy were also reported to have more Internalizing and Total Behavior problems is the CBCL than healthy children, but no differences were demonstrated in Externalizing behavior problems.



Note. Between groups *$p < .05$, ** $p < .01$, ***$p < .001$

Figure 4. Mean *T* Scores for the CBCL Internalizing, Externalizing and Total Problems in children with uncomplicated and complicated epilepsy and in healthy children.

5. Discussion

The purposes of this dissertation were to investigate both neurocognitive function and social competence in preschool-aged (i.e. three to six years old) children. The specific aims were to describe the medical and cognitive characteristics in a cohort of preschool-aged children with epilepsy, to evaluate their neurocognitive functioning, and to assess social competence in children with epilepsy compared to healthy controls. In addition, a systematic review of studies on social competence in childhood epilepsy was conducted.

5.1 Overview of the results

Epilepsy in preschool-aged children

In this study, prevalence of epilepsy (3.2 per 1,000 children) concurs with that previously reported (3.4 – 5.1) in Scandinavia (Eriksson & Koivikko, 1997; Rejnö-Habte Selassie et al., 2008; Waaler et al., 2000). When compared to idiopathic etiology, cryptogenic and symptomatic etiologies were overrepresented in the study cohort. This is partly in contrast with other studies reporting a lower proportion of symptomatic (or non-idiopathic) and idiopathic etiology in early onset epilepsy, e.g. 40 vs. 60% in Vanderlinden and Lagae (2004), 58 vs. 42% in Datta and Wirrell (2000). This may partly reflect the differences in the use of these term and practices in epilepsy classification. Seizure control in this study was partial or poor for 60%. Antiepileptic medication was used for 91% of the participants. Thus this study represents children with relatively early onset (mean age at the onset of seizures 27 months) and severe epilepsy.

Neurocognitive functions in preschool-aged children with epilepsy

Normal intellectual functioning was demonstrated in half of the participants, and an intellectual impairment was evident in half of children with epilepsy (Study I). This concurs partly with earlier studies (Berg et al., 2008; C. Camfield & Camfield, 2007; Sidenvall et al., 1996; Sillanpää, 1992, 2004) in which estimates of cognitive impairment in children with epilepsy have varied (ranging from 20 to 51%). However, the proportion of impairment reported in Study I was significantly higher than that reported e.g. by Berg et al. (2008), who demonstrated global cognitive impairment in 33% of children with seizure onset before five years of age. Sillanpää (2004) in his longitudinal study found that onset of epilepsy before six years was one of the significant predictors of mental retardation and a subsequent learning disorder. Higher frequency of intellectual impairment has typically been demonstrated in children with refractory epilepsy and recurrent seizures, such as candidates for epilepsy surgery. Cormack et al. (2007) reported cognitive impairment in 57% of surgical candidates with temporal lobe epilepsy, and Freitag and Tuxhorn (2005) in 70% of children treated surgically between 3 and 7 years of age.

The distribution of the intelligence quotients in the study cohort was twofold, and overall mean IQ was significantly lower than the normative mean. The intellectual impairment was more apparent in children with complicated epilepsy (mean FSIQ 63) than in children with uncomplicated epilepsy (mean FSIQ 91). In fact, the level of cognitive functioning in the complicated epilepsy group was lower than demonstrated with the mean IQ since the neurologically and cognitively most severely impaired participants unable to participate in standardized testing were excluded from the analysis. This difference in intellectual functioning between the UCE and the CE groups was expected in light of earlier studies on school-aged children (Bailet & Turk, 2000; Mandelbaum & Burack, 1997). It reflects the importance of underlying pathology and / or additional neurologic conditions for intellectual functioning. However, among children with uncomplicated epilepsy, the distribution of IQ scores was also at the lower end of normal distribution. A similar trend of a downward shift in the distribution of intelligence in children with epilepsy has been reported by Cormack et al. (2007) and Høie et al. (2005).

Specific neurocognitive functions were investigated in children with uncomplicated epilepsy and mild impairments in language, verbal short-term memory and attention were indicated (Study II and IV). Language impairments (i.e. lower and more discrepant VIQ from PIQ, weaker performance in comprehension of instructions) demonstrated are in line with earlier studies (e.g. Cohen & Le Normand, 1998; Danielsson & Petermann, 2009). Although findings of language problems in preschool-aged children have been reported, partly contradictory findings have also been reported by Rejnö-Habte Selassie et al. (2008) in six-year old Swedish children with epilepsy and without learning difficulties. They reported intact Verbal IQ, expressive and receptive grammar and receptive vocabulary, but lower test scores in oral motor ability, articulation, emerging literacy, and rapid word retrieval. Verbal short-term memory of preschool children with uncomplicated epilepsy was considered to be mildly affected compared to those of healthy controls (Study II). This finding is consistent with various memory problems, including short-term memory problems (Nolan et al., 2004; Northcott et al., 2005) demonstrated earlier. Similarly, a recent study reported short-term memory and narrative memory problems in six-year old children with epilepsy (Rejnö-Habte Selassie et al., 2008). Contradictory findings have also been reported e.g. by Pavone et al. (2001), who found relatively intact verbal memory, but impaired nonverbal memory in children with absence epilepsy. In addition to language and verbal short-term memory problems, earlier studies (for a review, see Plioplys et al., 2007; Rodenburg, Stams et al., 2005) have shown attention problems to be specific to childhood epilepsy. The results presented in this dissertation confirm this to be true also for young children with epilepsy. Behavioral ratings by parents included attention problems, especially impulsivity, in preschool-aged children with epilepsy (Study IV). A similar trend for attention problems was found in neuropsychological assessments (Study II), but due to limited number of participants this finding did not reach statistical significance.

Contrary to these earlier studies and expectations, visuospatial and sensomotor impairments were not confirmed (Study II). Problems in visual (or non-verbal) (e.g. Germanó, Gagliano, Magazú, Sferro, Calarese, Mannarino, et al., 2005; Høie et al., 2005; Rejnö-Habte Selassie et al., 2008), visuospatial functions (Pavone et al., 2001) and psychomotor speed (Bailet & Turk, 2000) have been suggested in earlier studies. Instead, the results of Study II are in line with e.g. Boelen et al. (2005), who found that overall psychomotor development was comparable to that of controls. This unexpected

finding may be partly related to a poorer reliability of sensomotor subtests in younger children, as suggested by Korkman (2000) and Korkman et al. (1997). There seems to be individual maturation and differentiation of sensomotor skills in healthy children, too. This greater variability in sensomotor skills may in turn affect the reliability of the subtests.

To conclude, the results of Studies I-II, IV suggest subtle and diffuse neurocognitive impairments in preschool-aged children with relatively early onset epilepsy. These problems also seem to be evident in the children with uncomplicated epilepsy. Similar patterns of subtle, generalized or diffuse neurocognitive impairments (e.g. intellectual, language, executive, attention and / or psychomotor speed) have been suggested in school-aged children and adolescents with epilepsy (e.g. Germanó et al., 2005; Hermann, Jones, Sheth, Dow, Koehn & Seidenberg, 2006; Oostrom et al., 2003; Williams et al., 1998).

Social competence in preschool-aged children with epilepsy

A model of social competence, its subcomponents (social skills, social performance and social adjustment), and hypothetical links was proposed in Study III (see also Rantanen et al., 2011). A similar recommendation for a broader perspective to study of social competence in the CNS related conditions has also been made by Cavell (1990). The review indicated that although a number of studies have been published on the field over the past twelve years, definitions of social competence were still lacking in the studies reviewed. On the basis of the implicit definition of social competence as the absence of psychiatric, behavioral or emotional problems, the perspectives were narrowed down to overt behavior. Most of the studies reviewed were cross-sectional (83%) and seven were follow-up studies. The studies reviewed used either population- or community-based cohorts. In the majority of studies, the focus was only on social adjustment (i.e. behavioral problems), and less attention was paid to positive aspects of social competence, namely social skills and social performance. The results of this review (covering the period 1998–2010) therefore concurred with the earlier work by Nassau and Drotar (1997), who reported that the majority of studies from 1975 to 1997 assessed social competence at the social adjustment level, with only few studies addressing the social performance or social skills level. Thus the earlier

recommendations to expand the conceptualizations of social competence specific to children's CNS conditions have not affected the study field.

In Study IV poorer social skills and social adjustment problems were reported in preschool-aged children with epilepsy, such as elevated internalizing and total behavior problems. These problems have not previously been studied in preschool-aged children with epilepsy, but similar social adjustment problems have frequently been reported in school-aged children with epilepsy (see e.g. Plioplys et al., 2007; Rodenburg, Stams, et al., 2005; see also Study III). Moreover, and as expected, the results showed that behavioral and attention problems were more frequently encountered in children with complicated epilepsy (Study IV). Also, others have earlier concluded that behavioral problems are related to low IQ (Buelow, Austin, Perkins, Shen, Dunn & Fastenau, 2003), and recurrent seizures (Austin et al., 2002; Dunn et al., 2003). An association between behavioral problems and younger age at onset of epilepsy (Dunn, Austin & Perkins, 2009) has been suggested. The results of Study IV suggested further that children with relatively early onset epilepsy seem to be at risk for behavior problems already during their preschool years. In addition to behavioral problems, lower social skills in preschool-aged children with epilepsy compared to their healthy peers were demonstrated. Only one study (Tse et al., 2007) focused on social skills in school-aged children with epilepsy and reported similarly poorer social skills in children with epilepsy compared to their siblings.

Associations between epilepsy related factors, neurocognitive functions and social competence

The findings reported in this dissertation (Study I, II and IV) support the conclusion that early onset epilepsy is a risk factor for both neurocognitive impairment and poorer social competence. Further, these impairments can already be demonstrated during the preschool years in children with relatively short duration of epilepsy. In addition to etiology, age at onset of seizures was the most important predictor of cognitive impairment supporting the relevance of time at onset of seizures in the developing brain in a population based cohort of preschool-aged children with epilepsy. This supports the conclusion by Vasconcellos et al. (2001) and Vendrame et al. (2009), who demonstrated the importance of age at onset of seizures independent of etiology. Normal development before seizure onset is reported to predict a good cognitive outcome (Battaglia et al.,

1999). Therefore, early onset seizures may be particularly harmful for later development.

One possible explanation for the overall developmental impairments in both neurocognitive function and social competence evident at young age is a developmental delay. Alternatively, these impairments may be an early indication of a mental arrest, where a cognitive decline becomes more evident later in the course of epilepsy (Neyens, Aldenkamp & Meinardi, 1999). This cascade model of deterioration, in which children with epilepsy are in a process of mental deterioration shortly after the onset of epilepsy, has been suggested (Meinardi, Aldenkamp & Nunes, 1992; Neyens et al., 1999). Neyens et al. (1999) found that during one year follow-up, the children with epilepsy achieved lower FSIQ scores. Mangano et al. (2005) suggested that early seizure activity during the maturation of the brain may induce an abnormal arrangement of the underlying processes involved in the organization of more complex cognitive functions. This would result in later emergence of problems in higher-order cognitive functions, and thus in long-term neurocognitive and behavioral disabilities (Mangano et al., 2005). However, given the general instability and variability of test-scores in young children, the lower scores during preschool years may also partly be an indication of developmental delay rather than mental retardation. An investigation of questions relating to possible developmental trajectories requires prospective long-term follow-up studies, and therefore conclusions regarding these issues remain unanswered in this dissertation.

Both neurocognitive impairments and social competence problems are nowadays regarded as elementary parts of epilepsy itself rather than as secondary problems due to adjustment problems of a chronic condition (Hamiwka, Jones, Salpekar & Caplan, 2011). However, it is also possible that the chronic condition itself explains or moderates, at least partly, the development of poorer social competence. In general, an increased risk of developing social problems among children with chronic illnesses relates to limited ability to participate in social activities and social opportunities (La Greca, Bearman & Moore, 2002). The risk is high, especially for children with CNS condition or other stigmatizing medical conditions (La Greca et al., 2002; Nassau & Drotar, 1997). Similar conclusions were drawn in a recent meta-analysis by Martinez, Smith Carter and Legato (2011), who compared social competence in different chronic illness categories (e.g. asthma, diabetes, juvenile arthritis, cancer and neurological

disorders). They also concluded that when compared to other chronic conditions, epilepsy patients (and other neurological conditions) had poorest social competence. Therefore, the nature of the chronic condition seems to moderate social competence outcomes (Martinez et al., 2011).

The relationships between epilepsy related factors, and both cognitive function and social competence are complex. Despite the risk factors for neurocognitive problems and behavioral problems identified in children with epilepsy, knowledge of the interaction and mechanism of these factors and developing behavioral problems is lacking (Caplan et al., 2005). It is well recognized that underlying neurologic pathology is one of the most important factors. But, epilepsy is characterized in part by fluctuating cognitive and behavioral problems and diversity of underlying or associated brain pathology and manifestation of seizures. This is especially true in children with poor or partial seizure control that is often related to early onset seizures (Deonna & Roulet-Perez, 2005). In this dissertation, seizure control was good for 40% of the children and partial or poor for the remaining 60% (Study I). Hence, the neurocognitive problems encountered in half of the children could be partially related to recurrent seizures.

Neurocognitive problems are typically reported in school-aged children with epilepsy. As seen in typically developing children, underlying or comorbid neurocognitive problems, e.g. verbal intelligence (Caplan et al., 2004) or inattention (Drewel et al., 2009) have been demonstrated to be associated with social adjustment problems and peer difficulties in children with epilepsy. In fact, these neurocognitive problems (instead of epilepsy related factors) may be more closely related to poorer social competence, especially social adjustment problems in children with epilepsy (Turky et al., 2008). Or alternatively, there may be underlying deficits in basic socio-cognitive skills relating to social adjustment problems, as Golouboff et al. (2008) suggested in children with temporal lobe epilepsy. Social skills problems may impede the development of age-appropriate social competence. There is still a need for studies focusing on the developmental course and early assessment after the onset of seizures.

5.2 Theoretical considerations and future directions

As recently suggested in the ILAE classification (Berg et al., 2010), the term benign epilepsy is no longer valid. This is due a growing body of studies showing problems in both neurocognitive and social function. In this dissertation, impairments reported in language, verbal short-term memory and attention may be related to the active development of these functions in preschool age. Possibly the most vulnerable functions associated with epileptic activity at a given time are those still developing (Svoboda, 2004). Especially the vulnerability of language function, that seems to be evident in preschool-aged children with epilepsy, may partly be related to ongoing development (e.g. vocabulary, semantic categories) during the preschool years (Kagan & Herschkowitz, 2005). Thus an interruption via epileptic activity may alter, delay, or arrest the expected developmental course of language (Deonna & Roulet-Perez, 2005; Svoboda, 2004). Similarly, short-term memory performance shows a linear increase during preschool years (Gathercole et al, 2004). There are contradictory findings regarding memory function in children with epilepsy which may be alternatively explained by underlying impairments in language and attention (Kadis, Stollstorff, Elliott, Lach & Smith, 2005). Although attention functions are easily disrupted in CNS conditions, the impairments reported in this dissertation may also reflect active development of inhibition and impulse control in preschool-aged children (Klenberg, Korkman & Lahti-Nuuttila, 2001). It is also possible that diffuse impairments are an indication of active epilepsy, possibly disappearing after remission, as has typically been reported in benign rolandic epilepsies (Lindgren et al., 2004; Northcott, Connolly, McIntyre, Christie, Berroya, Taylor, et al., 2006).

Given the number of studies conducted on both neurocognitive function and social adjustment in children with epilepsy, little is known about the developmental pathways leading to neurocognitive or social impairments. This is due to the descriptive and comparative nature of earlier studies. However, different neurodevelopmental trajectories are suggested as probable in the course of childhood epilepsy (Seidenberg et al., 2007). In future, it would be beneficial to change the focus to the investigation of possible mediating factors between epilepsy, neurocognitive factors, and social competence. The proposed conceptual framework (Figure 1) hypothesizes that underlying CNS lesions or dysfunction along with environmental and familial factors

may have a direct effect on social competence. Alternatively, this effect may be mediated through epilepsy related or / and neurocognitive factors which, in turn, may both also have an independent effect on social competence [see also Noeker et al., 2005). The studies reviewed (Study III) provided some support for this hypothetical link between epilepsy-related factors, neurocognitive functions (e.g. **v**erbal cognitive impairments, socio-cognitive skills) and social competence (Caplan et al. 2004; Golouboff et al., 2008). However, in order to confirm these hypothetical links and mediating factors, more studies are needed. Studies also need to determine whether poorer social competence in children with epilepsy is related to an underlying deficit or developmental delay in social skills or attributed to inability in social performance. Future studies on the associations between various variables and social competence would also be beneficial in identifying possible protective factors.

Compared to studies on cognitive functions and epilepsy, fewer studies have focused on various aspects of social competence. There has been a lack of theoretical consideration that is obviously a significant limitation is earlier studies of social aspects of childhood epilepsy. In future studies, definition of the key concept, social competence, need to be theoretically clarified. This, in turn, requires a theoretical and conceptual background of social competence that integrates current views and results from both developmental psychology and developmental neuroscience. A conceptual model or theoretically justified definition would also help to distinguish subcomponents and potential outcomes related to social competence. Subcomponents of social competence should also be defined in individual studies. Rather than keeping the perspective at the social adjustment level, positive aspects of social competence (e.g. social participation) should be considered in future studies. In addition, more studies are needed on the basic socio-cognitive skills related to social competence. A broader perspective would also be beneficial regarding intervention and protective factors of coping with chronic condition.

Some methodological considerations for future research must be addressed. These methodological questions may partly explain the contradictory findings between studies regarding neurocognitive functions. The first and possibly most important consideration for studies is the representativeness of study designs; especially regarding participants' age. Studies on social competence have typically included fairly large population- or community-based samples and have been quite representative with

respect to age range. However, the age range of the participants has varied considerably (from 1 to 18 years). Typically participants have been school-aged children with mean age over ten years. Thus, school-aged children are overrepresented. This is decidedly problematic from the developmental perspective because the childhood years are a phase of rapid cognitive and social development. Subsequently the demands for social competence increase as a function of child's age and developmental level. Therefore, in future studies, subgrouping of participants is recommended (e.g. infants, early childhood years, school-aged children, and adolescents). Some aspects of social competence (e.g. social skills) may be assessed at a younger age, but other aspects, like social participation, can be more reliably evaluated at school-age.

Secondly, there have been differences between epilepsy related factors (e.g. seizure types, seizure frequencies and, and age at onset) in study samples. Typically, most of the studies on neurocognitive functions have focused on specific syndromes (e.g. on rolandic epilepsy), and therefore the generalizability their findings is compromised (Seidenberg et al., 2007). In addition, most severe epilepsies with high seizure frequency and mental retardation (i.e. learning disabilities) are often excluded from studies. This does not represent the whole heterogeneous population of children with epilepsy, and possibly leads to more favorable cognitive and social outcomes. Neurocognitive function has typically been assessed several years after the onset of seizures. However, some evidence supports the idea that both neurocognitive and social competence may already be affected at diagnosis or prior to the first seizure (e.g. Austin et al., 2001; Austin et al., 2002; Dunn et al., 2003). Evidently, all these factors affect the representativeness of the study groups. Therefore, more population-based cohort studies on children with epilepsy will be needed in the future to confirm the diffuse pattern of the neurocognitive impairments suggested.

The final methodological consideration relates to the assessment of social competence. Different rating scales are most often used. The review (Study III) indicated that the assessment methods had been quite stable over the past 12 years with the majority of studies using the CBCL. However, Perrin, Stein and Drotar (1991) pointed out several years ago that the CBCL is neither designed nor recommended for children with chronic illnesses (see also Berg, Vickrey, Testa, Levy, Shinnar, DiMario, et al., 2007; Oostrom, Schouten, Kruitwagen, Peters & Jennekens-Schinkel, 2001). The CBCL problem scales have been argued to be problematic especially in children with

epilepsy due to fact that behavioral ratings may be confused with or based on seizure features rather than behavior (Oostrom et al., 2001). Moreover, the Social Competence Scales measure more accomplishments and social participation skills or competence in social interactions. Therefore restrictions and limitations on participation in social activities due to epilepsy should not be mistaken for social incompetency (Nassau & Drotar, 1997; Martinez et al., 2011). Based on the review, inclusion of all aspects of social competence is recommended for a comprehensive assessment of social competence. This would require reconsideration of the assessment methods used; rating scales for social skills and prosocial behavior such as the SSRS (Gresham & Elliott, 1990) and the SDQ (Goodman, 1997) should be considered. But, more studies are needed to assess the reliability and validity of the rating scales in children with epilepsy. Finally, the age of the participants and the assessment methods used should be thoroughly considered. The assessment of social competence, especially in young children, may be problematic. For example, the CBCL scales for young children under school-age do not include social competence scales. More attention should be paid to the use of rating scales for young children.

5.3 Limitations

The strength of this study is its population based cohort representing the heterogeneity of epilepsy with several seizure and epilepsy types and also including epilepsies secondary to congenital and progressive neurological diseases with severe phenotype. The strength of the Studies II and IV was the use of age and gender matched healthy controls. The methodological choice inevitably causes to some limitations. First, the study cohort was heterogeneous with respect to epilepsy related variables, e.g. different etiologies, epilepsy and seizure types. Thus, early onset and severe epilepsies are overrepresented in the study cohort, which should be taken into account when interpreting the results. Also, there was limited number of participants in Studies II and IV. Due to the limited number of children, subgrouping of participants was not feasible. Therefore it was not possible to explore the relationships between epilepsy related variables and neurocognitive functions and social competence in greater detail. The number of children in subgroup analysis remained low, and only limited analyses were possible. Secondly, due to the cross-sectional nature of this dissertation, no conclusions

regarding different developmental trajectories can be drawn. On the basis of the results presented in the original studies, early onset epilepsy seems to be a risk factor for subsequent development. However, it remains to be seen in follow-up studies whether the impairments reported here develop into long-lasting disabilities. Thirdly, neurocognitive functions and social competence were assessed with standardized tests and rating scales completed by parents, providing a limited perspective on the children's competence. Assessments from day-care or caregivers would have broadened the picture and improved the ecological validity of the results. A follow-up study with assessment of learning and academic skills would also improve the ecological validity of the neuropsychological assessment.

A systematic review of social competence in children with epilepsy was conducted to investigate which aspects of social competence have been studied. First, the limitations of this review relate partly to the terms used in the original search. The terms and their combinations used in the search yielded numerous studies. Given the number of studies drawn from the electronic database in the first phase (4,509 articles) and second phase (344 articles), it was not possible to review them in detail. Due to this some relevant articles may have been excluded. Secondly, the quality of this review would have improved if the quality of the study indices (QSI) (e.g. Downs & Black, 1998; Ferro & Speechley, 2009) had been calculated. The QSIs would also have helped readers to put the results of this review into context. Alternatively, a meta-analysis of social adjustment problems and social participation would have given to conclusions more power, but due to descriptive nature of this review and the limited number of studies conducted on social skills no meta-analysis was conducted.

5.4 Clinical implications

The present study provides additional evidence for the conclusion that epilepsy is more than overt seizures or the tip of the iceberg (Aicardi, 1999). In addition, this dissertation emphasizes the heterogeneous nature of epilepsy and the variable impact on a child's development. Due to increased risk for cognitive impairment in preschool-aged children with epilepsy, a neuropsychological assessment is recommended as a standard procedure in clinical practice. Neuropsychological evaluation is also suggested for those

with idiopathic (i.e. genetic) epilepsies with presumably more favourable cognitive long-term outcome. A large and growing body of literature in recent years has demonstrated specific neurocognitive problems among this subgroup of children with epilepsy. The assessment is proposed early in the course of epilepsy (e.g. at the time of seizure onset) rather than after parents have become more concerned.

In clinical practice, the emphasis has more often been on cognitive assessments rather than behavioral assessments. A more comprehensive and multilevel perspective in psychological evaluation, including standardized tests, and behavioral rating scales along with observations from day-care or school for the assessment of social competence is suggested for the multidisciplinary, holistic treatment of epilepsy. This would be beneficial in determining individual developmental pathways and possible protective factors. In epilepsy guidance, more attention should be paid to supporting the acquisition of age-appropriate social skills and social competence (Rantanen et al., 2011). Social competence in the preschool years forms a basis for the subsequent development of academic skills and prosocial behavior. Therefore developmental, social and behavioral problems during the preschool years may have long-lasting effects on later development. Behavioral and social issues are of special importance for those children with refractory epilepsy and additional cognitive problems. It is important that parents have a realistic understanding of the condition and its consequences, including possible restrictions on participation. In particular, avoidance of unnecessary and unwarranted restrictions in everyday life should be emphasized.

6. Summary and conclusions

1) Prevalence of active epilepsy in a cohort of preschool-aged children with epilepsy was 3.2 / 1,000. Cryptogenic and symptomatic etiologies were most typically found in the cohort, and only a minority of children had idiopathic epilepsy. This study therefore represents children with early onset seizures and severe epilepsies.
2) Intellectual function was found to be normal in half of the children with epilepsy, and a proportion of moderate to severe mental retardation was reported in 28 %. However, specific neurocognitive impairments in verbal skills, short-term memory, and attention were also reported in some children with normal intellectual function.
3) A review of studies demonstrated that definitions of social competence were lacking. The focus of the studies and hence the assessment methods used were mostly at the social adjustment level. Little is known about socio-cognitive or social skills or social participation.
4) Poorer social competence was demonstrated in preschool-aged children with uncomplicated and complicated epilepsy. When compared to healthy controls, children with epilepsy had poorer social skills, and more behavioral problems.

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FULL-LENGTH ORIGINAL RESEARCH

Cognitive impairment in preschool children with epilepsy

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Summary

Purpose: **Studies have shown that underlying pathology and early onset of seizures are both significant factors contributing to cognitive impairment in children with epilepsy. However, there are only few studies focusing on cognitive impairment in preschool children with epilepsy. The purpose of this study was to describe the cognitive performance in a population-based cohort of preschool children with epilepsy. The aims of the study were to determine frequency of cognitive impairment, level of cognitive functions, and epilepsy-related factors correlating with cognitive impairment.**

Methods: **The study group consisted of a population-based cohort (N = 64) of preschool children (3–6 years 11 months) with active epilepsy. Medical data and results from previous psychological evaluations were reviewed retrospectively from the medical records. A logistic regression model was used for the prediction of cognitive impairment.**

Key Findings: **Prevalence of epilepsy was 3.2 per 1,000 children. Cognitive function was considered to be within normal or borderline range for 50%, mildly retarded for 22%, and moderately to severely retarded for 28%. Cognitive impairment was related to complicated epilepsy, age at onset of epilepsy, abnormal magnetic resonance imaging (MRI), and additional neurologic problems. Age at the onset of seizures was the only significant predictor of cognitive impairment.**

Significance: **The results concur with those of earlier studies on cognitive impairment in childhood epilepsy. Age at onset of epilepsy is also an important factor for cognitive impairment on young children with epilepsy. The results suggest that cognitive impairment is evident early in the course of epilepsy.**

KEY WORDS: **Cognitive function, Cognitive impairment, Preschool children, Epilepsy.**

Many factors may contribute to cognitive impairment in childhood epilepsy. Underlying brain abnormalities are associated with impaired cognitive functions in children with epilepsy (Nolan et al., 2003). Children with symptomatic epilepsy are more likely to have mental retardation (Vasconcellos et al., 2001). Instead, children with idiopathic epilepsy are reported to have cognitive performance at the lower end of normal distribution, although differing from healthy controls (e.g., Høie et al., 2005; Cormack et al., 2007). Generally, the proportion of intellectual dysfunction (IQ <80) in children with epilepsy varies between 26% and 57% (Cormack et al., 2007; Berg et al., 2008) and in population-based studies, about 20–40% of children with epilepsy are reported to have mental retardation (Sillanpää, 1992; Sidenvall et al., 1996; Waaler et al., 2000; Camfield & Camfield, 2007). In addition, Sillanpää (1992) indicated other neurocognitive difficulties; about 28% have speech disorders and 23% learning difficulties. It has also been suggested (Keene et al., 2005) that the cognitive problems in epilepsy are likely to be related to a common preexisting underlying pathology influencing both.

Although the underlying etiology is perhaps one of the strongest predictors of cognitive impairment, several studies have demonstrated that early age at onset of seizures seems to be another major risk factor contributing to cognitive impairment (Bourgeois et al., 1983; Battaglia et al., 1999; Bulteau et al., 2000; Smith et al., 2002; Freitag & Tuxhorn, 2005; Mangano et al., 2005; Cormack et al., 2007), even independently of the pathology of epilepsy (Vasconcellos et al., 2001). Both animal and clinical studies demonstrate that early seizures affect brain development and increase the subsequent vulnerability of the mature brain to the effects of seizures (Squier et al., 2003; Holmes, 2004). Children with seizure onset during the first year of life are especially likely to have poorer cognitive outcome (Vanderlinden & Lagae, 2004; Mangano et al., 2005; Cormack et al., 2007).

In addition to etiology or age at onset, longer duration of epilepsy (Elger et al., 2004) or proportion of life with

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epilepsy (Smith et al., 2002) has been found to be associated with cognitive function. Some (Aldenkamp & Bodde, 2005) have emphasized the association between seizure control or seizure frequency and cognitive function. Furthermore, current antiepileptic medication (AED) has been found to be associated with cognitive function (Bulteau et al., 2000; Berg et al., 2008), but some (Smith et al., 2002) have reported contradictory findings.

Early onset of seizures is also often related to underlying neurologic pathology, that is, to symptomatic epilepsy (Rodin, 1989; Svoboda, 2004). In addition to early onset of seizures, high seizure frequency or intractable epilepsy has been found to coincide with both symptomatic etiology and additional neuroimpairment (Eriksson & Koivikko, 1997; Ramos-Lizana et al., 2009). Therefore, it is not surprising that mental retardation and cognitive and behavioral problems are common among children with complicated epilepsy (Kobayashi et al., 2001; Vasconcellos et al., 2001). In addition, mental retardation or cognitive problems are overrepresented in surgical candidates with severe refractory epilepsy. For example, Freitag and Tuxhorn (2005) reported that >70% of preschool surgical candidates were mentally retarded (IQ <70). Despite the well-recognized fact that early onset seizures may affect cognitive function, there are only few studies (e.g., Battaglia et al., 1999; Chaix et al., 2003; Mangano et al., 2005) on preschool-aged children. In addition, children with additional neuroimpairment (e.g., cerebral palsy) and learning disability/mental retardation (IQ <70) are often excluded from studies (e.g., Rejnö-Habte Selassie et al., 2008).

Purpose

The purpose of this present study is to describe the full range of cognitive performance in preschool children with epilepsy. First, the aim of this study was to describe the characteristics of a population-based cohort of preschool children with epilepsy and to determine the frequency and the level of cognitive impairment in more detail. Secondly, the associations between the neurologic variables (e.g., age at onset, seizure control, AEDs used) and cognitive functions were studied. For descriptive purposes the cohort was divided into two subgroups: children with uncomplicated (n = 26) and complicated (n = 38) epilepsy. Uncomplicated epilepsy refers to idiopathic or cryptogenic epilepsy and complicated epilepsy refers to epilepsies with remote symptomatic cause or an epileptic encephalopathy (Berg et al., 2008). On the basis of earlier studies conducted on school-aged children with epilepsy, it was first hypothesized that the intellectual functioning of children in the uncomplicated group would be within normal range and impaired among children with complicated epilepsy (Mandelbaum & Burack, 1997; Bailet & Turk, 2000; Vasconcellos et al., 2001). The second hypothesis was that cognitive impairment in preschool children would be associated with underlying etiology, age at onset of seizures, duration of epilepsy, and seizure frequency that studies (Battaglia et al., 1999; Vasconcellos et al., 2001; Elger et al., 2004; Cormack et al., 2007) have previously shown to contribute to cognitive functions.

This research was conducted in collaboration with the Department of Psychology at the University of Tampere, the Pediatric Neurology Unit of Tampere University Hospital, and the Pediatric Research Centre at the University of Tampere. The ethical committee of Tampere University Hospital approved the study. Parents of children participating in psychological assessment gave their informed written consent. For retrospective review of medical and psychological data, the approval of the ethical committee was sufficient.

Methods

Participants

A population-based cohort of preschool-aged children with active epilepsy (N = 64) was identified through the medical records of the Pediatric Neurology Unit, Tampere University Hospital, Finland, which is the only center for pediatric neurology services in the hospital district. On the point prevalence day, September 30, 2004, the total population of the hospital district was 464,976, of whom 19,821 were children aged 3–6 years 11 months. The study cohort consisted of all children aged 3–6 years 11 months with epilepsy.

Medical and psychological assessment data

All medical and psychological records, neurophysiologic recordings, and available clinical data were reviewed retrospectively. Medical data including demographic factors, duration of epilepsy (at the time of psychological assessment), seizure and epilepsy type, seizure control during the period of the study, electroencephalography (EEG), imaging of the brain with 1.5T MRI, current AEDs, and most recent AED levels were analyzed retrospectively from children's medical records. Examiner's comments and observations during the psychological assessment were also checked. According to the medical reports there were nine children in the complicated group with daily seizures, no seizures during the assessment day or the previous night were reported by parents. Of the total cohort (N = 64), psychological assessment of cognitive abilities were available for 47 children, 14 children were neurologically too impaired for reliable assessment, and 3 children with idiopathic epilepsy did not consent to psychological assessment. The Finnish versions of Wechsler's Primary and Preschool Scale of Intelligence – Revised, WPPSI-R (Wechsler, 1995) or Wechsler Scale of Intelligence for Children –III, WISC-III (Wechsler, 1999) were used. Thirty-seven were assessed with WPPSI-R and 10 with WISC-III. Five of the nonparticipating children were assessed at the age of 18–28 months

with the Bayley Scales of Infant Development, BSID-II (Bayley, 1994). Due to different nature of the Bayley Scales, these results have been excluded from the analysis. The psychological evaluations were administered by a clinical psychologist or neuropsychologist. For those children unable to participate in standardized psychological evaluation, the level of cognitive functioning was determined from medical and psychological records, parental reports, and, when available, observations from daycare. Cognitive functioning was classified as within normal (IQ ≥70), mildly retarded (IQ = 50–69), moderately retarded (35–49), and severely/profoundly retarded (<34).

Statistical analysis

Statistical analyses were done with the Statistical Package for Social Sciences (SPSS, version 16.0; SPSS Inc., Chicago, IL, U.S.A.). Continuous and normally distributed variables were compared with Student's *t*-test, and chi-square test was used for categorical variables. Spearman's rho was used to explore the linkage between epilepsy-related factors and cognitive impairment. P-values <0.05 were considered statistically significant. A logistic regression analysis was used to predict cognitive impairment. Level of cognitive function was dichotomized into normal (IQ ≥70) and impaired (IQ ≤69, including the severe, unassessable participants). Predictors considered included age at onset seizures, duration, etiology (idiopathic/cryptogenic vs. symptomatic), MRI (normal vs. abnormal), seizure frequency (good, partial vs. poor), and AED (AED vs. no AED). First, all the independent variables were tested by univariate logistic analysis. Thereafter, the predictive model was executed using a multivariate logistic analysis.

Due to the severity of cognitive and other neurologic impairment, we were not able to reliably assess the cognitive functions of 14 children with standardized measures. This unassessable group included children with severe psychomotor retardation without specific etiology (n = 6), infantile neuronal ceroid lipofuscinosis (INCL, Hagberg-Santavuori disease, n = 3), Rett syndrome (n = 2), congenital CNS malformations (n = 2), and Charge syndrome and mental retardation (n = 1). In some instances (e.g., in analyzing IQ scores), this unassessable group was excluded in order to ensure that they did not influence the findings. For the logistic regression analysis cognitive function for the unassessable group was classified as impaired.

Results

Medical and clinical data

The total cohort consisted of 64 children with epilepsy; 33 girls and 31 boys participated in the study. The total point prevalence was 3.2 per 1,000 in children aged from 3 to 6 years 11 months. Mean age was 65.16 months (SD = 13.38) and age at onset of epilepsy varied between 0 and 75 months (mean 26.98 months, SD = 21.05). About 55% of children had normal MRI and 45% had abnormal MRI. Twenty-seven children had focal seizures, 31 had generalized seizures, and six were unclassified. Monotherapy was used in 64.1% children, polytherapy in 26.6% children, and 9.4% of children had no AED. Valproate was the most common AED used (n = 43, 67.1%). Seizure control was good in 37%, partial in 16%, and poor in 47% of the participants. There were differences in epilepsy-related variables between the uncomplicated and complicated groups. The children with complicated epilepsy were significantly younger at the onset of seizures (mean: 21.89 vs. 32.42, $t_{62} = 2.43$, $p < 0.02$) and had, therefore, longer duration of epilepsy (mean: 43.05 vs. 30.42, $t_{62} = -2.07$, $p < 0.05$) than those with uncomplicated epilepsy. They also had higher seizure frequency than children with uncomplicated epilepsy ($\chi^2_5 = 11.8$, $p < 0.05$). Detailed characteristics are presented in Table 1.

Cognitive function

Cognitive function was considered to be within the normal range (IQ ≥70) for 50% of the participants. However, some of these children (n = 6, 9%) may be considered to have borderline (IQ 70–79) cognitive function. Mild mental retardation was found in 21.9% of the participants and moderate to severe retardation in 28.1% of the cohort. The mean IQ (n = 47) of the cohort was 76.00 (SD = 26.06), which was significantly lower than normative mean ($t_{46} = -6.32$, $p < 0.001$). As demonstrated in Fig. 1, cognitive impairment was more common in children with complicated epilepsy, and cognitive function in children with uncomplicated epilepsy was within normal range. Children with complicated epilepsy had significantly lower overall IQ (91.27 vs. 62.56, $t_{45} = 4.49$, $p < 0.001$) than children with uncomplicated epilepsy. In fact, the level of cognitive functioning in this group was lower than the mean IQ, since the neurologically and cognitively most severely impaired participants had to be excluded from the analysis.

Cognitive impairment in relation to epilepsy variables

Some epilepsy-related variables were associated with cognitive functioning (Table 2). Significant correlations were found between cognitive impairment and group, that is, uncomplicated versus complicated epilepsy ($r = 0.636$, $p < 0.001$), additional neurologic diagnosis ($r = 0.565$, $p < 0.001$), age at onset ($r = -0.309$, $p = 0.01$), and MRI ($r = 0.258$, $p < 0.05$). However, no significant associations were found between cognitive impairment and seizure frequency, etiology, duration, status epilepticus, most recent EEG, or number of AED.

A logistic regression model was used to study the predictors of cognitive impairment. Cognitive impairment was a dependent variable. First, the predictive significance of each independent variable was determined by univariate logistic analysis. Thereafter, the best combination of predictors was computed using a forward stepwise regression model. In the

Table 1. Clinical and demographic characteristics of the study groups

	All subjects	Uncomplicated group	Complicated group
N	64	26	38
Gender			
Female	33	12	21
Male	31	14	17
Age (months)[a]			
Mean (SD)	65.16 (13.38)	64.85 (11.61)	65.37 (14.61)
Range	36–83	43–79	36–83
Etiology			
Idiopathic	6	6	0
Symptomatic	27	0	27
Cryptogenic	31	20	11
MRI			
Normal	35	26	9
Abnormal	29	0	29
Age at onset of seizures (months)			
Mean (SD)	26.98 (21.05)	34.42 (20.93)	21.89 (19.83)
Range	0–75	6–72	0–75[b]
Duration (months)[a]			
Mean (SD)	37.92 (23.99)	30.42 (20.31)	43.05 (25.20)
Range	2–83	2–71	2–83[c]
Epilepsy type			
Focal	27	9	18
Generalized	31	16	15
Unclassified	6	1	5
Seizure control			
Daily	9	0	9
Weekly	10	2	8
Monthly	8	5	3
Yearly	11	6	5
>1 year remission	6	2	4
>2 year remission	20	11	9[d]
Status epilepticus			
No	50 (78%)	20	30
Yes	14 (22%)	6	8
AED			
No AED	6 (9%)	2	4
Monotherapy	41 (64%)	20	21
Polytherapy	17 (27%)	4	13

[a]Age was calculated at the time of psychological assessment.
[b]$t_{62} = 2.43, p < 0.02$.
[c]$t_{62} = -2.07, p < 0.05$.
[d]$\chi^2_5 = 11.8, p < 0.05$.

final model age at onset of seizures, etiology, MRI (normal, abnormal), additional neurologic diagnosis (yes, no), and seizure frequency (good, partial, poor) were entered as predictors of cognitive impairment. The overall model predicted about 32% of the cognitive impairment ($\chi^2 = 17.54$, d.f. = 5, $p = 0.004$, Pseudo $R^2 = 0.32$), with age at onset of seizures being the only significant predictor (Wald = 4.52, d.f. = 1, $p < 0.05$).

Discussion

To the best of our knowledge, there are no other studies available focusing on cognitive impairment in population-based cohorts of preschool children with epilepsy. In most studies (e.g., Rejnö-Habte Selassie et al., 2008), children with additional neurologic impairments and lower IQ (<70) are often excluded. The present population-based study of preschool children with epilepsy included all the 3–6 years 11 months aged children with epilepsy in the hospital district. The prevalence rate 3.2 of this study was consistent with earlier studies conducted in Finland (Eriksson & Koivikko, 1997) and other developed countries (Beilmann et al., 1999; Waaler et al., 2000; Larsson & Eeg-Olofsson, 2006). In the present study, we described the medical and cognitive characteristics of a population-based cohort of preschool children with epilepsy, that is, with no exclusion criteria. The children with uncomplicated epilepsy differed clearly from the complicated group regarding age at onset of epilepsy, duration of epilepsy, and seizure control. It was characteristic of the complicated group that they were younger at onset of seizures, had longer duration, and had higher seizure frequency than the uncomplicated group. Other studies (e.g., Vasconcellos et al., 2001) confirm this to be typical for children with symptomatic or complicated epilepsy.

First, the frequency and the level of cognitive impairment were determined. The mean overall IQ (m = 76.00) of the whole cohort is significantly below normal. In this study, cognitive function was considered normal in 40% and borderline in 9% of the cohort. Moderate to severe mental retardation was found in 28% of the children. These results are consistent with earlier studies (Sillanpää, 1992; Sidenvall et al., 1996; Waaler et al., 2000; Camfield & Camfield, 2007; Berg et al., 2008) suggesting that about 20–57% of children with epilepsy are cognitively impaired. Berg et al. (2008) have recently shown in their large, representative community-based cohort that about 26% of subjects had subnormal cognitive functions and in those with seizure onset before 5 years the percentage was 33%. However, in our study, about 50% had cognitive impairment. The high proportion of participants with low cognitive functioning was somewhat unexpected. As we hypothesized in the light of Mandelbaum and Burack (1997), Bailet and Turk (2000) and Vasconcellos et al. (2001), impaired cognitive functioning was more common among children with complicated epilepsy and within normal range in children with uncomplicated epilepsy. In our study, only one of six children with idiopathic epilepsy had mild cognitive impairment.

Secondly, the associations between the epilepsy-related variables and cognitive functions were studied. The hypothesis was that cognitive impairment in preschool children would be associated with four factors, that is, underlying etiology, age at onset of seizures, seizure duration, and seizure frequency, that other studies have previously shown to contribute to cognitive functions (Battaglia et al., 1999; Vasconcellos et al., 2001; Elger et al., 2004; Cormack et al., 2007). As expected, cognitive impairment was related

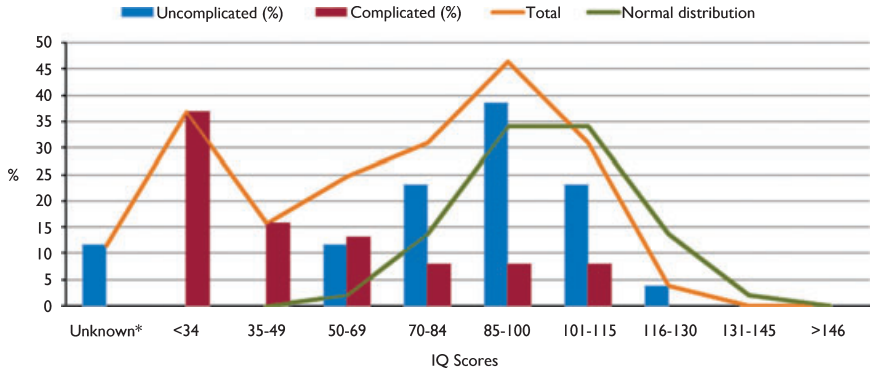

Figure 1.
Cognitive functioning in preschool children with epilepsy.
*No psychological assessment data available (n = 3). The level of cognitive functioning was determined to be normal on the basis of medical records, parental reports, and, when available, observations from day care.
Epilepsia © ILAE

Table 2. Cognitive impairment in relation to epilepsy-related variables

	Cognitive impairment		Level of mental retardation		
	No (≥70)	Yes (≤69)	Severe (<34)	Moderate (35–49)	Mild (50–69)
Etiology[a]					
Idiopathic	5	1	–	–	1
Symptomatic	9	18	7	5	6
Cryptogenic	18	13	3	3	7
MRI[b]					
Normal	24	16	5	3	8
Abnormal	8	16	5	5	6
Seizure type					
Focal	16	11	3	1	7
Generalized	16	15	4	3	8
Unclassified	1	5	–	–	5
Age at onset, months					
1–24	12	21	5	8	8
25–48	12	8	4	–	4
49–60	8	3	1	–	2
Seizure control[c]					
Good	14	10	3	2	5
Partial	6	4	–	2	2
Poor	12	18	7	4	7
AED					
No AED	4	2	–	–	2
Monotherapy	22	19	7	3	9
Polytherapy	6	11	3	5	3

[a] $\chi^2_2 = 6.25$, $p < 0.05$.
[b] $\chi^2_1 = 4.27$, $p < 0.05$.
[c] Seizure control: Good: Seizure remission >1 year, Partial: Seizures ≤1 per month, Poor: Seizures >1 per month.

to age at onset of seizures, abnormal MRI, and additional neurologic diagnosis. A strong relationship between early onset epilepsy and cognitive impairment has been recognized in the literature (Battaglia et al., 1999; Bulteau et al., 2000; Vasconcellos et al., 2001; Chaix et al., 2003; Freitag & Tuxhorn, 2005; Kaaden & Helmstaedter, 2009; Vendrame et al., 2009). Evidently, our study cohort represents children with early onset epilepsy.

Some, for example, Vasconcellos et al. (2001) have demonstrated that early age at seizure onset is a risk factor for cognitive impairment independent of etiology. However, even among this narrow age group there was a significant difference in age at onset of epilepsy between uncomplicated and complicated epilepsy. Complicated epilepsy is closely related to earlier onset of seizures and higher seizure frequency. In addition to early onset, almost half of the children had poor seizure control. Again, seizure control or frequency was poorer in the complicated group. Interestingly, seizure frequency was not associated with level of cognitive impairment, but, this may be partly due to small sample size.

This study provides further evidence of the importance of the age at onset of seizures for cognitive functioning. In addition, in their recent study, Kaaden and Helmstaedter (2009) concluded that cognitive impairment is more related to age at onset of epilepsy than to longer duration or cumulative effects of seizures. In the present study, cognitive impairment was evident in young children (i.e., preschoolers) with relatively short duration of epilepsy supporting the hypothesis that cognitive deterioration or impairment is likely to occur early in the course of epilepsy, as Meinardi and Nunes (1992) and Neyens et al. (1999) have suggested. The developing, immature central nervous system is vulnerable to the effects of damage or harmful internal or external conditions (Aylward, 1997). Therefore, any interruption (e.g., the presence of an active electrophysiologic epileptic focus or repetitive epileptiform generalized discharges) may disrupt the expected

developmental course and impede or impair the normal maturation of the central nervous system and cognitive functions (Elger et al., 2004; Hommet et al., 2006; Kaaden & Helmstaedter, 2009). This may be one explanation for the cognitive impairment in young children with epilepsy. Or possibly early seizures affect the brain development and exacerbate subsequent vulnerability of the mature brain to the effects of seizures (Squier et al., 2003; Holmes, 2004). Note also that children with uncomplicated epilepsy may be at risk for neurocognitive difficulties despite normal cognitive capacity (Bailet & Turk, 2000; Henkin et al., 2005; Northcott et al., 2005). According to our earlier studies of this same cohort (Rantanen et al., 2009, 2010), the preschool children with uncomplicated epilepsy demonstrated more problems in neurocognitive functions (e.g., in attention and language) and social competence than their healthy peers.

One of the main benefits of this study is that the focus is on preschool-aged children, a group of children with epilepsy that has been paid little attention in the earlier studies. The strengths of the study also include a targeted and population-based cohort with a narrow age range and the detailed review of the clinical data and epilepsy variables. However, some limitations must be conceded. First, because we focused on a population-based cohort in a narrow age range, the sample size remains small. Due to the methodologic decision to use the population-based cohort, the study group was inevitably heterogeneous, representing the whole range of different types of epilepsy. Because of this, the associations between cognitive impairment and epilepsy-related factors may not be regarded as definite. Failure to find independent effects of MRI abnormalities and etiology in logistic regression may partly reflect inadequate power due to small number of participants. Due to definition used in this study, it is also possible that there may be some overlap between etiology and uncomplicated versus complicated epilepsy. Therefore, the failure of etiology to predict impairment may partly relate to the method of defining etiology. The generalizability of our findings is limited and, therefore, these data must be interpreted with caution.

To conclude, early onset epilepsy is a risk factor for cognitive impairment. Furthermore, the cognitive impairment can already be demonstrated during preschool years in children with relatively short duration of epilepsy. However, due to the general instability of test scores in young children, the lower scores during preschool years may partly be an indication of developmental delay rather than mental retardation. A follow-up study of this cohort would be beneficial to study this and also the association between a longer duration of illness and development of cognitive function. In clinical practice, we should pay more attention to early intervention to improve the subsequent cognitive and psychological outcomes of these children. In addition, further longitudinal, especially prospective studies, are needed to investigate the developmental course of children with epilepsy.

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Disclosure

None of the authors has any conflict of interest to disclose. We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

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Neurocognitive functioning of preschool children with uncomplicated epilepsy

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Only few studies are available on the cognitive functioning of preschool children with uncomplicated epilepsy. The aim of this study was to describe the neurocognitive functioning of 3–6-year-old children with uncomplicated epilepsy. A subgroup of children with uncomplicated epilepsy from a population based cohort of preschool children with active epilepsy ($N = 64$) participated in the study. The neurocognitive functioning of these children ($N = 13$) was compared to that of matched healthy controls ($N = 13$). The Wechsler's Primary and Preschool Scale of Intelligence – Revised and the Developmental Neuropsychological Assessment were administered. The intellectual functioning of the children with uncomplicated epilepsy was within normal range, but differed significantly from that of healthy controls, which was contrary to expectations. Statistically significant differences emerged between the study and the control group in Verbal IQ and Full Scale IQ, but no differences were found in Performance IQ. The children with uncomplicated epilepsy also had minor neurocognitive difficulties in verbal short-term memory ($p < .01$) compared to healthy children. The result suggests that uncomplicated epilepsy in preschool children may interfere with language and verbal short-term memory functions. Further studies with detailed neuropsychological assessments and follow-up time are needed to gain more insight into the developmental course of children with uncomplicated epilepsy. Also, because of the developmental risks reported in this study, psychological screening and detailed neuropsychological assessment are recommended in clinical practice.

Epilepsy, a chronic condition characterized by recurrent seizures, is one of the most common neurological disorders in childhood. The prevalence of active epilepsy in children is generally estimated between 3 and 11 per 1,000 children (Larsson & Eeg-Olofsson, 2006) and in Finland between 2 and 4 per 1,000 in children less than 16 years of age (Eriksson & Koivikko, 1997; Sillanpää, Jalava, Kaleva, & Shinnar, 1998). The developing, immature brain is more epileptogenic than the mature brain (Moshé, 1987, 1993). Therefore, the incidence of epilepsy is highest during the first year of life and

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declines with increasing age during childhood (Anderson Northam, Hendy, & Wrennall, 2001; Hauser & Annegers, 1993). During the sensitive period the central nervous system (CNS) is vulnerable to the effects of damage or harmful internal or external conditions (Aylward, 1997). Any interruption (e.g. the presence of an active electrophysiological epileptic focus or repetitive epileptiform generalized discharges) during a critical period of CNS development may disrupt the expected developmental course and interfere with the normal maturation of CNS and cognitive functions (Elger, Helmstaedter, & Kurthen, 2004; Hommet, Sauerwein, De Toffol & Lassonde, 2006; Motamedi & Meador, 2003).

Animal and clinical studies demonstrate that early seizures may profoundly affect the brain development and increase the later vulnerability of the mature brain to the effects of seizures (Holmes, 2004; Squier, Salisbury, & Sisodiya, 2003). However, recovery may be achieved with age, but in part this may be more of compensation and rewiring of the developing nervous system (Elger *et al.*, 2004; Nieminen & Eriksson, 2008). The epilepsy related factors contributing to the neurocognitive impairment in children with epilepsy include the underlying etiology and neuropathology, electroencephalographic (EEG) discharges and seizures, and antiepileptic drugs (Nieminen & Eriksson, 2008). An early onset, long duration of the disease and poor seizure control are generally associated with poor cognitive outcome (Battaglia *et al.*, 1999; Elger *et al.*, 2004; Mangano, Fontana, & Cusumano, 2005). Cognitive functions may already be impaired at the onset of epilepsy (Kolk, Beilmann, Tomberg, Napa, & Talvik, 2001; Oostrom, Smeets-Schouten, Kruitwagen, Peters, & Jennekens-Schinkel, 2003). Also, the maturation of cognitive functions in children is susceptible to the adverse influence of epilepsy (Elger *et al.*, 2004).

Developmental and cognitive problems are common in children with epilepsy, especially symptomatic epilepsy (Rodin, 1989; Svoboda, 2004). Idiopathic epilepsy refers to epilepsies with no underlying structural brain lesion or to age-dependent clinical manifestation and assumable genetic etiology (Engel, 2006; Hommet *et al.*, 2006). Most idiopathic epilepsies are uncomplicated which implies that there are no other neurological signs or symptoms and cognition is within normal range or only slightly impaired (Elger *et al.*, 2004; Hommet *et al.*, 2006; Mandelbaum & Burack, 1997; Motamedi & Meador, 2003). In general, children with focal seizure types have been found to perform better than children with generalized seizures (Dodrill, 2004; Mandelbaum & Burack, 1997). In spite of the favourable medical and intellectual prognosis, various neurocognitive deficits have been reported also in children with idiopathic, either focal epilepsies (FEs) or generalized epilepsies (GEs). Frequently, reported neurocognitive problems in school-aged children with idiopathic or uncomplicated epilepsy include slower reaction times (Aldenkamp & Arends, 2004; Leonard & George, 1999), overall attention problems (Gülgönen, Demirbilek, Korkmaz, Dervent, & Townes, 2000; Oostrom, Teeseling, Smeets-Schouten, Peters, & Jennekens-Schinkel, 2005), and specific deficits in visual and verbal attention (Henkin *et al.*, 2005; Williams, Griebel, & Dykman, 1998). Attention problems more often include inattentive than impulsive type (Dunn & Kronenberger, 2005), although attention-deficit-hyperactivity disorder has also been associated with epilepsy (Leonard & George, 1999; Williams, Schulz, & Griebel, 2001). In addition, various memory problems have been reported; impairments in short-term memory (Bailet & Turk, 2000; Oostrom *et al.*, 2005), delayed recall (Henkin *et al.*, 2005; Pavone *et al.*, 2001), verbal memory (Gülgönen *et al.*, 2000; Henkin *et al.*, 2005; Northcott *et al.*, 2005), and in visual and non-verbal memory (Gülgönen *et al.*, 2000; Northcott *et al.*, 2005, 2007; Pavone *et al.*, 2001) have been demonstrated in school-aged children with uncomplicated epilepsy.

Deficits in language function have also been reported, for example, in word fluency (Henkin *et al.*, 2005) and phonological awareness (Northcott *et al.*, 2005, 2007). In addition, specific neurocognitive impairment in school-aged children with uncomplicated epilepsy includes impairments in controlled fine motor responses (Henkin *et al.*, 2005) and psychomotor speed (Bailet & Turk, 2000; Boelen *et al.*, 2005).

Although there are many studies showing various neurocognitive impairments in children with uncomplicated epilepsy, contradictory findings have also been reported. For example, Pavone *et al.* (2001) found intact verbal memory and language functions. Also, Boelen *et al.* (2005) reported overall psychomotor development comparable to that of controls. These disparate findings demonstrate that there is no single pattern of neuropsychological impairment in idiopathic epilepsy (Deonna, Zesiger, Davidoff, Maeder, & Roulet, 2000; Seidenberg, 1989) or in childhood epilepsy in general (Williams *et al.*, 1998). Instead, a more diffuse neuropsychological profile with uncomplicated childhood epilepsy (Germanó *et al.*, 2005; Williams *et al.*, 1998) has been proposed. It is also possible that the impairments do not necessarily persist (Northcott *et al.*, 2006; Oostrom, Schouten, Kruitwagen, Peters, & Jennekens-Schinkel, 2002). Lindgren *et al.* (2004) showed that after active phase of rolandic epilepsy (i.e. when most of the children were seizure free), cognitive development resembled that of healthy children. It is clear that the association between epilepsy and comorbid neurocognitive deficits is complex and no direct causality has been demonstrated**.** See also Doddrill (2004) and Vingerhoets (2006) for an overview of the effects of seizures on cognition.

As Nolan *et al.* (2003) pointed out the majority of studies have been conducted on school-aged children. Studies on the impact of early onset seizures and on subsequent development are relatively scarce, but some do exist (e.g.Chaix *et al.*, 2003; Mangano *et al.*, 2005). The purpose of the present study was to describe the intellectual and neuropsychological functioning of preschool children from 3 to 6 years of age with uncomplicated epilepsy. In this study, children with epilepsy but without any associated neurological disorder or other chronic illnesses are referred to as uncomplicated epilepsy or 'epilepsy only' (Sillanpää, 1992), i.e. children with apparently age appropriate neurological and social development. The neurocognitive functioning of the uncomplicated children was compared to that of matched healthy controls. The two primary research questions were (1) Do the preschool children with uncomplicated epilepsy differ from healthy controls in their intellectual functioning and (2) Do preschool children with uncomplicated epilepsy differ from healthy controls with respect to neurocognitive functions? Also, the associations between intellectual, neurocognitive variables, and epilepsy related factors (e.g. epilepsy type, seizure control, and age at onset of epilepsy) were studied. In light of earlier studies, conducted on school-aged children with idiopathic or uncomplicated epilepsy, it was hypothesized firstly that the intellectual functioning of the study group would be within normal range and no statistical difference between the study group and the control group would emerge (Bailet & Turk, 2000; Mandelbaum & Burack, 1997). The second assumption was that if any neurocognitive deficits were to be found, they would demonstrate a diffuse pattern with various impairments in attention, memory, and / or visuomotor skills as in school-aged children with uncomplicated epilepsy (Aldenkamp, Overweg-Plandsoen, & Diepman, 1999; Boelen *et al.*, 2005).

This research was conducted in collaboration with the Department of Psychology at the University of Tampere, the Pediatric Neurology Unit of Tampere University Hospital and the Pediatric Research Centre at the University of Tampere. The ethical committee of Tampere University Hospital approved the study.

Methods

Participants

This study was part of a larger research project on neurocognitive functioning and social competence of preschool aged children with epilepsy. A population-based cohort of preschool aged children with active epilepsy ($N = 64$) was identified through the medical records of the Pediatric Neurology Unit, Tampere University Hospital, Finland, which is the only centre for pediatric neurology services in the hospital district of 460,000 inhabitants. The study cohort consisted of all children aged 3–6 years with epilepsy on the point prevalence day of 30 September 2004 (Rantanen *et al.*, 2009). The inclusion criteria for the uncomplicated epilepsy study group were definite diagnosis of epilepsy based on clinical, EEG, and imaging data, no other neurological disorders or severe learning difficulties assessed according to routine clinical practice by standardized psychological tests (IQ >75 was required), normal magnetic resonance imaging (MRI), age between 3 years 0 months and 6 years 11 months. A total of 38 (59%) children from the cohort were excluded on the basis of symptomatic epilepsy and/or other associated neurological disorders (e.g. cerebral palsy, neurodegenerative disease) and/or severe learning difficulties. Twenty-six (41%) children had uncomplicated epilepsy. The parents of 13 children gave their written, informed consent for the participation of detailed neuropsychological part of the study. There were no differences between those who participated in this neuropsychological part of the study ('participants') and those whose general intellect had been assessed earlier according to clinical practice ('non-participants') on IQ scores or epilepsy related factors (see Table 1), except for age. The non-participants were significantly older than participants; their mean age was 71.7 months compared to 58.7 months of the study group ($t(24) = -3.69$, $p < .001$).

Intelligence tests and detailed neuropsychological assessments were conducted on 13 children with epilepsy. Two children failed to complete the full neuropsychological assessment due to oppositional behaviour and/or other behavioural problems. The number of participants in the study group therefore varied between 11 and 13, depending upon the subtest in question. Neuropsychological assessment was performed at Tampere University Hospital, Department of Psychology, University of Tampere or at the child's day-care centre.

Healthy controls were age and gender matched healthy volunteers with the same exclusion criteria as the study group; no chronic illness or neurological disorder. These children were from two municipal day-care centres in the municipality of Lempäälä, near Tampere. The managers of the day-care centres were asked to exclude those children who had some chronic illness or developmental problems (e.g. specific language impairment, mental retardation, autism) or who needed special assistance or special education for a medical and/or developmental reason. A total of 28 parents gave their written consent for the participation of their healthy children, and of these 13 children were matched according to age (± 3 months) and gender with the study group. Neuropsychological assessments took place at the day-care centres.

Medical and background data

Medical data including demographic factors, duration of epilepsy, seizure, and epilepsy type, seizure control during the study period, EEG recordings, brain imaging with 1.5 T, MRI, current antiepileptic drugs (AEDs), and most recent AED levels were analyzed retrospectively from the children's medical records. The results of previous

Table 1. Background data of participants and non-participants

	Participants ($N = 13$)	Non-participants ($N = 13$)	t test/χ^2, p-value
Age (months)	58.7	71.7	$t(24) = -3.69$, $p < .001$
Gender			
Male/female	6/7	8/5	$\chi^2(1) = .62$, $p = .70$
Epilepsy type			
Generalized/focal	7/6	9/4	$\chi^2(1) = .65$, $p = .69$
Age at onset (months)	27.85	41.00	$t(24) = -1.66$, $p = .11$
AED			
No AED	1	1	ns.
Mono-/polytherapy	12	12	
Seizure control[a]			
Good/poor	4/9	9/4	$\chi^2(1) = 3.85$, $p = .12$
Maternal education			
Basic	1	All mothers have	
Vocational training	5	completed at least nine	
High school/college	6	years of basic education in	
University	1	mainstream schools.	
VIQ mean (*SD*)	92.5 (10.5)	90.9 (13.6)[b]	$t(19) = .30$, $p = .77$
PIQ mean (*SD*)	99.4 (13.3)	90.3 (18.3)[b]	$t(19) = 1.33$, $p = .20$
FSIQ mean (*SD*)	94.6 (12.2)	91.4 (14.0)[b]	$t(19) = .56$, $p = .58$

Note. VIQ, Verbal intelligence quotient; PIQ, Performance intelligence quotient; FSIQ, Full scale intelligence quotient.

[a] Seizure control: good – seizure remission $>$ 1 year; poor – seizures $\geq$ 1 per month.

[b] $N = 8$. There were no neuropsychological evaluation data available for five non-participants.

psychological evaluations made according to clinical practice during earlier routine visits to the pediatric neurology unit were also reviewed. Additional data was collected using a background information questionnaire, which included questions of the child's medical and non-medical everyday life (e.g. need for day-care, therapies, and play).

Intellectual and neuropsychological assessment methods

Clinical neuropsychologist assessed all the subjects and controls with the same standardized tests. Finnish standardized version of the Wechsler's Primary and Preschool Scale of Intelligence (WPPSI-R; Wechsler, 1995), was used to assess intellectual functioning. Scores for Full Scale IQ (FSIQ), for Verbal IQ (VIQ), and for Performance IQ (PIQ) were estimated on the basis of following subtests: Information, Similarities, Arithmetic, Picture completion, Block Design, and Object Assembly. The subtests used are considered good or accurate measures of general ability (Kaufman & Lichenberger 2000). The short form of the WPPSI-R as proposed by Sattler (2001) was chosen, including subtests Block Design, Picture completion, Information, Arithmetic, Similarities. The fact that Object Assembly is regarded as a marginally reliable subtest at various age groups (Sattler, 2001; Wechsler, 1995), was considered at the selection of the subtests. But, given the motivational factors and variability of subtests used, Object Assembly was selected as an additional subtest. Here the reliability (Cronbach alpha) of the subtests selected is .79. The exclusion of the Object Assembly subtest would have not changed the reliability.

Neurocognitive functions were assessed by the Developmental Neuropsychological Assessment (the NEPSY test) (Korkman, Kirk, & Kemp, 1997). The Finnish version of the NEPSY test was selected because it has been standardized on a single sample of children (Korkman, 2000) and is widely used in clinical practice. The subtests of the Finnish version correspond to the English version of the NEPSY (Korkman, Kirk & Kemp, 1998). The NEPSY test consists of five domains: attention and executive function, language function, sensomotor function, visuospatial function, and memory and learning function. Ten subtests (two per function) were selected to obtain the core assessment of neurocognitive development, i.e. a brief overview of the five complex, cognitive domains mentioned. From the available subtests for core assessment the ten recommended by Korkman *et al.* (1997) for both ages 3–4 and ages 5–6 were chosen. For the attention and executive function subtests visual attention and statue, for the language function subtests comprehension of instructions and phonological processing, for the sensomotor function subtests visuomotor precision and imitating hand positions, for the visuospatial function subtests block construction and copying, and for the memory and learning function subtests sentence repetition and narrative memory were administered. Thus, the neuropsychological assessment consisted total of 16 subtests and the assessment took two to three sessions (á 45 min).

Statistical analysis

Statistical analyses were done with the SPSS (Statistical Package for Social Sciences, version 15.0). For the comparison of the intellectual functioning of the study group and the control group, FSIQ, VIQ, and PIQ were calculated. Standard scores for age groups were used in the analysis of the group differences. Continuous and normally distributed variables were compared with Student's *t* test. The Shapiro–Wilk test was used to evaluate the normality of the scores, and the Levene's test the equality of variances. Fisher's exact test was used for categorical variables. Spearman's rho was used to explore the linkage between epilepsy related factors and neurocognitive variables. The Bonferroni correction procedure was used. Clinically, significant neurocognitive impairment was considered to exist when a child scored two standrard deviations below the neuropsychological test mean (i.e. standard score < 4; Korkman, 2000; Lezak, 1995).

Results

Data

The data consisted of 13 children (6 boys and 7 girls) with uncomplicated epilepsy and their matched controls. The study and the control group had a comparable socioeconomic status (Table 2). Mean age was 4 years 10 months (i.e. 58.7 months, $SD = 11.3$) in the study group and 5 years (i.e. 60.8 months, $SD = 10.2$) in the control group. In the epilepsy group the age at onset of epilepsy varied between 6 and 64 months, mean age at onset was 2 years 4 months. Six children were under 24 months and 7 children between 25 and 64 months at the onset of epilepsy. FE was diagnosed in 6 children and GE in 7 children. MRIs were normal for all children, and EEGs were consistent with the clinical seizure and epilepsy diagnosis. Nine children were on AED monotherapy, three children on duotherapy and one child had no AED. Valproate was the most common AED used ($N = 10$). Seizure control was good (i.e. seizure free of

Table 2. Education backgrounds of the study and control parents

	Epilepsy $N = 13$	Controls $N = 13$
Maternal education		
Basic	1	1
Vocational training	5	3
High school/college	6	5
University	1	3
N	13	12[a]
Paternal education		
Basic	1	0
Vocational training	6	5
High school/college	3	3
University	2	2
N	12[a]	10[a]

[a] No information available concerning the education of one father in the epilepsy group and one mother and three fathers in the control group.

at least 1 year at the time of the study) in four children, partial (i.e. seizures less than one / month) in six children, and poor (i.e. one or more seizures / month) in three children. The clinical characteristics of the study group are presented in Table 3. All the children in the study group had received special day-care services due to the diagnosis of epilepsy, but none in the control group. In Tampere University Hospital District, special day-care services are commonly available for all children with diagnosis of chronic illness.

Intellectual functioning

IQ scores were at the lower end of the normal distribution in the epilepsy group and at the upper end in the controls. VIQ was 92.5 ($SD = 10.5$) in epilepsy group and 113.2 ($SD = 10.2$) in controls, PIQ was 99.4 ($SD = 13.3$) and 109.7 ($SD = 13.4$) with controls, and FSIQ was 94.6 ($SD = 12.2$) and 113.6 ($SD = 12.2$) with controls. VIQ and FSIQ differed significantly between the study and control groups (VIQ $t(24) = -5.12$, $p < .001$ and FSIQ $t(24) = -3.97$, $p < .001$, respectively), but no significant differences between the two groups was found in PIQ $t(24) = -1.97$, $p = .06$). There was a trend of VIQ being more discrepant than PIQ (i.e. VIQ scores lower than 1 *SD*, −15 IQ points from PIQ) in the study group compared to controls ($t(24) = -2.10$, $p < .05$). There were six children in the study group with VIQ over 1 *SD* lower than PIQ, but none in the control group.

Neurocognitive functioning

All the NEPSY subtest scores were in the study group within 2 *SD* compared to the norms and within 1 *SD* in the control group (Table 4). The study group performed somewhat better than the controls in three subtests: phonological processing, visuomotor precision, and block construction, although the differences were not significant. Children with epilepsy had lower scores on several NEPSY subtests compared to the scores of the healthy controls. Children with epilepsy had mild

Table 3. Clinical characteristics of the study group

Subject number	Gender, age	Epilepsy type	Age at onset	EEG	AED	Seizure control[a]
1	Boy, 4 years 8 months	CAE	3 years	Generalized epileptiform abnormality	Valproate	Poor
2	Girl, 6 years 10 months	CAE	3 years 9 months	Generalized epileptiform abnormality	Valproate	Partial
3	Boy, 5 years 3 months	GE	1 year 9 months	Normal	Valproate	Good
4	Girl, 3 years 9 months	GE	2 years 11 months	Generalized epileptiform abnormality	Levetiracetam, valproate	Partial
5	Boy, 6 years 3 months	GE	2 years 1 month	Generalized epileptiform abnormality	Oxcarbazebine, valproate	Partial
6	Boy, 3 years 11 months	GE	1 year 11 months	Focal epileptiform abnormality	Valproate	Partial
7	Boy, 5 years 9 months	GE	3 year 8 months	Generalized epileptiform abnormality	Lamotrigine	Good
8	Boy, 5 years 6 months	FE	5 years 4 months	Focal epileptiform abnormality	Oxcarbazebine	Partial
9	Girl, 4 years 2 months	FE	2 years 11 months	Abnormality of background activity	Valproate	Poor
10	Girl, 6 years 3 months	FE	6 months	Abnormality of background activity	no AED	Good
11	Girl, 4 years 4 months	FE	6 months	Abnormality of background activity	Valproate	Poor
12	Girl, 5 years 6 months	FE	9 months	Generalized epileptiform abnormality	Topiramate, valproate	Good
13	Girl, 3 years 7 months	FE	1 year 1 month	Normal	Valproate	Partial

Note. CAE, Childhood absence epilepsy; GE, Generalized epilepsy; FE, Focal epilepsy.

[a] Seizure control: good – seizure remission $>$ 1 year; partial, seizures $<$ 1/month; poor – seizures $\geq$ 1/month.

Table 4. Standard scores of NEPSY subtests

	Group					
	Study ($N = 13$)		Control ($N = 13$)			
NEPSY subtest	*M*	*SD*	*M*	*SD*	*t* test	*p*-value[a]
Visual attention	10.17[c]	4.53	13.85	3.00	$t(23) = -2.39$	.025
Statue	7.09[b]	3.24	8.69	3.88	$t(22) = -1.09$	.290
Phonological processing	9.33[c]	1.97	9.08	1.32	$t(23) = 0.39$	.704
Comprehension of instructions	6.77	2.71	9.77	2.35	$t(24) = -3.01$	.006
Imitating hand positions	6.36[b]	3.08	7.08	2.87	$t(22) = -0.59$	.563
Visuomotor precision	9.00[b]	3.82	8.92	3.71	$t(22) = 0.05$	.961
Copying	8.69	4.98	9.38	3.02	$t(24) = -0.43$	.672
Block construction	11.00[b]	3.38	10.69	2.53	$t(22) = 0.26$	.801
Narrative memory	9.09[b]	2.59	10.85	2.79	$t(22) = -1.59$	.127
Repetition of sentences	5.55[b]	3.14	9.23	2.71	$t(22) = -3.09$	.005[a]

[a] Bonferroni correction was used, $p > .005$ are considered significant.
[b] $N = 11$.
[c] $N = 12$.

difficulties (standard scores below 1 *SD*, i.e. standard score < 7) in comprehension of instructions and repetition of sentences. The study group performed significantly weaker than healthy controls in the subtest repetition of sentences ($t(22) = -3.09$, $p < .005$). Also, a similar trend of the study group performing weaker was found in the comprehension of instruction ($t(24) = -3.01$, $p < .006$). Although the difference did not reach statistical significance. No clinically significant neurocognitive impairments (i.e. subtest scores 2 *SD* below the neuropsychological test mean, standard score < 4) (Korkman *et al.*, 1997; Lezak, 1995) were found in the children with epilepsy as a group.

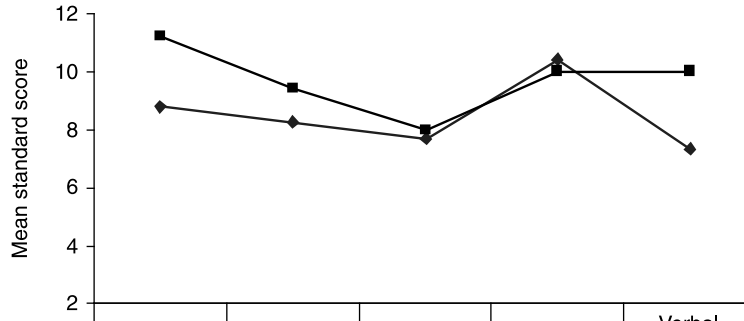
At the individual level this pattern of performance (>1 *SD*, mild difficulties) was maintained in six children with uncomplicated epilepsy in comprehension of instructions and in eight children in repetition of sentences compared to four and two children in the control group. In visual attention four children with epilepsy had mild difficulties, but none of the healthy controls. In statue there was also a greater variation between healthy children: there were five children in the epilepsy group against four in the control group with mild difficulties in inhibitory functions. The variations of visuospatial and visuomotor subtests within both the study and the control groups were wide and no differences between the two groups were found. Children with epilepsy were a heterogeneous group: some children with poor seizure control performed well in all neurocognitive domains (e.g. Subject 1) whereas others had neurocognitive problems despite good or partial seizure control (e.g. Subjects 3, 5, and 12). Also, the only child with no AED (Subject 10) and average intellectual capacity demonstrated problems in attention, sensomotor, and verbal memory functions. Detailed performances in the IQ test and neurocognitive domains of the study group are presented in Table 5.

The mean standard scores for the main neurocognitive domains were calculated from the domain subtests in the NEPSY test. The only statistically significant difference between the groups was found in verbal short-term memory ($t(22) = -2.68$, $p < .01$), but not in other domains (See Figure 1).

Table 5. Intellectual and neurocognitive data of study group

Subject number	Gender, age	VIQ	PIQ	FSIQ	Attention standard score	Language standard score	Sensomotor standard score	Visuospatial standard score	Verbal memory standard score
1	Boy, 4 years 8 months	104	122	116	11.00	8.50	9.00	15.50	10.50
2	Girl, 6 years 10 months	111	110	112	8.50	9.00	9.50	13.00	8.00
3	Boy, 5 years 3 months	77	93	81	–[a]	7.50	–[a]	–[a,b]	–[a]
4	Girl, 3 years 9 months	83	83	78	–[a,c]	–[a,c]	–[a]	–[a,c]	–[a]
5	Boy, 6 years 3 months	77	96	83	5.50	5.00	4.00	8.00	5.00
6	Boy, 3 years 11 months	96	107	101	10.50	10.50	10.00	16.50	11.50
7	Boy, 5 years 9 months	100	98	98	9.50	9.00	8.00	7.00	8.00
8	Boy, 5 years 6 months	84	104	93	10.00	7.50	8.00	9.00	10.00
9	Girl, 4 years 2 months	96	104	100	13.50	8.50	7.00	10.00	4.00
10	Girl, 6 years 3 months	102	91	96	5.00	8.50	6.00	9.00	5.00
11	Girl, 4 years 4 months	93	110	101	7.50	8.00	10.50	9.00	5.50
12	Girl, 5 years 6 months	93	70	77	7.00	6.00	4.50	5.50	5.50
13	Girl, 3 years 7 months	86	104	94	9.00	10.50	8.00	12.00	7.50

[a] Missing data in either a single subtest or both subtests required for domain score.
[b] The subject was able to complete copying (standard score 3).
[c] The subject was able to complete visual attention (6), comprehension of instructions (3), and copying (2).



	Attention	Language	Sensomotor	Visuospatial	Verbal memory*
Epilepsy	8.82	8.27	7.68	10.41	7.32
Healthy	11.27	9.42	8.01	10.04	10.04

**Note.* Bonferroni correction was used, *P* values >.01 are considered significant.

Figure 1. Mean standard scores of the study and control groups for neurocognitive domains of the NEPSY test.

Studying the associations between intellectual functioning and epilepsy related variables, revealed no differences between GE ($N = 7$) and FE ($N = 6$) types (GE / FE: VIQ = 92.6/93.6, PIQ = 101.3/95.8, FSIQ = 95.6/93.4). Also, correlations between seizure control, antiepileptic medication used, age at onset of AED treatment or seizure foci, and neurocognitive variables were not statistically significant. Only one epilepsy related variable was associated with the neurocognitive domain: age at onset of seizures was associated with attention ($\rho = .91$, $p < .001$).

Discussion

The aim of this study was to describe the intellectual and neurocognitive functioning of children with uncomplicated epilepsy in early childhood and to compare these to the functioning of healthy controls. Idiopathic or uncomplicated epilepsy is generally regarded as having a good medical prognosis and the intellectual functioning of these children at school age has been found to be within normal limits (Bailet & Turk, 2000; Mandelbaum & Burack, 1997). Therefore, the intellectual functioning of children with uncomplicated epilepsy was expected to be normal. In this study, the intellectual functioning of the children with uncomplicated epilepsy was indeed within the normal range, but differed clearly from that of the matched healthy controls which was contrary to expectations. Maternal IQ was not assessed in this study even though a genetic component in uncomplicated, especially in idiopathic epilepsy has been suggested. However, all the mothers of the study group had at least 9 years of basic education, which was equivalent to that of the mothers of the control group.

Based on earlier studies, some diffuse impairment in memory functions, attention, and/or visuomotor skills were anticipated. Firstly, verbal short-term memory of preschool children with uncomplicated epilepsy may be considered moderately affected compared to those of healthy controls. The epilepsy group differed from controls with respect to verbal short-term memory. Various memory problems, including short-term memory problems (Nolan *et al.*, 2004; Northcott *et al.*, 2005) have

been demonstrated also earlier. The neurocognitive impairments found in verbal short-term memory was not clinically significant, if clinical significance is defined as a performance below 2 *SD* from the norms (Korkman, 2000; Lezak, 1995). Secondly, in contrast to earlier findings, no significant evidence of attention problems was found. This is somewhat surprising, since the previous findings suggest that attentional problems are possible in preschool children with uncomplicated epilepsy: the parents of the same cohort with uncomplicated epilepsy have reported more attention problems, especially impulsive behaviour compared to healthy controls (Rantanen *et al.*, 2009). Also, several other studies have demonstrated various attention problems to be typical with school-aged children with idiopathic epilepsy (e.g. Gülgönen *et al.*, 2000; Henkin *et al.*, 2005). The fact that no differences between the study and the control groups were found in subtest of behavioural inhibition (statue) may partly reflect the individual maturation of inhibitory functions during preschool years (Klenberg, Korkman, & Lahti-Nuuttila, 2001) and also explain the variation in the performance in healthy children. Given the developmental variability in the performance, the reliability of the statue test is poorer.

An unanticipated finding was that the visuospatial and sensomotor functions were intact and no differences were found from the corresponding functions of controls. Previously, deficits in psychomotor speed (Bailet & Turk, 2000; Boelen *et al.*, 2005), in visuospatial (Pavone *et al.*, 2001), and in visuoperceptual abilities (Germanó *et al.*, 2005) have been reported in school-aged children with uncomplicated epilepsy. Our findings are supported by Boelen *et al.* (2005), who found that overall psychomotor development was comparable to that of controls. In this study, in one sensomotor subtest, imitation of hand positions, both the study group and the healthy children performed at the lower end of the norms. However, the reliability of sensomotor subtests may be poorer in younger children (Korkman, 2000; Korkman *et al.*, 1997) possibly due to individual maturation and differentiation of sensomotor skills in healthy children, too.

Contrary to previous research and our initial expectations, language was mostly impaired in preschool children with uncomplicated epilepsy. There was a difference between the epilepsy and control groups in VIQ and comprehension of instructions. At the individual level, there were six children in the study group with VIQ significantly lower than PIQ, which may be regarded as a clinically significant indicator of language difficulties (Lezak, 1995). In addition, the verbal short-term memory difficulty found in this study could be explained with primary impairment in receptive language, because pure memory deficits are rarely seen in young children (Aylward, 1997) and verbal memory deficits in children are often associated with language impairments (for an overview see Baddeley, 2003). Further, one could also argue that memory functions in early childhood are not yet matured and differentiated as a specialized function (Gathercole, 1998; Tideman & Gustafsson, 2004).

Language development may be adversely affected by epileptic activity (Gordon, 2000). An association between epileptic activity and language development is demonstrated in children with benign childhood epilepsy with focal spikes (Monjauze, Tuller, Hommet, Barthez, & Khomsi, 2005; Svoboda, 2004). For example, various language deficits (Monjauze *et al.*, 2005) and difficulties in phonological processing skills (Northcott *et al.*, 2005) have been reported in benign rolandic epilepsy. Deficits in auditory perception, lexical skills, and comprehension of speech have also been reported in children with new onset FE (Kolk *et al.*, 2001). Resently, Rejnö-Habte Selassie, Viggedal, Olsson, and Jennische (2008) reported affected expressive language

and verbal short-term memory functions despite normal VIQ in preschoolers with epilepsy. Cohen and Le Normand (1998) also found deficits in linguistic comprehension and production in their longitudinal study on children with early onset simple focal seizures of the left hemisphere. Even though the delay in speech comprehension persisted for years, it reached normal levels by the age of seven. Instead, problems in language production persisted longer. On the other hand, according to a study by Pavone *et al.* (2001) verbal memory and language capacity should be intact in idiopathic GE.

In our study, there were only four children with good seizure control. Therefore, the language deficits found may also be an indication of active epilepsy, possibly disappearing after remission as has been reported typical in benign rolandic epilepsies (Lindgren *et al.*, 2004; Northcott *et al.*, 2006). Early childhood is a critical period for language acquisition and establishment. It is possible that electrophysiological epileptic activity, seizures, and/or antiepileptic medication at that time especially may interfere with language development, which is active at that age period. Gordon (2000) emphasized the importance of the association between epileptic activity and language especially in small children, but not all studies (Monjauze *et al.*, 2005) found a correlation between age at seizure onset and language performance. With respect to seizure type, Mandelbaum and Burack (1997) found that on cognitive functioning children with focal seizures performed better than children with generalized seizures. In our study, possibly due to the small sample size, no difference was found in cognitive functioning between focal and generalized seizures. In the correlation analysis, only one epilepsy related factor (i.e. age at the onset of seizures) was associated with the neurocognitive domain of attention. This epilepsy related variable contributing to neurocognitive functioning has also been recognized before (e.g. Elger *et al.*, 2004; Mangano *et al.*, 2005).

The strengths of this study are the narrow age group from a population-based cohort, a matched control group and consistent and widely used psychological testing measures. Usually, in order to obtain sufficient data (i.e. patients), participants have been recruited from a wider age group (e.g. children from 3 to 16 years of age). Neuropsychological assessments with standardized tests are time-consuming and require trained neuropsychologists. Therefore, the total number of the participants often remains quite small in clinical studies. Also, the results of the present study are based on a limited number of participants. There were no differences on overall intellectual functioning between participating and non-participating children with uncomplicated epilepsy. Therefore, the study group may be considered to be a fairly representative sample of neurocognitive functioning of preschool children with uncomplicated epilepsy. Nevertheless, due to the small sample size, the results may be best regarded as tentative.

Developmental changes in cognitive processes during childhood have not been fully studied, although there is consensus that developmental changes may occur in the level and also in the structure of performance (Korkman *et al.*, 1997). Studies focusing on early childhood or preschool years with epilepsy are mostly lacking. Some studies do exist (e.g. Battaglia *et al.*, 1999), but the focus in them has been on medical aspects and the remission of seizures rather than on the psychological outcome. Some studies with psychological assessments have been conducted (e.g. Chaix *et al.*, 2003; Mangano *et al.*, 2005; Rejnö-Habte Selassie *et al.*, 2008). Further studies with detailed neuropsychological assessments and follow-up time are needed to gain more insight to the developmental course of children with uncomplicated epilepsy. Studies at the level of

overall intellectual functioning (IQ) no longer suffice. It seems unlikely that there is a specific pattern of neuropsychological impairment in idiopathic epilepsy (Deonna *et al.*, 2000; Seidenberg, 1989). Rather, a more diffuse neuropsychological profile with uncomplicated childhood epilepsy (Germanó *et al.*, 2005; Williams *et al.*, 1998) has been proposed. This may partly reflect the inconsistency of the results concerning the association between neurocognitive functioning and seizure related factors. Previously, lower intellectual functioning was associated with childhood epilepsy, but the studies were based on heterogeneous groups. Subsequently, the overall cognitive development with uncomplicated childhood epilepsy was regarded as normal, but there are an increasing number of studies demonstrating subtle, but perceptible neurocognitive problems with benign epilepsies. Today, these subtle neurocognitive difficulties may be regarded as quite common in children with idiopathic epilepsy despite good cognitive overall capacity. However, there is no consensus about an association between epilepsy related factors and neurocognitive deficits.

In conclusion, the neurocognitive deficits found in this study were subtle and their clinical significance for further development of these preschool children is difficult to determine. It is also important to note that the subtle neurocognitive impairments are not necessarily socially disabling cognitive deficits (Elger *et al.*, 2004), but definite answers would require a long-term follow-up study. Also, multi-centre studies are needed in order to obtain sufficient data. Because of the developmental risks reported in this study, psychological screening and detailed neuropsychological assessment are recommended in clinical practice. Buelow and McNelis (2002) have also suggested that neuropsychological assessment should be considered in the initial evaluation of children with epilepsy. So far, it is unclear whether the mild neurocognitive deficits during development persist or whether they resolve after seizure remission or during age. Therefore, the psychological follow-up evaluations of children with early onset uncomplicated epilepsy is necessary as a standard procedure.

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Review

Social competence in children with epilepsy — A review

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Children

ABSTRACT

This systematic review focuses on definitions of social competence and assessment methods and provides an overview of the main findings in childhood epilepsy. A total of 45 studies drawn from MEDLINE and PsycINFO (1998–2010) and their reference lists met the selection criteria. Social competence was not defined in the studies reviewed. The study samples varied and consisted mostly of school-aged children. The majority of the studies focused on social adjustment and addressed problems in this area. Little is known about other aspects of social competence, namely social skills or social performance. A broader perspective on and definition of the assessment of social competence in children with epilepsy are proposed. More studies of the abilities underlying social competence, such as social and socio-cognitive skills, are needed in order to gain insight into the developmental pathways of social competence and protective factors for later development.

1. Introduction

Childhood years are a phase of rapid cognitive and social development. Social competence is related to cognitive and socio-emotional development and to developmental changes occurring with increasing age [1,2]. The development of social competence is regarded as one of the best predictors of later behavioral, social and academic success, and of present and future behavioral and emotional problems [3]. Children with chronic conditions affecting the central nervous system (CNS), such as epilepsy, have been found to have an increased risk for poorer social competence, such as developing behavioral problems (e.g., [4]) or mental health problems [5].

There is no agreement on the definition of social competence; numerous and heterogeneous definitions and models have been proposed. Differing approaches to social competence have emphasized either social adaptness as a property of a person or the inherent nature of prosocial and inappropriate behaviors or the situation specificity of social competence [6]. Social competence has, accordingly, been defined as an individual's ability to function in a manner consistent with age-appropriate and cognitive abilities [7], as a battery of social skills (e.g., [8]) or, simply, as a manifestation of prosocial and antisocial behavior [9] or, more broadly, as effectiveness in interaction as Rose-Krasnor [10] suggested. Different subcomponents of social competence entail social skills, social adjustment, and social performance [11–13]; see Fig. 1 (modified from [14]). These are proposed as key subcomponents of a conceptual framework for social competence in childhood epilepsy. Social skills refers to the underlying abilities (e.g., listening, sharing) required to perform competently in specific social tasks [11,12]. Social adjustment is defined as absence of behavioral problems or antisocial behavior (e.g., aggression and disruptive behavior) and manifestation of prosocial actions (e.g., [9]). Social performance refers to an actual behavior and the degree to which a child's responses to relevant, primarily social situations meet socially valid criteria [12]. The basis of the conceptual framework proposed in Fig. 1 lies in Cavell's [12] tri-component model of social competence, which is considered to be sensitive to the effects of CNS conditions (like epilepsy or cerebral palsy). The associations between epilepsy and social competence are complex, and no direct causality has been demonstrated. However, the conceptual framework proposed hypothesizes that both pathophysiological (i.e., CNS dysfunction or lesions) and environmental factors, including family-related ones, may affect the development of social competence. This effect may be direct or mediated through epilepsy-related or/and neurocognitive factors which, in turn, may also have an independent effect on the development of social competence (see [5]).

In the assessment of social competence in typically developing children, either requisite skills of social functioning (e.g., stimulus encoding skills) or social functioning per se (e.g., frequency of peer interactions, specific social behaviors) or products of social functioning (e.g., social attainments, peer acceptance) have been measured [12,15]. Assessment methods of social competence include sociometric and peer nomination procedures, observational procedures, and rating scales [6]. Laboratory settings have also been utilized to study

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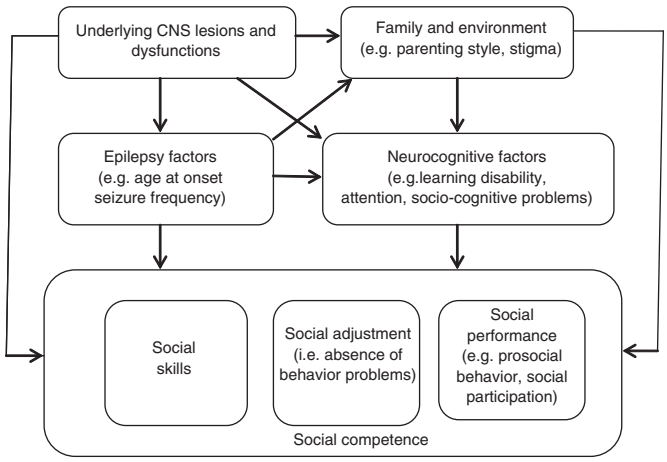

Fig. 1. A conceptual framework of social competence, its subcomponents and hypothetical connections in childhood epilepsy.
Modified from Rantanen, Eriksson and Nieminen [14].

the perception and interpretation of social cues (see e.g., [16]). For clinical and research purposes, different rating scales are most often used. Typically, a parent, a teacher, or a child assesses the frequency and/or severity of a given behavior. The most frequently used assessment methods include the Child Behavior Checklist (CBCL [17,18]), the Conners' Rating Scales (CRS-R [19]), and the Social Skills Rating System (SSRS [20]).

In their review, Nassau and Drotar [4] evaluated the studies on social competence among children with CNS conditions. They found that between 1975 and 1997, the overwhelming majority of studies evaluated the social competence at social adjustment level but neglected the aspects of social skills and social performance. For future research, they recommended the utilization of theoretical frameworks and reconceptualization of the concept of social competence, and more studies focused on the relations between social competence and CNS conditions. They also raised methodological concerns, for example, about the measurement of social competence, representativeness of study designs, and sample characteristics. Since the review by Nassau and Drotar [4], the number of studies on the behavioral issues and social correlates of childhood epilepsy has increased considerably. Two systematic reviews or meta-analyses have been published [21,22], and other reviews [23–28] have presented selective or clinically relevant studies. The focus of the earlier reviews has been on behavior problems, neuropsychiatric aspects, and/or psychiatric problems, i.e., factors related to one of the subcomponents of social competence in children with epilepsy. Similarly, in clinical practice, attention has often been paid to cognitive aspects and possible behavioral problems rather than to overall psychosocial functioning. The studies investigating social aspects or social functioning in other chronic illnesses have taken a broader approach (see e.g., [29,30]). To our knowledge, no systematic reviews with a broader approach, like that of the Cavell model [12], have been conducted on social competence in childhood epilepsy. The purpose of this review was to summarize studies of social competence in children with epilepsy over the past twelve years. The specific aims of the study were 1) to describe how social competence has been defined and which aspects of social competence have been studied in childhood epilepsy, 2) to evaluate the study designs (e.g., representativeness of age) for the assessment of social competence, 3) to describe what assessment methods have been used, and 4) to provide an overview of the main empirical findings of social competence on children with epilepsy. The framework of the analysis in this review is the model presented in Fig. 1.

2. Methods

2.1. Literature search and main terms

A systematic literature search was conducted. Data were identified in January 2011 by searches in MEDLINE and PsycINFO (January 1998–December 2010). In addition, cross-references from relevant articles were checked out. The search focused on the past twelve years because Nassau and Drotar [4] published an exhaustive review evaluating the social competence of children with CNS conditions covering the years 1975–1997. For MEDLINE and PsycINFO, the search terms were: epilepsy, behavior, behav* and social competence or social function*, social adjustment, social performance, social skills, psychosocial or peers, and combinations of these. The inclusion criteria for the original studies reviewed were the following: 1) children diagnosed with epilepsy between 0 and 18 years of age, 2) all types of seizures, epilepsies, and epilepsy syndromes, 3) empirical studies with behavioral or social assessments, either questionnaires or structured interviews, and 4) articles in English or articles with a detailed abstract in English. Since the purpose was to conduct an overview of studies on social competence in childhood epilepsy, both children with normal cognitive function and those with cognitive impairment or learning disability were included. If possible, the results of subgroups of children (normal development vs. cognitive impairment) were reported. Observational studies of behavior in a natural setting would have also been included, but no such studies were found. Exclusion criteria were as follows: adults (over 18 years), qualitative studies, review articles, non-human studies, intervention studies (e.g., on the effects of epilepsy treatment, antiepileptic medication, surgery, or psychological interventions), and studies focusing on health-related quality of life (HRQL).

3. Results

3.1. Literature search

The original search yielded 4509 articles (Fig. 2), but a total of 567 articles remained after the limitations (e.g., age range, children 0–18 years, human studies). These were exported to EndNote© (version 8.0) reference manager. Duplicates were then removed, leaving 344 studies in the EndNote database. Titles and abstracts were inspected, and those not meeting the inclusion criteria were excluded. Of these, 105 articles remained after removing studies not meeting the selection criteria and duplicates. An additional 21 articles were included after reviewing the reference lists. Thus, the abstracts of these remaining 126 articles were reviewed, resulting in the removal of 70 articles meeting the exclusion criteria. Finally, 56 articles were fully reviewed, and of these, 45 articles met the eligibility criteria (see Table 1; the articles reviewed are listed in alphabetical order [31–75]).

3.2. Definitions of social competence

Despite the various definitions of social competence (e.g., [10–12]) available, definitions of the key concept were mostly absent from the studies reviewed. None of the studies reviewed included definitions of social competence, except for that by Rantanen et al. [69] and a theoretical model proposed by Drewel et al. [45]. Social competence was defined as age-appropriate social skills acquired and absence of behavioral problems [69]. Instead of providing a definition, Drewel et al. [45] proposed a model of neurocognitive functioning as a mediator for peer difficulties, i.e., social performance. Other studies with a focus on social performance as opposed to social adjustment problems did not specify this key concept. In these studies [37,43,57], the term social competence refers to a concept operationalized on Achenbach's scales [17]. The three-quarters of the studies reviewed (about 76%) focused on one

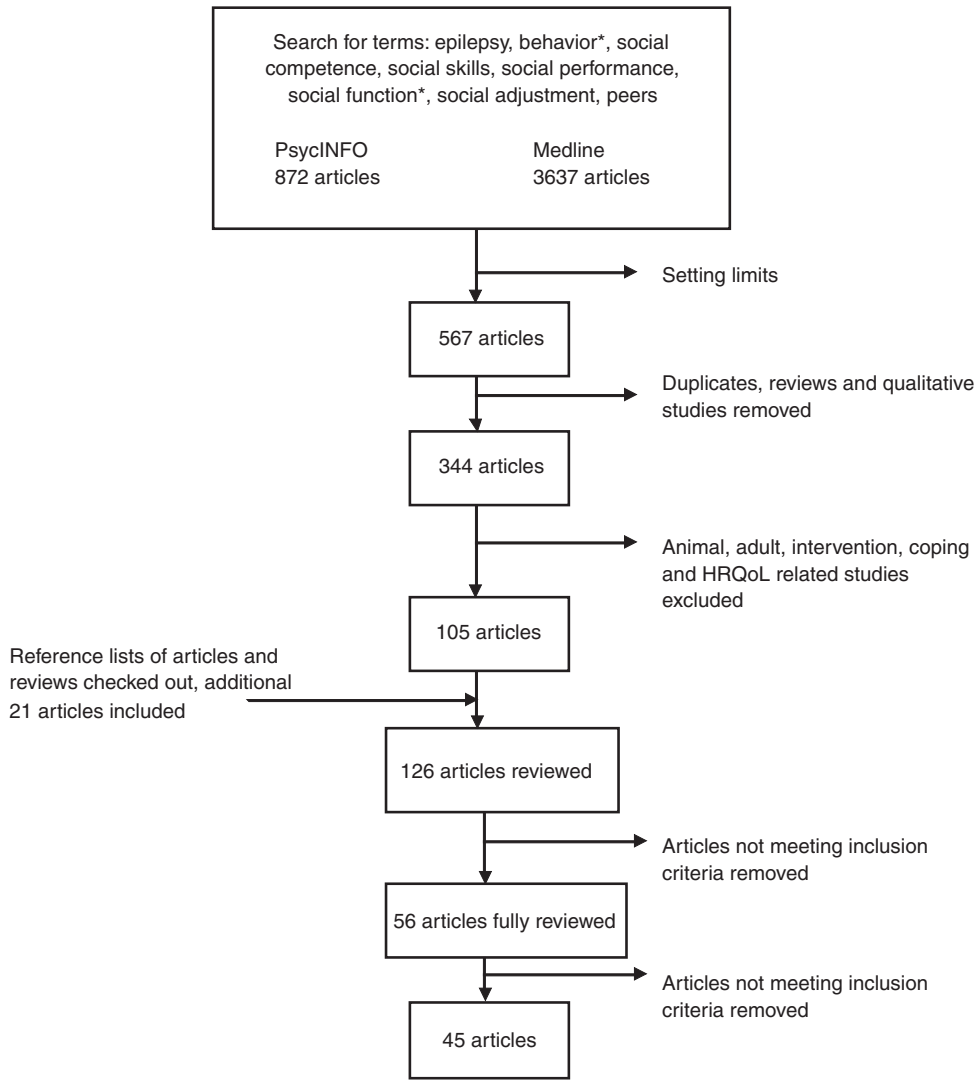

Fig. 2. Results of the systematic literature search.

aspect of social competence, namely social adjustment, and a quarter of the studies on other aspects (e.g., social skills or prosocial behavior) (see Table 1).

3.3. Study designs and participants

Most of the studies reviewed were cross-sectional (38/46), and seven were follow-up studies [32–34,37,47,64,66]. The studies reviewed used either population- or community-based cohorts. Participants were drawn from consecutive series of patients from medical centers in seven studies [49,50,59,64–66,72]. Two studies [33,52] did not specify the selection of participants. Additional neurologic or metabolic disorders and/or abnormal neuroimaging were excluded in 24 studies. Developmental problems and/or learning disability, usually defined as IQ<70 (or <80–90; [34,57]) or based on school placement, were excluded in 32 studies. A total of 29 studies out of 45 included control groups, but only nine studies had age- and gender-matched controls [35,52,55,56,58,61,63,65,69], and three of these [34,44,53] had two control groups (healthy siblings, other chronic disease). Healthy or normal children were used as controls in 18 studies, siblings or children with other chronic diseases (e.g., asthma) both in six studies, and cousins in one study. In 16 studies, there were no control groups; however, two of them [40,54] compared different epilepsy types.

The number of participants ranged from 26 to 226 (median: 87). Typically, the age ranges in articles reviewed varied widely. The ages of the children ranged from 1 to 18 years. Twenty-five studies included participants whose age varied by ≥10 years and in 21 studies from 3 to 9 years. The mean age ranged from 4.9 to 15.0 years (median 10.9 years). One study did not report the mean age [72]. There was only one study on children with mean age under 6 years [69]. Age at onset of epilepsy ranged from 1 to 15 years, mean age at onset of epilepsy ranged from 1.8 to 11.59 years (median: 6.1). Mean duration of epilepsy ranged from 0 months to 8.8 years (median: 3.9), and eight studies [31,32,38,46,47,64–66] focused on recent onset seizures. Behavioral problems were reported 6 months before the first recognized seizure [31] or within 6 weeks of the first recognized seizure (mean 35 days) [32,46,47] or immediately after diagnosis and before antiepileptic medication started [38,64–66]. Some studies did not report age at onset (13 studies) or duration (21 studies) of epilepsy.

3.4. Assessment methods

As seen in Table 2, Achenbach's CBCL [17,18], which includes problem scales and social competence scales, was utilized in the majority of studies (73%). With the exception of the study by Jakovljevic and Martinovic [57], the scores of the problem scales were reported in all studies. The results were reported at the level of broadband scores

Table 1
Characteristics of the studies included in the review.

Reference	N	Age range (mean)[a]/controls[b]	Aspect of social competence studied[c]
1. Austin et al. [31]	224	4–14 (8.4)/siblings	SA
2. Austin et al. [32]	224	4–14 (8.4)/siblings	SA
3. Austin et al. [33]	115	8–13 (10.5)/asthma	SA
4. Bailet and Turk [34]	74	8–13 (9.6)/siblings, migraine	SA
5. Baker et al. [35]	70	12–18 (15.0)/healthy[b]	SA
6. Baki et al. [36]	35	7–19 (12.8)/healthy	SA
7. Berg et al. [37]	226	8–17 (13.0)/siblings	SA, SP
8. Bhise et al. [38]	57	6–17 (10.1)/–	SA
9. Buelow et al. [39]	164	9–14 (11.8)/–	SA
10. Caplan et al. [40]	149	5–16 (9.6–10.6)/–	SA, SP
11. Caplan et al. [41]	101	5–16 (10.7)/normal	SA
12. Caplan et al. [42]	171	5–16 (9.9–10.9)/healthy	SA, SP
13. Caplan et al. [43]	152	5–16 (10.3)/normal	SA
14. Davies et al. [44]	67	5–15 (10.2)/diabetes, normal	SA
15. Drewel et al. [45]	173	8–15 (11.7)/–	SA
16. Dunn et al. [46]	192	4–14 (8.4)/asthma	SA
17. Dunn et al. [47]	209	4–14 (8.3)/asthma	SA
18. Dunn et al. [48]	173	9–14, (11.7)/–	SA
19. Ettinger et al. [49]	44	7–18, (12.4)/–	SA
20. Freilinger et al. [50]	108	5–18 (11.5–11.8)/–	SA
21. Giordani et al. [51]	200	4–13 (8.2)/–	SA
22. Golouboff et al. [52]	37	8–16 (12.6–13.3)/healthy[b]	SA
23. Hamiwka et al. [53]	59	8–16 (11.8)/renal disease, healthy	SA, SS, SP
24. Hernandez et al. [54]	32	8–16 (11.2–12.4)/–	SA, SP
25. Høie et al. [55]	117	6–13 (10.7–11.0)/controls[b]	SA
26. Høie et al. [56]	162	6–12 (10.2)/healthy[b]	SA
27. Jakovljevic and Martinovic [57]	70	11–18 (14.3)/controls	SP
28. Jones et al. [58]	53	8–18 (12.7)/cousins[b]	SA
29. Keene et al. [59]	158	6–18 (11.3)/–	SA
30. Lossius et al. [60]	124	13–16 (15.1)/control	SA
31. Mathiak et al. [61]	30	6–15 (11.0)/healthy[b]	SA
32. McCusker et al. [62]	48	2–12 (7.1)/–	SA, SP
33. Oguz et al. [63]	35	9–18 (12.9)/healthy[b]	SA
34. Oostrom et al. [64]	66	5–16 (8.2)/classmates	SA
35. Oostrom et al. [65]	51	5–16 (10.1)/classmates[b]	SA
36. Oostrom et al. [66]	42	7–16 (8.8)/controls	SA
37. Ott et al. [67]	114	5–16 (10.5)/–	SA
38. Ott et al. [68]	87	5–16 (9.7–11.3)/controls	SA
39. Rantanen et al. [69]	26	3–6 (4.8–5.0)/healthy[b]	SA, SS
40. Sabbagh et al. [70]	185	3–16 (10.9–11.2)/–	SA
41. Schoenfeld et al. [71]	57	7–16 (10.8)/siblings	SA, SP
42. Thome-Souza et al. [72]	55	4–18/–	SA
43. Tse et al. [73]	101	3–17 (11.2)/siblings	SA, SS
44. Turky et al. [74]	56	4–17, 12.0/–	SA
45. van Mil et al. [75]	51	6–16 (10.2)/–	SA

[a] Mean ages for the epilepsy group.
[b] Age and gender matched controls.
[c] SA: social adjustment, SS: social skills, SP: social performance.

(e.g., internalizing scores, 9 studies) or at the level of narrow-band scores (e.g., aggression, 4 studies) or both (15 studies). The results of the Total Problem Scale were only reported in three studies [64–66]. The social competence scores of the CBCL were reported in 10 studies [37,40,42,43,50,54,57,62,71,73]. The CBCL with other assessment methods was applied in nine studies. The next most often used assessment methods included a semi-structured interview, the Schedule for Affective Disorders and Schizophrenia for School-Aged Children (K-SADS [76,77]), and the Children's Depression Inventory (CDI [78]). Other assessment methods included the Conners' Parent Rating Scales [19], the State-Trait Anxiety Inventory (STAI [79]), the Revised Children's Manifest Anxiety Scale (RCMAS [80]), and the Piers–Harris Children's Self-Concept Scale (CSCS [81,82]). Scales designed specifically to assess social skills and prosocial behavior, namely the SSRS [20] and the Strengths and Difficulties Questionnaire (SDQ [83]), were utilized in fewer studies [44,53,60,70,73,74]. For the assessment of social skills and adaptive behavior, the Vineland Social Maturity Scale (VSMS) [7] was applied in one study [69]. Only one assessment method (including different forms of the scale, e.g., parent and teacher reports of the CBCL) was used in 25 studies, two methods in 12, and three or more methods in nine studies. A multi-informant perspective (i.e., parent report, teacher report and/or self-report) was taken in 20 studies (43%). Parent reports were only utilized in 33 studies and teacher reports in two studies, while one study focused on self-reports.

3.5. Overview of the empirical findings on social competence

The majority of the studies reviewed focused on social adjustment and the minority on social performance and social skills (see Tables 1 and 3). For a more detailed description of behavioral problems and psychopathology, see also the reviews by Rodenburg et al. [21,22] and by Plioplys et al. [24]. Children with epilepsy were found to have social adjustment problems. They had statistically significantly higher rates of behavior problem scores than siblings [31,32,37,47,71] or children with other chronic illness [33,44,46,47]. Between studies, there was variability in the proportion of clinically significant social adjustment problems (e.g., internalizing, externalizing and total problems) reported (see Table 3). Problems were more frequently encountered in children with low IQ [39], with recurrent seizures [32,47], and of younger age [48]. Clinically significant problems were reported most consistently in attention, depression, and anxiety. For attention problems, both inattentive and impulsive/hyperactive types were found [45,70,72,75]. There were studies showing that although attention problems were common in children with idiopathic or cryptogenic epilepsy, they were not persistent [64]. Children and adolescents with epilepsy were noted to have high levels of depression [35,49,72] and anxiety [42,49,72]. Baki et al. [36] found that the frequency of depressive but not anxiety symptoms was statistically significantly higher than in the general population of healthy children. Also, in one study [63], more symptoms of depression were reported in older children (12–18 years) than in younger children (9–11 years). Studies also reported varying findings on other problems, e.g., thought problems, somatic complaints, and delinquent or disruptive behavior (e.g., [31,40,43,46,51]). An association between social adjustment problems and deficit in underlying socio-cognitive skills (i.e., recognizing emotional expression) was reported [52]. The study by Golouboff et al. [52] was the first to demonstrate such an association in children with early-onset temporal lobe epilepsy.

Only few studies focused on social skills. Statistically significantly lower social skills compared to healthy children [69] and siblings [73] were demonstrated in children with epilepsy. Tse et al. [73] found in school-aged children that social skill impairment was apparent in 13% of children with epilepsy, and they were statistically significantly less assertive than their siblings. However, these differences between groups in the proportion of clinically significant social skill deficits were not significant. Statistically significantly lower social skills (e.g., lower sociability scores) were also evident in preschool children with complicated epilepsy [69] and in those attending special institutions compared to those children with epilepsy in mainstream schools [70].

When social performance is defined as the degree to which a child's responses to social situations meet socially valid criteria [12], the relevant social competence scales of the CBCL comprise items relating the social performance in daily situations (e.g., participation in sports, other recreational activities, group activities, and social relationships). Therefore, the results are presented here. The overall scores of the CBCL Social Competence Scale were within the normal range in children with epilepsy [37,40,43,54,57,62,71,73]. However, the proportion of clinical or borderline scores in children with epilepsy was statistically significantly higher than in healthy children or siblings. Most frequently, problems were encountered in School Competence when compared to that of healthy children or siblings (10–22 vs. 1–2%). An exception to the reported proportion of problems within

Table 2
Overview of the assessment scales most often used in the studies reviewed.

Scale	Description, purpose	Number of studies using the scale (reference to original articles)
Child Behavior Checklist (CBCL) [17,18]	For 3–18 years. Includes Problem Behavior and Social Competence Scales. Parent, teacher, and self-report (for 11–18 years) forms include 110–113 problem items and VII–VIII social competence (parent, self-report) and academic and adaptive functioning items (teachers) depending on age. Social competence scales comprise subscales: activities, social, school, and total scale. The total competence score is obtained by summing the raw scores of the activities, social, and school scales.	33 [31–34,37–43,45–48,50,52,54–57,59,62,64–71,73,75]
Schedule for Affective Disorders and Schizophrenia for School-Aged Children (K-SADS) [76,77]	For 6–18 years. A semi-structured interview that covers a broad spectrum of child psychiatric diagnoses.	8 [40–43,58,67,68,72]
Children's Depression Inventory (CDI) [78]	For 7–17 years. A self-report screening tool to measure depressive symptoms. Includes 27 items, domains total depression, negative mood, interpersonal problems, inaffectiveness, anhedonia and negative self-esteem.	8 [35,36,38,39,42,49,53,63]
Strengths and Difficulties Questionnaire (SDQ) [83]	For 4–16 years, same version with 25 items for parents and teachers and a self-report for 11– to 16-year-olds. Assesses both strengths and difficulties, five dimensions: conduct problems, emotional symptoms, hyperactivity, peer relationships and prosocial behavior.	4 [44,60,70,74]
Conners' Parent Rating Scale—Revised (CPRS-R) [19]	For 3–17 years, includes parent (80 items) and teacher (59 items) forms and a self-report (87 items) form for 12–17 years. Assesses attention deficit/hyperactivity disorder and evaluates problem behavior in children and adolescents. Consists of 8–10 subscales depending on the form.	3 [51,69,70]
Revised Children's Manifest Anxiety Scale (RCMAS) [80]	For 6–19 years. A self-report, 37 items to measure anxiety. Includes Total Anxiety Score and Anxiety Subscale Scores.	3 [38,49,53]
Piers-Harris Children's Self-Concept Scale (CSCS) [81,82]	For 7–18 years, self-report including 60 items. Includes Total Scales and 6 domain scales Behavioral Adjustment, Intellectual and School Status, Physical Appearance and Attributes, Freedom from Anxiety, Popularity, Happiness and Satisfaction.	3 [39,45,53]
State-Trait Anxiety Inventory (STAI, STAI-C) [79]	For 9–12 and 6–14 years. Self-report including 20 items that measure the level and nature of anxiety: state anxiety (S-Anxiety) and trait anxiety (T-Anxiety).	2 [36,63]
Social Skills Rating System (SSRS) [20]	For 3–18 years. Includes teacher, parent and student rating forms. Provides Social Skills Scale (with subscales of cooperation, empathy, assertion, self-control, and responsibility), Problem Behaviors Scale (with subscales externalizing, internalizing problems and hyperactivity) and Academic Competence Scale.	2 [53,73]

the borderline or clinical range was reported by McCusker et al. [62]. They demonstrated a higher proportion of clinically significant impairments in those children with intractable epilepsy, ranging from 35.5 to 43.8% in the social competence subscales of the CBCL.

Little attention was paid to peer problems in children with epilepsy. In their population-based survey, Davies et al. [44] showed statistically significantly more problems with greater impact and peer problems reported by parents in children with epilepsy than in healthy children. Children with epilepsy were demonstrated to be less active and socialize less with their friends [57]. Difficulties in relating to peers were found to be more evident in those children with epilepsy attending specialized institutions than in those children with epilepsy attending mainstream schools [70]. In a recent study [53], peer problems were manifested in bullying behavior. Hamiwka et al. [53] reported children with epilepsy to be more frequently victims of bullying (42%) than healthy controls (21%) or children with chronic kidney disease (18%). This suggests that factors related to bullying behavior could be associated with epilepsy rather than with chronic disease. However, the predictors of victim status were not related to the epilepsy factors (e.g., early age at seizure onset, seizure type, and refractory epilepsy) nor were relations between victim status and poor social skills, increased problem behaviors and emotional problems found. One possible explanation for these results is that bullying behavior and other peer difficulties in children with epilepsy could be related to inattentive and anxious behavior, as seen in typically developing children [45].

Associations between social competence and epilepsy-related variables were also studied, and the results varied. Some studies reported findings of associations between epilepsy-related variables and social competence. In addition to etiology [50,56,64], social competence was most often reported to be associated with seizure frequency [33–35,37,56,63] and seizure type [35,42,56,57,61,74,75], although not all studies confirmed these results [34,53,63]. More inconsistent associations were reported between social competence and age at onset [34,50,53,56,63,75], duration [62,63,75], and antiepileptic medication [37,50,53,54,63,67,75].

4. Discussion

The purpose of this review was to summarize the definitions of social competence, assessment methods, and study design used in studies from 1998 to 2010 and to provide an update of the main findings. The model presented in Fig. 1 (modified from [14]) was used as a theoretical framework of this review.

4.1. Definitions and assessment of social competence

There are some theoretical and methodological problems regarding the studies reviewed. Most importantly, the earlier recommendation by Nassau and Drotar [4] that future studies should expand the conceptualizations of social competence specific to children's CNS conditions has not affected the field. Although a number of studies have been published in the field during the past twelve years, definitions of social competence were still mostly absent from the studies reviewed, and the perspectives were confined to overt behavior. Only one study [69] provided a definition of '*age-appropriate social skills acquired and absence of behavioral problems*'. This definition entails two aspects of the subcomponents of social competence but neglects social performance. In the other studies reviewed, social competence was regarded implicitly as a manifestation of behavioral

Table 3
Proportion of problems in social competence reported in the studies reviewed.

Domain of social competence (rating scale)	Proportion of problems reported (% in clinical or at-risk range[a])	Study number
Social adjustment		
Psychiatric disorder (K-SADS)	26.2–60.5	[44,67,68,74]
Internalizing problems (CBCL)	12.7–70	[31,32,37,39,41,46,48,59,67]
Externalizing problems (CBCL)	11.4–43	[31,32,37,39,41,46,48,59,67]
Total problems (CBCL)	15.5–68	[31–33,37,39,41,46,48,50,59,67]
Attention problems (CBCL)	8.4–67.0	[31,37,39,48,50,58,59,62,72]
Depression (CDI)	7.5–39.6	[36,37,39,49,58,63,72,74]
Anxiety (STAI)	4.5–49.0	[31,37,39,42,48,49,58,67,72]
Social problems (CBCL)	6.3–51.0	[31,37,39,48,50,62]
Social performance		
Activities (CBCL)	2.0–37.5	[37,43,57,62,73]
Social competence (CBCL)	4.0–41.7	[37,43,57,62,73]
School competence (CBCL)	10.0–43.8	[37,43,57,62,73]
Total competence (CBCL)	6.5–33	[37,43,73]
Social skills		
Social skill deficit (SSRS)	13	[73]

[a] Social adjustment: Psychiatric disorder was determined according to DSM-IV criteria and with the K-SADS. For the CBCL broadband scales, at-risk range defined as T score ≥ 60 and clinical range as T score > 63, and for the syndrome scales, at-risk range $T \geq 67$ and clinical range $T \geq 71$. The CDI cutoff score at-risk defined as > 13, and the STAI-C cutoff score defined as > 35. Social performance: Clinical range for the CBCL subscales was T score ≥ 37 (Total) or ≥ 30. Social skill deficit was determined as the SSRS standard score -1.5 SD below the normative mean.

problems, where the absence of a psychiatric diagnosis and/or emotional and behavioral problems as rated by parents and/or teachers was regarded as an indicator of socially competent behavior. In the majority of studies, this implicit definition of social competence limited their focus to social adjustment problems. Less attention was paid to positive aspects of social competence, namely social skills and social performance. The results of this review, therefore, concur with the earlier review by Nassau and Drotar [4] who reported that the majority of studies before 1997 assessed social competence at the social adjustment level, and only few studies addressed it at the social performance or social skills level. This lack of theoretical consideration is evidently a significant limitation in the research of social aspects of epilepsy. There is still a need for a conceptualization and more carefully justified conceptual background of social competence that integrates the current views and results from developmental psychology and developmental neurosciences among typically developing children (see also [13,84]). A conceptual model with an exhaustive definition of social competence would also help the future research to distinguish potential outcomes related to social functioning or areas of weaknesses of social competence among children with childhood epilepsy. Socio-cognitive and social information processing skills that are considered especially critical determinants of social competence [13,16,84] should be integrated in future conceptualizations. Instead of outcome variables, socio-cognitive skills were integrated as possible modifying factors in the hypothetical model proposed in Fig. 1.

There are two important methodological limitations in earlier studies of social competence. First, the assessment methods used in epilepsy-related studies focused on one or two aspects of social competence (e.g., the social adjustment and social performance scales of the CBCL). Second, they relied mostly on parental and/or teacher reports. The assessment methods remained quite unchanged over the past 12 years. The failure to conceptualize social competence is reflected in the operationalization of social competence as an absence of psychiatric disorders. This was demonstrated in the utilization of the CBCL. The vast majority of studies (73%) still used only the CBCL to assess social competence, although as Perrin, Stein and Drotar [85] pointed out several years ago, the CBCL is neither designed nor recommended for children with chronic illnesses. Others have also expressed criticism of the assessment methods (see [37,86]), especially the CBCL for not being designed for children with chronic health conditions (see e.g., [86]). Oostrom et al. [86] demonstrated that the CBCL problem scales may be quite problematic in assessing the behavior of children with epilepsy. They concluded that ratings (such as the item 'Staring blankly') may be based on seizure features rather than behavior, leaving the behavioral scores ambiguous. The use of the standard version of the CBCL would result in overestimation of social adjustment problems [86]. However, some have reported findings supporting the validity of the CBCL. Gleissner et al. [87] demonstrated that when compared to the standard version of the CBCL, the adjusted version (i.e., scoring ambiguous items as missing) did indeed indicate fewer social adjustment problems before epilepsy surgery. However, the difference between the adjusted and standard versions persisted 12 months after surgery, indicating true difficulties in behavior and not merely seizure features. Further, the social competence scales measure accomplishments and social participation rather than skills or competence in social interaction [85]. Possible restrictions and limitations on participation in social activities due to epilepsy should not be mistaken for social incompetency [4]. The social competence scales of the CBCL are designed for children over 6 years of age, which partly explains the extensive use of problem scales in studies on younger participants. In the future, in order to broaden the perspective to include all aspects of social competence, it would be beneficial to utilize assessments of social skills and prosocial behavior and to consider use of other validated rating scales, such as the SSRS and the SDQ. The SSRS provides a comprehensive assessment tool for social skills with good reliability and validity that covers behaviors such as cooperation, assertion, responsibility, self-control, and empathy [20]. Similarly, the SDQ [83] also includes subscales, for example, for kind and helpful behavior. Both these scales are examples of possible and practical assessment tools for a broader perspective in the assessment of social competence. The SSRS was standardized in a sample of over 4000 children with and without disabilities (e.g., learning-disabled and behaviorally-disordered children) [20]. The normative data for the well-validated measure SDQ have also been published [88–90] (see also www.sdqinfo.com). Studies have also provided evidence for a high sensitivity and specificity of the SDQ among children with epilepsy or other chronic illness (e.g., [82,88,90]). However, the reliability of these most commonly used rating scales should not be taken for granted among clinical populations, such as those with epilepsy. More studies are, therefore, still needed to determine the reliability and validity of the rating scales or checklists used for the assessment of social competence among children with epilepsy.

The second methodological limitation of the studies reviewed is the use of parent and/or teacher report as the only means of assessing social competence. However, in typically developing children, the assessment of social competence has included other methods than behavioral rating scales, for example, sociometric and peer nomination procedures, observational procedures [6], and also laboratory settings (see e.g., [16]). For example, assessment methods like the Multisource Assessment of Social Competence Scale (MASC [9]) that provides peer assessments would be theoretically justified in future studies. To the best of our knowledge, these methods mentioned above have not been employed in epilepsy research. This is somewhat surprising, given how common these methods are in the field of developmental psychology. If we are to enhance our understanding of social competence in various settings and develop better focused interventions for children with epilepsy, these alternative methods should not be overlooked or neglected in the field of epilepsy research.

4.2. Study designs and data

Considerations relating to study designs, especially regarding participants' ages, must be addressed. Studies on social competence in childhood epilepsy were typically conducted with fairly large population- or community-based samples and were quite representative with respect to age range. However, in order to increase the number of participants, the age range varied considerably (from 1 to 18 years). Typically, participants have been school-aged children with mean age over 10 years. This is quite problematic since from the developmental perspective, the childhood years are a phase of rapid cognitive and social development. It is, therefore, decidedly problematic to include a wide age range in a study without distinguishing between young children from older children. Some important information is lost when the results are presented by means of the total sample: social competence in five-year-olds is somewhat different from that in twelve-year-olds. Expectations of social competence increase as a function of child's age and developmental level. Therefore, in future studies, it would be more informative to divide participants into subgroups, according to their age; e.g., infants, early childhood years from 2 to 6 years of age, school-aged children from 7 to 13 years (i.e., middle childhood) and adolescents (children over 13 years of age). Some aspects of social competence (e.g., social skills) may be assessed at a younger age, although some aspects, like social participation, can be more reliably evaluated at school age.

4.3. Recommendations for future studies

Studies have shown that chronic illnesses per se may affect a child's social competence (e.g., [29,30]). However, when compared to other chronic illnesses, the risk for developmental problems is increased in CNS-related conditions [4,5]. Therefore, studies focused on children with epilepsy are justified. Moreover, due to the discontinuous and potentially reversible nature of epileptic activity, the effects of epilepsy on neurocognitive and social functions should also be differentiated from static congenital or acquired brain disorders (e.g., cerebral palsy or traumatic brain injury) [91]. The extensive number of studies on social adjustment during the past 12 years is evidently a strength in the epilepsy research area. Nowadays, there is also a growing agreement that problems in social competence and neurocognitive functions are elementary parts of epilepsy itself rather than secondary problems due to adjustment problems of a chronic condition [92]. The results of the studies reviewed on social adjustment problems support this view and are also concurrent with the earlier meta-analysis by Rodenburg et al. [22]. However, due to the limited number of studies on social skills and participation, there is an imbalance between the number of studies investigating different aspects of social competence. Only a few of the reviewed articles focused on social skills and provided some evidence for the social skill impairments when compared to healthy controls [69] or siblings [73]. But, the proportion of children with problems in social performance was lower than the proportion of children with social adjustment problems. The scores of the CBCL Social Competence Scale were usually within normal range, except for the children with intractable epilepsy [62]. Still, problems in social activity, peer relations, and bullying [45,53,57] were reported. According to this review, a conclusion that social performance and social skills may be less affected than social adjustment in children with epilepsy cannot be drawn. This conclusion needs to be confirmed in future studies. Also, more descriptive and comparative studies are also suggested for young children with epilepsy. Studies focusing on younger children would be beneficial in order to understand overall social competence at young ages. The need for a broader perspective on social competence or behavioral issues as recommended in this review was also recently proposed by Hamiwka, Jones, Salpekar and Caplan [93].

Considering the number of studies in the last decade conducted on social adjustment in children with epilepsy, very little is known about the developmental pathways leading to these problems. This is because earlier studies have mostly been descriptive and comparative. It would, therefore, be beneficial to change the focus to investigating possible mediating factors between epilepsy and social competence. The conceptual framework proposed (Fig. 1) hypothesizes that underlying CNS lesions or dysfunction along with environmental- and family-related factors has a direct effect on social competence. Alternatively, this effect may be mediated through epilepsy-related and/or neurocognitive factors which, in turn, may both also have an independent effect on social competence (see also [5]). The neurocognitive functions may be one of the most important mediating factors between epilepsy-related variables and social competence. The studies reviewed provided some support for this hypothetical link between neurocognitive functions and social competence. The neurocognitive impairments relating to social adjustment included verbal cognitive impairments [41] and socio-cognitive skills [52]. For example, Caplan et al. [41] demonstrated that seizure-related variables were unrelated to social adjustment problems, but they predicted cognitive and linguistic deficits. More precisely, studies are needed to determine whether poorer social competence in children with epilepsy is related to an underlying deficit or developmental delay in social skills or to be attributed to inability in social performance. A social skill deficit may be one of the crucial factors associated with poorer social competence scores in children with epilepsy [73].

In typically developing children, social skill deficit is associated with later social adjustment problems and psychopathology [17,94]. There may also be underlying impairments in socio-cognitive and social information processing skills considered critical determinants of social competence [10,13,16], i.e., the prerequisite skills for enabling a child to encode and interpret social situations and problems, execute and evaluate plans to solve problems arising in social situations [94]. Golouboff et al. [52] have presented some preliminary evidence suggesting compromised development of recognizing facial expressions of emotion in children with temporal lobe epilepsy. Another possible explanation for the difficulty in developing age-appropriate social competence and peer relations is that an overt manifestation of the condition may be a risk factor leading to reduced opportunities to engage in age-appropriate peer activities [5,32,67].

There are contradictory findings regarding the importance of several epilepsy variables (e.g., etiology, seizure frequency, and seizure type) to be associated with problems in social competence. This relationship between epilepsy-related variables and social competence is probably indirect rather than direct [5,67]. Poorer social competence (i.e., social adjustment problems) may be related to a chronic condition (see e.g., [21,30]), or, as seen in typically developing children, peer problems may also be associated with neurocognitive functions (e.g., inattention and social cognition) [45,52]. These neurocognitive functions, for example cognitive impairment or learning problems [39,43,74,75] and verbal IQ [41,42,67], are proposed to be moderators of development of social competence in children with epilepsy [45]. It is possible that early-onset epilepsy with comorbid cognitive impairment is associated with poorer social skills or delayed social skill acquisition (see [95]). This, in turn, may predispose to later behavioral and adjustment problems or lead to subsequent psychopathology. However, regarding childhood epilepsy, we do not know to what extent the behavioral adjustment problems are attributed to performance deficit or, alternatively, if there is an underlying basic social skill deficit that increases the risk for later social adjustment problems. Future studies in this area would also be beneficial regarding interventions for children with epilepsy. To conclude, it remains to be seen in future studies whether the hypothetical framework of social competence and subcomponents presented is valid.

4.4. Limitations and clinical implications

The limitations of this review relate in part to the terms used in the original search. The various terms and combinations of them used in the search yielded numerous studies. Given the number of studies drawn from the electronic database at the first phase (4509 articles) and second phase (344 articles), it was not possible to review them in detail. Due to this, some important articles may have been excluded. The quality of this review would have improved if we had calculated the quality of the study indices (QSI) (e.g., [96,97]). The QSIs would have also helped readers to put the results of this review into context. Alternatively, a meta-analysis would have given more power to the conclusions. However, meta-analysis was not the method of choice due to the descriptive nature of this review. Also, given the number of studies conducted on different aspects of social competence (especially social skills), this was not justified.

For clinical practice, we recommend that more attention be paid to all aspects of social competence. Social competence is acquired in a social context, so, more studies are needed concerning, for instance, peer relationships, leisure activities, parental and family support, and their role in the development of social competence in children with epilepsy. Also, a wider perspective on the assessment of social competence in an individual child is recommended. For example, problems or delay in social skill development may be recognized earlier before behavioral problems are evident. This detection of social skill problems or problems in basic socio-cognitive skills at a younger age would enable earlier intervention. For a developing child, it is important to receive all the support needed to grow up as a competent member of society in spite of epilepsy. It is equally important for parents to be aware of possible challenges to neurocognitive and social functions related to epilepsy. Therefore, the social aspects of epilepsy should be individually considered in epilepsy guidance.

To conclude, the findings reported in this review emphasize the need for more studies on social issues (especially social skills and social performance) and possible mediating factors related to the development of social competence in pediatric epilepsy. In particular, further studies are required to address these issues in younger children with epilepsy. This requires both theoretically and methodologically justified studies. We also need more insight into the development of overall social competence, its subcomponents, and associations between these and modifying factors. Early detection of impairments in social competence and targeting appropriate interventions in the developing child may also have an impact on subsequent social outcome.

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Social competence of preschool children with epilepsy

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ABSTRACT

The aims of this study were to describe the social competence of 3- to 6-year-old children with epilepsy ($n = 26$) compared with that of age- and gender-matched healthy controls ($n = 26$). Social competence was assessed with the Vineland Social Maturity Scale, Conners' Parent Rating Scales—Revised, and the Child Behavior Checklist. The results indicate that the children with epilepsy, especially with complicated epilepsy, had fewer age-appropriate social skills and more attention and behavior problems than the healthy children, as reported by parents. It is possible that the lack of age-appropriate social skills and the presence of attention problems predispose to behavioral problems. Also, epilepsy-related factors impaired the achievement of social competence. This study shows that the preschool children with complicated, early-onset epilepsy are at increased risk of difficulties in social competence.

1. Introduction

Social competence is broadly defined as the individual ability to function equivalent to age-appropriate and cognitive abilities [1]. Social competence also refers to the means for achieving the major developmental tasks expected of a child of a given age and gender in the context of his or her own culture, society, and time [2], that is, the flexibility and ability to solve developmental problems and to adapt to different social contexts and demands [3]. Thus, maladaptive behavior, behavioral problems, and/or psychopathology may be regarded as undesired characteristics that may interfere with the child's development of social competence. A large and growing body of literature has been published on behavioral issues in pediatric epilepsy. Children with epilepsy are at increased risk of developing behavioral problems [4,5]. Results from several studies indicate increased levels of behavioral problems and psychopathology in children with epilepsy when compared with healthy children [6–11], siblings [12,13], and children with other chronic illnesses, for example, cardiac conditions and diabetes [14,15]. In particular, children with epilepsy and intellectual disability have more behavior problems [16,17]. Also, children with new-onset seizures may be at increased risk of behavior problems [18], but these problems do not necessarily persist [11,19]. Kölfen et al. [20] demonstrated that after withdrawal of the antiepileptic medication, children who did not relapse did not have any psychiatric disturbances and their performance was comparable to that of healthy peers, but those children who experienced occasional seizures exhibited behavioral problems.

The incidence of psychiatric problems in children with epilepsy varies in most studies from 16 to 60% [15,21,22]. In a Norwegian study, up to 77% of the children and adolescents with epilepsy had a possible psychiatric disorder [23]. Studies have also indicated that severity of psychopathology is further exacerbated in children with both epilepsy and mental retardation [24]. Behavior problems reported in children with epilepsy include both internalizing problems (e.g., anxiety, depression) [12,21,25] and externalizing problems (e.g., aggression, disruptive behavior) [21]. Externalizing and disruptive disorders and impaired social communication, in particular, have been found to predict lower social competence scores [8]. Children with epilepsy differed from healthy controls with respect to overall sociability and activities. Surprisingly, girls with epilepsy have more problems than boys [10].

The effects of epilepsy on social competence and overall mental health may be indirect rather than direct [26]. One possible explanation is that both seizures and behavior problems are caused by the same underlying neurological disorder [19,21,26]. Other explanations are that seizures as such disrupt behavior or that children have negative psychological reactions to seizure activity [12]. Seizure frequency in the past year, but not age at seizure onset, has been found to predict behavioral problems [25]. Recurrent seizures predict behavior problems very early in the course of epilepsy [12]. Also, intractability has been reported to account for a significant portion of the variance in behavioral problems [13,19]. However, these seizure-related variables do not necessarily predict social competence [7,21]. Other variables associated with behavior prob-

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lems are family-related, for example, maternal anxiety, parenting abilities, and family problems [see, e.g., 27]. Although risk factors for behavior problems and psychopathology have been identified in children with epilepsy, knowledge of the interactions between and the mechanisms underlying these factors and development of behavior problems is lacking.

Earlier studies conducted on social competence and behavior in children with epilepsy have some limitations. First, they concentrated on psychiatric aspects of behavior. In these studies, the absence of a psychiatric diagnosis and/or emotional and behavioral problems as observed by parents and/or teachers was regarded as indicating socially competent behavior. Studies conducted on social skills and competence, for example, mastering of age-appropriate social skills and peer relations rather than psychopathology, are mostly lacking. Nevertheless, from the view that social competence refers to the individual's ability to function equivalent to age-appropriate and cognitive abilities [1], the child's ability to adapt to different social context and demands [3] is essential. Therefore, social skills and adaptive behavior, as opposed to psychopathology, should be emphasized [28]. Second, as Nolan et al. [29] pointed out, the majority of studies have been conducted on school-aged children. Hence, studies on preschool children with epilepsy and on their subsequent development and behavior are rare.

The purpose of this study was to investigate social competence in preschool-aged children (i.e., 3- to 6-year-olds) with epilepsy as compared with that of matched healthy controls. In this study, social competence is defined as age-appropriate social skills acquired and absence of behavioral problems. The first hypothesis was that children with uncomplicated epilepsy (i.e., nonsymptomatic epilepsy without any other neurological signs or symptoms) have succeeded in the major developmental tasks of social development and that there is no statistical difference between the study group and the control group. The second hypothesis was that if any behavior problems are to be found, they were more likely to be observed among children with complicated epilepsy (i.e., epilepsy and other neurological signs or symptoms). The Ethical Committee of Tampere University Hospital approved the study. Parents gave their informed written consent to participate in the study.

2. Method

2.1. Study design

This study was part of a larger research project on neurocognitive functioning and social competence of preschool-aged children with epilepsy. A population-based cohort of preschool-aged children with active epilepsy ($N = 64$) was identified through the medical records of the Pediatric Neurology Unit, Tampere University Hospital, Tampere, Finland, which is the only center for pediatric neurology services in the hospital district of 460,000 inhabitants. The study cohort consisted of all children aged 3 to 6 years with epilepsy on the point prevalence day of September 30, 2004.

2.2. Participants

The children with epilepsy were divided into two groups: those with uncomplicated epilepsy and those with complicated epilepsy. The inclusion criteria for the uncomplicated epilepsy group were a confirmed diagnosis of epilepsy based on clinical data, EEG recordings, and imaging data; absence of other neurological disorders or developmental delay assessed according to routine clinical practice with standardized psychological tests (IQ >75 was required); normal MRI findings; and age between 3 years 0 months and 6 years 11 months. Excluded were any children with associated neurological disorders identifiable from previous medical records, identified by a pediatric neurologist during routine follow-up epilepsy visits or reported by parents or caregivers. The second study group of complicated epilepsy consisted of children not included in the uncomplicated study group. Of the population-based cohort of 64 children, 26 (41%) children were included in the uncomplicated epilepsy group and 38 (59%) in the complicated epilepsy group. Thirteen parents of both groups gave their written, informed consent for participation in the detailed neuropsychological part of the study. Table 1 summarizes the seizure-related variables of the participants. Age at onset of epilepsy varied between 2 months and 5 years 4 months. According to previous definitions, MRI scans were normal in all children in the uncomplicated epilepsy group, whereas six children in the complicated epilepsy group had abnormal MRI findings (e.g., polymicrogyria, focal cortical dysplasia). EEGs were consistent with the clinical seizure and epilepsy types.

Table 2 summarizes the detailed demographic and cognitive features of the participants. Twenty-six children (11 boys, 15 girls) with epilepsy and 26 age- and gender-matched healthy controls participated in this detailed neurocognitive and social competence assessment phase of the research project. There were 13 children

Table 1
Seizure variables of children in the uncomplicated and complicated epilepsy groups

	Children with uncomplicated epilepsy	Children with complicated epilepsy
Age at onset of seizures (months), mean (SD), range	27.85 (17.42), 6–64	21.60 (17.33), 2–52
Seizure type		
Focal	6	8
Generalized	7	5
MRI		
Normal	13	7
Abnormal	0	6
Seizure control[a]		
Good	4	3
Partial	6	4
Poor	3	6
Antiepileptic drugs (AEDs)		
None	1	1
Monotherapy	9	5
Polytherapy	3	7

[a] Good: seizure remission >1 year, partial: <1 seizure per month, poor: >1 seizure per month.

Table 2
Demographics and background data for children in the study and control groups

	Children with uncomplicated epilepsy	Children with complicated epilepsy	Healthy children
Number of subjects	13	13	26
Mean (SD) decimal age	4.83 (0.90)	4.98 (1.21)	4.70 (0.92)
Gender			
Boys	6	5	11
Girls	7	8	15
Maternal education			
Basic	1	1	2
Vocational training	5	5	8
High school/college	6	5	12
University	1	2	4
IQ, mean (SD)			
Verbal IQ	92.46 (10.53)	56.15 (17.10)	114.30 (13.16)[a]
Performance IQ	99.38 (13.28)	58.38 (17.58)	107.70 (11.82)[b]
Full Scale IQ	94.62 (12.22)	53.15 (14.18)	113.65 (12.08)[c]

[a] $\chi^2(2) = 27.69$, $P < 0.001$.
[b] $\chi^2(2) = 21.75$, $P < 0.001$.
[c] $\chi^2(2) = 32.99$, $P < 0.001$.

with uncomplicated epilepsy and 13 children with complicated epilepsy. The control group comprised age- and gender-matched healthy children ($n = 26$). Exclusion criteria for the healthy controls were chronic illness, neurological disorder, developmental problems (e.g., specific language impairment, mental retardation, autism), and need for special assistance or special education based on medical and/or developmental cause. A total of 32 parents gave their written consent to participate, and from these volunteers, 26 healthy children were selected and matched according to age and gender with the children in the study groups. As shown in Table 2, both patient groups had significantly lower mean IQ scores than the healthy children. Full Scale IQ scores were at the lower end of the normal distribution in the children with uncomplicated epilepsy and at the upper end in the controls, but intellectual functioning varied from borderline intellectual capacity (IQ 70–75) to moderate mental retardation (IQ 35–49) in the complicated epilepsy group.

2.3. Medical and background data

Medical data including demographic factors, duration of epilepsy, seizure and epilepsy type, seizure control during the period of the study, EEG, brain imaging with 1.5-T MRI, current antiepileptic drugs (AEDs), and most recent AED levels were analyzed retrospectively from children's medical records. The results of previous psychological evaluations made according to clinical practice during earlier routine visits to the pediatric neurology unit were also retrospectively reviewed. Cognitive abilities were assessed with standardized tests: the Bayley Scales of Infant Development (BSID-II) [30], or Wechsler's Primary and Preschool Scale of Intelligence—Revised (WPPSI-R) [31]. Additional data were collected using a background information questionnaire that included variables on children's medical and nonmedical everyday living (e.g., need for day care, therapies, and seizure-related variables).

2.4. Measurements of social competence

Social competence was assessed with questionnaires on behavior and social skills completed by parents. Because social competence has not been fully studied and results on preschool children are mostly lacking, a wider range of assessment measures were used in this study. Conners' Parent Rating Scale—Revised [32] and the Child Behavior Checklist [2,33] were used because they are the most commonly used assessment methods in both clinical and research practice. Also, both of these behavioral assessments have good reliability. In addition to these problem scales, the Vineland Social Maturity Scales (VSMS) [1] was selected because it focuses on different aspects of social competence and adaptive behavior. Also, the VSMS is commonly used in clinical practice in children with disabilities.

First, the VSMS measures social competence, self-help skills, and adaptive behavior required to function in an age-appropriate manner. The VSMS provides an overall composite score for objective and uniform index for acquired social skills. In this study, the VSMS raw scores were converted to an age-equivalent score, expressed as social age. Second, behavior and behavioral problems (including attention problems) were assessed using the 80-item Conners' Parent Rating Scales—Revised (CPRS-R) [32]. For description of the data, the raw scores of the CPRS-R were individually converted into T scores. The CPRS-R includes the subscales Oppositional, Cognitive Problems/Inattention, Hyperactivity, Anxious/Shy, Perfectionism, Social Problems, and Psychosomatic and the indexes Attention Deficit Hyperactivity Disorder (ADHD), Restless–Impulsive, Emotional Lability, and Total Index. In the CPRS-R, the cutoff level for problems in the above average range is a T score >65 (1.5 SD), and in the very much above average range, $T > 70$ (2 SD). Third, psychopathology was assessed with the Child Behavior Checklist (CBCL) [2,33]. Raw scores were individually converted into T scores. The CBCL is available in two versions: a 100-item list for 2- to 3-year-old children and a 113-item list for 4- to 6-year-old children. It results in a Total Behavior Problems score and two broadband scores, Internalizing Problems and Externalizing Problems. For the syndrome scales, the average is $T = 50$, the borderline clinical range is $T = 67–70$, and the clinical range is $T > 70$. The cutoff point for Total, Internalizing, and Externalizing Problem scores for behavioral disorder is 60, as suggested by Achenbach [2].

2.5. Statistical analysis

SPSS (Version 15.0) was used for the statistical analyses. Social composite score and social age obtained from the VSMS were used in the analysis of group differences. T scores of the CPRS-R subscales and CBCL Total Behavior Problems, Internalizing Problems, and Externalizing Problems were used for the comparisons between children with epilepsy and healthy children. The nonparametric Mann–Whitney and Kruskall–Wallis tests were used. P values less than 0.05 were considered statistically significant.

3. Results

3.1. Social skills

As a group, the children with epilepsy had lower scores on the VSMS than the controls. The mean social age was 5.51 years (SD = 0.05) in the uncomplicated epilepsy group, 4.05 years (SD = 1.35) in the complicated epilepsy group, and 6.12 years (SD = 0.57) in the healthy controls (Fig. 1). This difference between study and control groups was significant ($\chi^2(2) = 20.36$, $P < 0.01$). Also, social age of the uncomplicated epilepsy group differed from that of the complicated epilepsy group ($U = 29.5$, $P < 0.01$) and from that of healthy controls ($U = 96.0$, $P < 0.05$). The social age of the healthy controls was significantly higher (+16.6 months) than their chronological age (56.40 months). Similarly, this trend of the social age being higher than chronological age was observed in the uncomplicated epilepsy group (+8 months). However, the social age of the complicated epilepsy group was significantly lower (−22 months) than their chronological age.

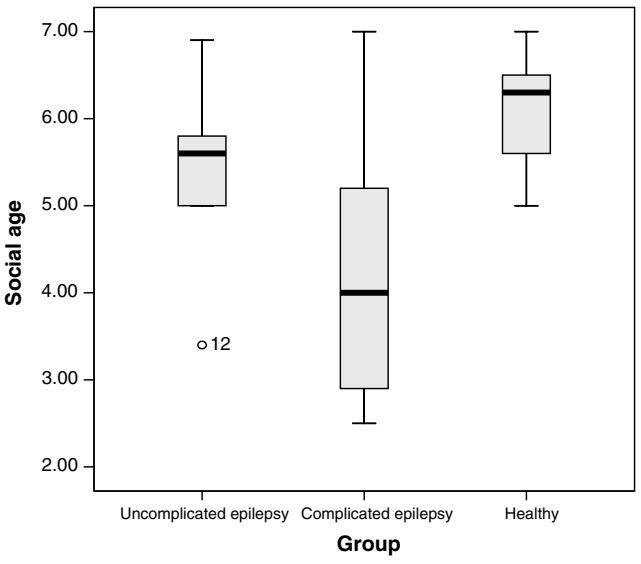

Fig. 1. Social age, as assessed with the Vineland Social Maturity Scale, of children with uncomplicated and complicated epilepsy and healthy children: $\chi^2(2) = 20.36$, $P < 0.001$.

3.2. Behavior problems

The children with epilepsy were found to have more attention problems than the controls according to the CPRS-R (Fig. 2). All differences were consistently in the direction of the control group performing better and within normal range than the two groups of children with epilepsy. The uncomplicated epilepsy group performed better than the complicated epilepsy group, but the differences between their scores were not statistically significant. Children with epilepsy had higher scores than healthy controls on the following CPRS-R subscales: Conners' Global Index (CGI) ($\chi^2(2) = 6.47$, $P < 0.05$), Restless–Impulsive Index ($\chi^2(2) = 9.15$, $P < 0.01$), and ADHD Index ($\chi^2(2) = 8.72$, $P < 0.01$). No differences were found in these indexes between the uncomplicated and complicated groups. In addition, there were differences on the Social Problems ($\chi^2(2) = 10.70$, $P < 0.01$) and Psychosomatic ($\chi^2(2) = 6.25$, $P < 0.05$) subscales between the study groups and the controls. In more detail, differences were found between the complicated epilepsy group and the controls on the Social Problems subscale (U = 63.5 $P < 0.001$), Psychosomatic subscale ($U = 88.0$, $P < 0.05$), and ADHD Index ($U = 77.0$, $P < 0.01$), but no differences were found between the uncomplicated epilepsy group and the controls. Conners' Restless–Impulsive Index was the only test on which the scores of the uncomplicated epilepsy group and healthy controls differed ($U = 97.0$, $P < 0.05$).

Among the children with epilepsy, the numbers in the at-risk or clinical range (i.e., $T > 60$) were 9 (35%) for the CBCL Total Problems scale, 5 (19%) for the Internalizing Problems scale, and 6 (23%) for the Externalizing Problems scale. Both the Total Problems and Internalizing Problems scores of the healthy control children were within the normal range, and only two (8%) children had an at-risk Externalizing Problems score.

Scores (means and SD) on the CBCL Internalizing Problems, Externalizing Problems, and Total Behavior Problems scales are summarized in Table 3. Children with epilepsy had significantly higher Total Problems ($\chi^2(2) = 15.08$, $P < 0.001$) and Internalizing Problems ($\chi^2(2) = 13.20$, $P < 0.001$) scores compared with their matched controls, but no difference was found in Externalizing Problems scores. In more detail, both groups of children with epilepsy had elevated Total Problems ($U_{only} = 79.0$, $P < 0.01$, $U_{plus} = 59.5$, $P < 0.001$) and Internalizing Problems ($U_{only} = 85.5$, $P < 0.01$, $U_{plus} = 51.0$, $P < 0.001$) scores compared with controls, but no differences were found between these epilepsy groups. There were no differences in the scores for the CBCL scales between the two groups of children with epilepsy, although the children with complicated epilepsy had more behavior problems.

4. Discussion

Several studies have reported behavioral and psychiatric problems in school-aged children with epilepsy. The aim of this study was to describe the social competence of preschool children with epilepsy as compared with that of healthy controls. In previous studies, only little attention has been paid to this developmental age range, which represents a period of rapid development in cognitive and social skills. The first hypothesis was that children with uncomplicated epilepsy have succeeded with the major developmental tasks of social development and there are no statistical differences compared with healthy controls. The second hypothesis was that if any behavior problems were to be found, they would be observed in children with complicated epilepsy.

First, as anticipated, the social skills of children with uncomplicated epilepsy were within the normal range but delay in social skills was evident in children with complicated epilepsy. The Vineland Social Maturity Scale was initially designed for use in mentally disabled children, and therefore, the scale may not discriminate effectively between non-disabled but disturbed and non-disturbed children [1]. Most children with normal intelligence

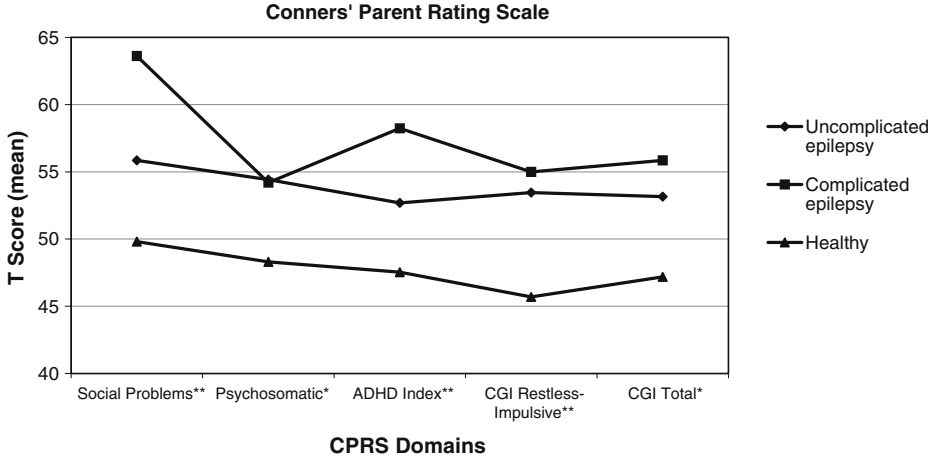

Fig. 2. Scores on Conners' Parent Rating Scale for children with uncomplicated and complicated epilepsy and healthy children. The average T score is 50 and the upper limit of normal is 64 points. $^{*}P < 0.05$, $^{**}P < 0.01$.

Table 3
CBCL Internalizing Problems, Externalizing Problems, and Total Problems scores of children with uncomplicated and complicated epilepsy and for healthy children

CBCL scale[a]	T score			Kruskall–Wallis test
	Children with uncomplicated epilepsy	Children with complicated epilepsy	Healthy children	
Internalizing Problems	48.31 (8.7)[b]	51.54 (8.7)	41.50 (5.7)	$\chi 2(2) = 13.20$ $P < 0.001$
Externalizing Problems	52.85 (8.5)	52.69 (8.4)	49.65 (7.0)	$\chi^2(2) = 2.06$ P = ns
Total Problems	53.31 (8.3)	56.38 (8.3)	45.54 (5.9)	$\chi^2(2) = 15.08$ $P < 0.001$

[a] Different versions of the CBCL (for age ranges 2–3 and 4–18) were used.
[b] Mean (SD).

perform well on items designed for their chronological age level. This ceiling effect was also demonstrated in this study in healthy children and in children with uncomplicated epilepsy. Both of these groups performed significantly better with respect to their chronological age. It is surprising that despite this ceiling effect, the social skills of both groups with epilepsy differed significantly from those of the matched healthy controls.

Second, as expected, some subtle problems in behavior, especially attention, were found, but no severe problems with clinical significance. This result concurs with earlier neuropsychological studies on attention problems of school-aged children with idiopathic or uncomplicated epilepsy [34,35]. The results are also consistent with the findings of a meta-analysis of 46 studies by Rodenburg et al. [36] concluding that attention problems, thought problems, and social problems are specific to childhood epilepsy. This view was further supported in a more recent review by Plioplys et al. [37].

Contrary to initial expectations, preschool children with epilepsy, including the children with uncomplicated epilepsy, also had behavior problems. Behavioral and attention problems were frequent, especially in children with complicated epilepsy. Hence, our study supports the previous observations [16,21,24] that behavior problems are more prevalent in those children with both epilepsy and intellectual or neurocognitive disabilities.

It is possible that the behavioral problems we observed in children with epilepsy are related mainly to overall cognitive capacity and specific neurocognitive impairments (e.g., in attention). In this study, the children with complicated epilepsy had lower scores on behavioral assessments, and the performance of children with uncomplicated epilepsy was more comparable to that of their healthy peers. Still, the parents of children with uncomplicated epilepsy reported fewer age-appropriate social skills and more Total Problems and Internalizing Behavior Problems than the parents of the healthy children. However, it might be that the difference in social age is related more to the difference in IQ. The children with uncomplicated epilepsy had significantly lower Verbal and Full Scale IQ scores compared with their healthy peers. Although there may be an underlying neurological cause for behavioral problems, it is possible that the lack of age-appropriate social skills predisposes to behavioral problems, especially if attention problems are evident. This study shows that preschool children with early onset epilepsy are at increased risk of difficulties in social competence. In clinical practice, we should pay attention to the development of social skills and behavior of these children with epilepsy to support their overall psychosocial development and acquisition of age-appropriate social skills.

Studies focusing on children with epilepsy in early childhood or in their preschool years are rare. Some studies do exist [e.g., 38], but the focus has been on medical aspects and the remission of seizures rather than on the psychological or social outcome. Moreover, the social competence of children with epilepsy has mostly been measured with the CBCL and similar assessments focusing on psychopathology and behavioral problems. Only one recent study by Tse et al. [28] focuses on the social skills of children with epilepsy in addition to behavioral problems. Nevertheless, further studies are needed to gain more insight into the developmental course of the social competence of children with epilepsy.

The strengths of this study are that it was population-based, was targeted, focused on a narrow age range, reviewed in detail the clinical data and epilepsy variables, used consistent and widely used measures of behavior and social skills, and employed a matched control group. However, the results of the present study are based on a limited number of participants. In addition, the study groups are heterogeneous with respect to representation of different types of epilepsy. Preschool age (i.e., <7 years) is a period of rapid cognitive and social development, which, in turn, is the basis for the subsequent development of academic skills during school age. Developmental, social, and behavioral problems in this age range may have long-lasting effects on later development; therefore, the clinical implications of these studies are important. The two groups of children with epilepsy in this study may be considered to be a fairly representative sample of preschool children with epilepsy, as they were recruited from a population-based cohort. Nevertheless, because of the small sample size, the results have to be regarded as tentative.

In conclusion, the results of this study indicate that children with early-onset epilepsy are at risk for developing behavioral problems and/or impaired social competence during their preschool years. As pointed out by Kirsch [39], epilepsy-related factors possibly interfere with the achievement of social competence. Also, the children's social environment may be restricted and their social network altered because of epilepsy-related factors. All of these mediators are essential to the development of social competence. In addition, family-related factors (i.e., disorganized or unsupportive home environments) [e.g., 27,34,40,41] have been found to further affect neuropsychological and behavioral deficits. It remains to be seen in follow-up studies whether these behavioral and attention problems, as well as the lack of age-appropriate skills, persist among children with epilepsy. According to these results, assessments of social competence are needed in clinical practice [see also 19]. The social skills and development of children with epilepsy should be studied further to increase our understanding of the possible developmental pathways to psychiatric problems in children with epilepsy. This would also be beneficial with respect to early intervention. In addition, children with epilepsy should be encouraged to participate in age-appropriate social activities and to interact with peers. Normal participation, in turn, is important for the development of overall social competence.

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