Speech and language dysfunction in childhood epilepsy and epileptiform EEG activity

by

Gunilla Rejnö-Habte Selassie

UNIVERSITY OF GOTHENBURG

Division of Speech and Language Pathology
Institute of Neuroscience and Physiology
The Sahlgrenska Academy at University of Gothenburg, Sweden

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Gutta cavat lapidem, non vi sed saepe cadendo

To Ghermay, Hanna and Sara
ABSTRACT

In severe childhood language disorder, concomitant dysfunction in other areas may be present. There are indications that epileptiform EEG activity and epilepsy may influence speech and language development, but this relationship is poorly understood. The objective of this thesis was to investigate the relationship between speech and language disorder in children and other neurodevelopmental dysfunctions and, in particular, to study the influence of epilepsy and epileptiform activity on speech and language.

In the first study, the medical records of 28 children with persistent speech and language disorder were reviewed in terms of speech and language development, psychological assessments and medical history and co-occurrence with other dysfunction was analysed. The second and third studies investigated speech, language, auditory and cognitive functions in 20 children from a regional cohort of six-year-olds with epilepsy and normal intelligence. They were compared with 30 reference children without epilepsy. The individual patterns of dysfunction were analysed with respect to some epilepsy variables. In the fourth study, 19 individuals with sleep-activated epileptiform activity and language dysfunction in childhood were followed up with assessments for speech, language, auditory and cognitive functions and EEG registrations. Their medical history and earlier assessments were reviewed. The results of the follow-up assessments were analysed with respect to both the pattern of earlier language development and some prognostic factors.

The first study revealed that a higher percentage of children with language disorder had epilepsy and epileptiform activity than children in the normal population and a complex pattern of co-occurrence with other developmental dysfunctions was present. Diverse speech and language profiles and intellectual profiles were found. In the second and third studies, children with epilepsy but normal intelligence displayed an expressive language dysfunction. Language dysfunction was found in children with a variety of epileptic conditions, but it was worse in those with epileptiform activity in the left hemisphere. The fourth study revealed diverse long-term outcomes for children with language dysfunction and epileptiform activity and no obvious differences were found between those with slow language development and those with a deterioration in previously acquired language ability. The amount of epileptiform activity indicated a poorer outcome.

Key words: auditory ability, cognition, co-morbidity, epilepsy, epileptiform activity, follow-up, Landau Kleffner syndrome, language disorder, neurodevelopmental dysfunction, speech disorder

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CONTENTS

ABSTRACT .................................................................................................................. 3
LIST OF PAPERS ......................................................................................................... 9
ABBREVIATIONS ......................................................................................................... 10
INTRODUCTIO ............................................................................................................ 11
BACKGROUND .......................................................................................................... 11
  Development and disorder of speech and language during childhood .................. 11
  Speech and language disorders in childhood ......................................................... 13
    Prevalence and definitions ................................................................................... 13
    Association with other developmental conditions .............................................. 14
    Functional areas related to speech and language ................................................. 14
      General cognitive function ............................................................................ 14
      Auditory perception ....................................................................................... 15
      Memory function ............................................................................................. 15
      Attention ......................................................................................................... 16
      Motor ability ................................................................................................... 16
      Pragmatics ....................................................................................................... 16
  Brain areas associated with speech and language during different stages of development ..... 17
  Epilepsy in childhood ........................................................................................... 19
    Prevalence, definition and manifestations .......................................................... 19
    Association with other developmental conditions .............................................. 19
    Epilepsy and cognitive function .......................................................................... 19
    Epileptiform EEG activity .................................................................................. 20
    Neuroimaging ..................................................................................................... 20
    Neurophysiological investigation ....................................................................... 20
  Classification of epilepsies .................................................................................... 21
  Antiepileptic treatment ......................................................................................... 22
  Epilepsy, epileptiform activity and language disorder .......................................... 23
    General studies ................................................................................................ 23
    Epileptic conditions specifically affecting speech and language ....................... 23
    Landau Kleffner spectrum speech and language disorders ................................ 23
AIMS OF THE STUDY ................................................................................................. 25
MATERIALS AND METHODS ................................................................................. 26
  Participants ........................................................................................................... 26
  Study I .................................................................................................................. 26
    Studies II and III
      Epilepsy group ................................................................................................. 27
      Reference group ............................................................................................. 27
      Medical history and group characteristics ...................................................... 27
  Study IV ................................................................................................................ 28
  Procedure ............................................................................................................. 28
  Study I .................................................................................................................. 28
    Speech and language records ............................................................................. 28
    Psychological records ....................................................................................... 28
    Medical records ............................................................................................... 28

5
Analysis of co-occurrence

Studies II and III

Speech, language and auditory assessments

Neuropsychological assessments

Assessments in relation to epilepsy variables

Study IV

Retrospective investigation

Follow-up assessments

The assessment battery

Speech and language assessments

Test translation

Auditory assessments

Neuropsychological assessments

Pragmatic ability

Statistical methods

Reliability

Analysis of individual profiles of dysfunction: (Study III)

(Study IV)

Analysis of prognostic indicators (Study IV)

Ethics

RESULTS

Study I

Speech and language dysfunction

Cognitive profiles

Epilepsy, EEG and etiological factors

Co-occurring factors

Studies II and III

Group comparisons

Speech, language and auditory assessments (Studies II and III)

Neuropsychological assessments (Study II)

Individual profiles of dysfunction (Study III)

Speech and language

Speech and language profiles and IQ levels (Studies II and III)

Test results in relation to epilepsy variables

Group comparisons (Study II)

Individual profiles in relation to type of epilepsy (Study III)

Study IV

Medical history and EEG features

Developmental characteristics

Results of follow-up assessments

Speech, language, communication and auditory ability

Cognitive ability

Follow-up assessments in relation to developmental profiles

Prognostic indicators

Summary of results from the four studies
DISCUSSION

Epilepsy and EPFA in language disorders
Speech and language dysfunction in childhood epilepsy
Diagnostic boundaries or a continuum of LKS-related conditions?
Epilepsy variables and speech and language dysfunction
Heredity
Cognitive function
Attention and motor ability
Auditory ability and language laterality
Word retrieval and memory
Phonology and literacy
Pragmatics
Prognosis
Treatment
Gender aspects
Limitations

SUMMARY AND CONCLUDING REMARKS
CLINICAL IMPLICATIONS AND FUTURE RESEARCH
ACKNOWLEDGEMENTS
REFERENCES
SUMMARY IN SWEDISH (Svensk sammanfattning)
LIST OF PAPERS

This thesis is based on the following papers, which will be referred to in the text by their roman numerals:


ABBREVIATIONS

ADHD  attention deficit hyperactivity disorder
AEA   acquired epileptic aphasia
ASD   autism spectrum disorders
AED   antiepileptic drug
BCECTS benign childhood epilepsy with centro-temporal spikes
BNT   Boston Naming Test
CAS   childhood apraxia of speech
CCC   Children’s Communication Checklist
CELF  Clinical Evaluation of Language Fundamentals
CPS   complex partial seizures
CSWS  continuous spikes and waves during slow wave sleep
CT    computerized tomography
CV-syllables consonant-vowel- syllables
DAS   developmental apraxia of speech
DL    dichotic listening
DLD   developmental language disorder
DVD   developmental verbal dyspraxia
EEG   electroencephalogram
ELD   epileptic language disorder
EPFA  epileptiform activity
FSIQ  full scale intelligence quotient
ILAE  International League Against Epilepsy
ITPA  Illinois Test of Psycholinguistic Abilities
KOLTIS Kommunikativ och lingvistisk bedömning av barn på ett tidigt stadium
LEA   left ear advantage
LI    language impairment
LKS   Landau Kleffner syndrome
MR    mental retardation
MRI   magnetic resonance imaging
NEA   no ear advantage
NEPSY Neuropsychological assessment of children
PET-scan positron emission tomography-scan
PIQ   performance intelligence quotient
PPVT  Peabody Picture Vocabulary Test
RCFN  Rapid Confrontation Naming test (Ordracet)
RDSL  Reynell Developmental Language Scales
REA   right ear advantage
SIT   Språkligt Impressivt Test
SLP   speech and language pathologist
SPECT single photon emission computerized tomography
SPS   simple partial seizures
TCI   transitory cognitive impairment
TROG  Test for Reception Of Grammar
WHO   World Health Organisation
VIQ   verbal intelligence quotient
WPPSI-R Wechsler Preschool and Primary Scale of Intelligence-Revised
WISC  Wechsler Intelligence Scales
INTRODUCTION

Speech and language disorders are among the most common developmental problems in childhood. Severe difficulties may restrict the child from social participation and academic achievement and lead to a permanent dysfunction in adulthood (Conti-Ramdsen et al., 2001, Young et al., 2002, Snowling et al., 2006). Researchers from different disciplines have previously focused on different aspects of speech and language disorders. Linguists have studied specific language functions and psychologists have dealt with explanations regarding the underlying nature, with particular emphasis on different aspects of cognitive processing capacity. Recent research has also highlighted the presence of additional disabilities, but it is unclear how they are related to speech and language disorders. New techniques for the study of cerebral functions and genetics have led to research that focuses more on neurobiological explanations of the origin of childhood speech and language disorders (Webster and Shevell, 2004). Interrupted cerebral activity in epileptic conditions results in disturbances in a variety of cognitive functions and may also affect speech and language development in a child, but it is not known how epileptiform discharges contribute to speech and language disorders. Research in the area of speech and language dysfunctions in children with epilepsy is scarce and the need for speech and language intervention has not received much attention (Svoboda, 2004).

This thesis focuses on the relationship between childhood epilepsy and epileptiform discharges in the brain and the various manifestations of speech and language dysfunctions which may be associated with them. It also looks into the co-occurrence with other negative developmental factors and with intellectual dysfunction.

BACKGROUND

Development and disorder of speech and language during childhood

The terms speech and language are sometimes used as synonyms. However, from a linguistic point of view, they are different sides of the same coin and are inseparably intertwined. Language refers to the cognitive set-up of the sounds of a language, the rules for their combination into words and sentences and the meaning behind them. Speech refers to the articulated utterances and the motor act and ability to perform them. Speech and language are mainly used for communication and this term also incorporates the use and understanding of social context and meaning. Language is usually described as consisting of phonology, which means the set-up of sounds and the rules for their combinations into words. It also consists of lexicon, meaning the vocabulary of a language and the meaning of words, which is also referred to as semantics. Additionally it consists of grammar, which refers to the combination of words into sentences, and pragmatics, which means the social use of language, or communication.

Children develop speech and language in a relatively short period of life. In most of them, language acquisition is smooth and seemingly effortless. However, some children experience a delay and some even experience serious difficulty in achieving their native language or
certain aspects of it. Locke proposed a neurodevelopmental theory of language acquisition and language disorder (Locke, 1997). He suggested that language develops in four phases, which occur in a fixed, interdependent sequence. Each phase is associated with a separate neural system. During the first phase, the child learns the characteristics of the face and voice of the caregiver. The second phase is affective and social and is dominated by the collection of utterances. The third phase is analytical and computational. As the child has reached the storage limit for words and utterances, he or she needs to analyse the different elements of language and the rules for their combinations in order to be able to continue to collect words and construct sentences. This stage of development is only reached after the child has collected enough words to activate their analytical mechanism. The most active phase of the neural mechanisms underlying the analytical computation is thought to be time locked. In children who are delayed in the second phase at the optimum biological moment, the capacity has begun to decline and this may lead to a language disorder. According to Locke, inactivation has the same effect as damage, leading to the compensatory use of other brain areas. During the fourth phase, extensive lexical learning takes place through integration and elaboration (Locke, 1997).

Linguistic theories have characterised language disorder as a disorder of grammatical competence. Children with language disorder are considered to have difficulty learning or using the grammatical rules of a language and this characteristic is thought to be the hallmark of language disorder (Bishop, 1997, Leonard, 1998). This involves both the rules of morphology, which refers to inflections and function words, and syntax, which refers to word order (Håkansson and Hansson, 2007). Another theory looks at the speech processing chain and is concerned with the way input and output are linked to meaning. According to this model, the speech signal enters via the auditory input, is matched to the stored lexical representations, or the mental lexicon, and computed for an output speech signal (Stackhouse and Wells, 1997). For speech production, lexical access is processed in two stages. The semantic representation of a word together with syntactic information is first retrieved and thereafter connected with the phonological information about how to pronounce the word. Children with language disorder may display a dysfunction on the input side, such as auditory discrimination of sounds or sequences of sounds, of the representations due to the imprecise storage of words, or on the output side, such as the inability to initiate, time and co-ordinate articulatory movements. This may lead to both speech and literacy difficulties (Stackhouse, 2000).

The cause of language disorder in children was unknown for a long period and children with this disorder often received the diagnosis “retardatio loquendi idiopatica”, meaning language delay without a known reason. Certain risk factors have subsequently been identified. Today, it is well known that genetic factors play a major role. Several researchers found a family aggregation of language disorder (Van der Lely and LA, 1996, Tallal et al., 2001) and both twin studies and adoption studies have confirmed these observations (Bishop et al., 1995, Felsenfelt and Plomin, 1997). Genetic studies have attempted to identify genes responsible for the disorder. No single gene that is responsible for language disorder has been identified, but several genes appear to be linked to the disorder (Newbury and Monaco, 2008). Perinatal factors have been suggested as a cause of language disorder, but they have not been found to be a major explanation. Being born small for gestational age (SGA) has, however, been
identified as a risk factor, as it appears to result in speech and language delay (Jennische and Sedin, 1998, Jennische and Sedin, 1999). Moreover, reduced hearing capacity due to middle ear infections has been suggested as a contributor to the disorder and it may be a risk factor in combination with others (Fox et al., 2002). A better understanding of the neurobiology of language disorder in children is critical for developing therapeutic strategies to treat this disorder (Webster and Shevell, 2004).

Speech and language disorders in childhood

Prevalence and definitions
Developmental lag in speech and language in children is the most common concern among parents and health supervisors. Speech and language delay affects around 15% of all children to such an extent that they need to be referred to a speech language pathologist (SLP) (Westerlund, 1994). The prevalence of speech and language disorder is 6-7% (Tomblin et al., 1997, Law et al., 2000) and in 2-3% severe language impairment is found (Law et al., 2000, Westerlund and Sundelin, 2000). Several studies have shown a gender ratio of two boys to one girl (Law J, 2000).

Terminology relating to speech and language disorders in childhood is inconsistent, as there is no generally accepted definition of the condition. Specific language impairment (SLI) is the term most often used in research on childhood language disorder and it was suggested by Stark and Tallal (Stark and Tallal, 1981). This term is based on exclusion criteria: language disorder in the absence of concomitant hearing impairment, mental retardation (MR) (defined as a full scale intelligence quotient (FSIQ) of < 70 measured with the Wechlsler scales), frank neurological impairment, autism and orofacial anomalies. It is also based on a discrepancy criterion: a difference of at least 1 standard deviation (SD) between verbal IQ (VIQ) and performance IQ (PIQ), the latter must be above IQ 85, which is 1 SD below IQ 100 (normal IQ). However, with this definition, 71% of clinically identified children with speech and language disorder were already excluded at the introduction of the term (Stark and Tallal, 1981). Developmental language disorder (DLD) has since been introduced as a less strict term, but the same exclusion criteria as those for SLI are still used. Several researchers include other children in SLI and DLD and the discrepancy criterion in particular has been challenged (Aram et al., 1992, Khami, 1998, Plante, 1998, Botting, 2005). Some researchers follow the interpretation of SLI and DLD in the International Classification of Diseases (ICD-10) of the World Health Organisation (WHO); there should be a discrepancy of at least 1 SD between a standardised language measure and a measure of non-verbal ability (Bishop, 1997). However, there are also studies in which SLI is the term used, without any clear inclusion criteria other than language disorder. The choice of terminology is sometimes arbitrary and different terms may refer to the same conditions. There is also an excluding assumption that there are no identifiable neurological diagnoses in children with SLI or DLD, but there is a lack of systematic studies of neurological function in these children (Trauner et al., 2000). The term language impairment (LI) has recently been used more frequently, as cognitive referencing is being abandoned to a greater degree (Norbury et al., 2008). It implies that the child’s language is poor for its age, without referencing to IQ level.
A generally accepted classification of language disorder is lacking, but the one that is most commonly used is that proposed by Rapin, categorising language disorder into expressive disorder, mixed expressive-receptive disorder and higher order processing disorder (Rapin and Allen, 1983, Rapin, 1996). These categories are also used in the ICD-10 (1993), and in the *Diagnostic and Statistical Manual* of the American Psychiatric Association (*DSM-IV*, 1994). There are also a number of psychometric approaches, which have attempted to classify children with language disorder using multivariate statistical methods (Conti-Ramsden et al., 1997, Van Weerdenburg et al., 2006). None of these approaches has as yet been adopted for clinical use.

In recent decades, research has also focused more heavily on disorders relating to speech sound production. Childhood apraxia of speech (CAS) is a term used for the severe forms; it involves difficulty with sensorimotor planning but without signs of paralysis or weakness in the muscles of the speech organs (Crary, 1993, Shriberg et al., 1997). Synonyms are developmental apraxia of speech (DAS) or developmental verbal dyspraxia (DVD). These difficulties interfere with the phonological development and are difficult to distinguish from a phonological disorder (Ozanne, 1995). There is a debate in the literature as to whether CAS should be understood as a motor speech disorder or a phonological disorder (Kent, 2000). Dysarthria, on the other hand, is the term used for an oral motor disorder due to paralysis or reduced motor ability.

**Association with other neurodevelopmental conditions**

Increasing evidence that language disorder is seldom specific is being presented (Sahlén and Nettelbladt, 1995, Goorhuis-Brouwer and Wijnberg-Williams, 1996, Bates, 2002). Several studies have shown that subtle signs of neurodevelopmental dysfunction often follow the speech and language impairment (Fernell et al., 2002, Westerlund et al., 2002, Conti-Ramsden and Hesketh, 2003, Webster and Shevell, 2004, Bruce et al., 2006, Miniscalco et al., 2006). Language disorder is often found in children with *attention deficit hyperactivity disorder* (*ADHD*) and *autism spectrum disorders* (*ASD*) (Gillberg et al., 1982, Miniscalco et al., 2006). ADHD is the most common additional disorder present in language impairment (Cohen et al., 2000). ASD are sometimes found in children with language disorder. Previously, a specific subgroup of semantic-pragmatic disorder in language disorder was identified (Rapin and Allen, 1983, Bishop, 1997). However, as the diagnostic boundaries for autism have been extended during the last few decades, some of those individuals who were previously diagnosed as having semantic-pragmatic disorder are now included in ASD. As a result, the percentage of diagnoses of autism among children with language disorder has increased (Bishop et al., 2008). Moreover, *late motor development* is a common additional phenomenon and is also seen in some children with neurological correlates (Trauner et al., 2000, Bishop, 2002, Hill, 2001). The degree of language disorder is related to the degree of co-occurrence with other developmental disorders (Westerlund et al., 2002).

**Functional areas related to language**

**General cognitive function**

Language development is related to general cognitive development and language disorder is common in mental retardation (MR) and is then regarded as part of the general delay in development. However, even in children with MR, language development can lag
substantially behind development in other areas (Kamhi, 1998). Different ideas have been put forward when it comes to problems associated with cognitive processing capacity that lie behind language disorder. Some researchers hold the view that difficulty with general processing capacity is the cause of language disorder and also with concomitant dysfunction in other areas (Johnston, 1994). These general limitations are thought to be found in space, energy or time (Kail and Salthouse, 1994). According to this model of explanation, there is a lack of space in the memory for linguistic processing, or there is a lack of energy. Lack of time means that the child is generally slow in cognitive computations. Other researchers have concentrated on processing deficits in particular areas as the cause of language disorder.

**Auditory perception**

The importance of auditory perception for speech and language development has been studied from different angles. Poor perception of rapid auditory stimuli has been suggested as an important factor underlying language disorder (Tallal, 2000). In a study using auditory brain stem audiometry, children with language disorder were found to have a longer latency responding to auditory stimuli (Ors et al., 2002), but contradictory results have also been found. Fernell et al. found no problems with temporal resolution in auditory perception in children with language disorder, but problems with speech discrimination and working memory were found (Fernell et al., 2002). In a study of speech perception in noise, children with language disorder were found to display more difficulty comprehending speech than children with typical development (Magnusson and Nauclér, 1987). However, these tests have generally been used for the assessment of hearing capacity in hearing disorders and seldom in language disorder. In a more recent study, Ziegler and co-workers found that children with language disorder were poorer than normal in identifying consonants in masking noise, particularly in terms of the voicing aspect of consonants (Ziegler et al., 2005). The metric hypothesis was proposed by Gerken, as an explanation of the way children learn language. The stress pattern of words in the child’s native language directs his or her attention to the different syllables, often leading to the omission of unstressed syllables in very young children. This is an effort-saving way of learning to speak and offers an explanation of some types of speech error found in children with language disorder (Gerken, 1994).

**Memory function**

Memory function is also important for language competence. Different types of memory have been suggested: working memory for the storage of information over a short period and computation and long-term memory for storing information over a long period. Baddeley proposed a model in which working memory consists of several components: a central executive, responsible for the planning, co-ordination and execution of different tasks, a phonological loop responsible for the storage of phonologically related information, a visual loop, responsible for the storage of visual and spatial information, and an episodic buffer, responsible for activation and retrieving information from the long-term memory (Baddeley et al., 1998, Repovs and Baddeley, 2006). The phonological loop in the working memory is considered to play a particularly important role in language acquisition and children with language disorder often have a poor phonological working memory (Montgomery, 2003). Poor results in tests of non-word repetition, which impose a heavy load on the phonological working memory, and in memory tests of digit span have been identified as risk markers of language disorder (Conti-Ramsden and Hesketh, 2003). Another view of memory functions
has been put forward by Ullman. His declarative/procedural model attempts to explain the neurocognitive systems responsible for the two language capacities: the memorisation of words and the rule-governed combination of words by the mental grammar (Ullman, 2001). The declarative memory system contains both semantic and episodic knowledge and the procedural memory system is used for learning new motor and cognitive skills and for controlling well-established ones. According to this model, the declarative memory is responsible for the storing of words and irregular grammatical forms, while the procedural memory is responsible for the storing of regular grammatical forms. The computation of morphologically complex forms is thought to involve both systems.

**Attention**
Several studies have revealed concomitant problems with attention (Westerlund et al., 2002, Gillberg et al., 1982, Miniscalco et al., 2006). In particular, sustained attention involves frontal brain areas which are also involved in speech and language activity (Cabeza and Nyberg, 2000). Selective and simultaneous attention to auditory stimuli is thought to play a role in language acquisition. Tests of dichotic listening have been used to assess both auditory attention and language laterality (Hugdahl et al., 1986, Hugdahl and Andersson, 1986). In dichotic listening, different speech signals are given to both ears simultaneously. Different tests of dichotic listening have used different types of speech signal, from single phonemes to consonant-vowel syllables to words and phrases.

**Motor ability**
Delayed oral motor development is sometimes found in children with language disorder (McAllister, 2008). In such cases, the general oral movements are immature and clumsy. In childhood apraxia of speech (CAS), articulatory movements are groping and vary from one moment to the other in the production of the same word. The child may also have difficulty producing articulatory movements on request and the difficulty tends to increase with longer sequences of syllables (Caruso and Strand, 1999). A rare genetic condition has been found in a large family with a severe form of CAS in three generations, tied to the FOXp2 gene (Varga-Khadem et al., 1998). A genetic predisposition is suspected in many cases of CAS, although no particular gene responsible for the disorder has been identified in these cases. Oral dyspraxia is sometimes found and also includes the disability of general oral movements. CAS is regarded as a severe variant of expressive language disorder (Rapin, 1998). Dysarthria, on the other hand, is due to a disease or damage affecting oral motor areas of the central nervous system or peripheral nerves to the speech organs and as such is separate from a language disorder.

**Pragmatics**
Pragmatic ability is linked to the semantic ability or understanding of a message. Children with language disorder may have difficulty processing longer utterances and drawing inferences about what has been said (Bishop, 1997). They may also have difficulty understanding the social context and use of language. Pragmatic ability requires an awareness of people’s beliefs, desires and knowledge. Pragmatic ability in children is often measured using different parental or teacher check-lists (Bishop, 1998b). Several studies have shown that there is a relationship between children’s ability to produce a narration and pragmatic ability (Reuterskiöld Wagner, 1999, Leinonen et al., 2000, Miniscalco et al., 2007).
According to Applebee, the structure of a narrative develops through different stages and is dependent on how well the child understands the knowledge of the listener (Applebee, 1978). This understanding reflects the set-up of the narrative, as in the framework of the story, the introduction of the subject, the building up of a conflict, the resolution and finally the concluding message or moral of the story. The ability to build up a story in this way also reflects the capacity to organise information. Moreover, the understanding of contextual cues about things that have not been openly stated, such as grammatical cues like pronouns and definite articles, develops gradually (Stein and Glenn, 1979). These difficulties may reflect problems both with the grammatical system of the language and with pragmatics.

**Brain areas associated with speech and language during different stages of development**

In most adults, the left hemisphere of the brain is dominant for language, i.e. language function is lateralised. When it comes to language, the left hemisphere is primarily characterised by a capacity to analyse and sequence linguistic information, while the right hemisphere is known for its holistic perception. The perception of prosodic aspects of language, whole word perception and the perception of social interaction are considered to be typical activities of the right hemisphere. Right-hemispheric damage often results in problems with social communication, also referred to as pragmatics. Locke argued, in his theory of language development, that the right hemisphere subserves language development during the first two phases, when the child is oriented towards interaction with the caregiver and the collecting of whole utterances (Locke, 1997). The left hemisphere gradually takes command, as the child starts to analyse the different elements of language and the rules for their combinations. In this way, language lateralisation develops. Recent fMRI studies suggest that early language processing is predominantly bilateral (Dick et al., 2008). Lateralisation toward the left hemisphere occurs gradually and a shift is found to occur around five years of age and it then continues through childhood and adolescence. The lateralisation occurs about one year earlier in girls than in boys, which corresponds with the earlier onset of puberty in girls. In children with brain damage, cognitive functions can be shifted to other brain regions, as for language, to the non-dominant and most often the right hemisphere. This possibility of brain repair, called plasticity, is more likely to occur before lateralisation is completed (Carlsson, 1994).

The main brain areas involved in language processing are Wernicke’s area for receptive language located in the posterior part of the temporal lobe and adjacent parts of the parietal lobe, close to the auditory cortex, and Broca’s area for expressive language located in the lower posterior part of the frontal lobe (Figure 1). These structures are integrated in a network and form a language implementary system. During childhood, these areas gradually increase in thickness, corresponding to increased grey matter (Dick et al., 2008). This results in an asymmetry between the hemispheres, where the left hemisphere is larger than the right, particularly in the area of the planum temporale. Absent or reversed asymmetry has been seen in studies of children with language disorder (Dick et al., 2008). The Rolandic area, located in the precentral gyrus at the Rolandic fissure, is the primary motor area involved in the motor
control of the speech act, while the secondary motor area for initiating speech motor activity adjacent to it overlaps partly with Broca’s area (Figure 1). The phonological encoding is considered to be localised in the periSylvian region, near the Sylvian fissure, of the dominant hemisphere, while articulatory retrieval is located in Broca’s area (Baddeley et al., 1998). Hickok and Poeppel proposed a dual-stream model of speech processing involving auditory fields of the superior temporal gyrus bilaterally (Hickok and Poeppel, 2007). A ventral stream processes speech signals for comprehension, projects towards the inferior posterior temporal cortex and is largely bilateral. The dorsal stream maps sound onto articulatory-based representations, involves a region in the posterior Sylvian fissure at the parietal-temporal boundary and ultimately projects to the frontal regions. It is strongly left-hemisphere dominant. A memory network within the limbic system, including the hippocampus, interacts with speech and language, as the left hippocampus is particularly important for memory for language. Moreover, associative areas within several regions in the temporal, frontal and parietal lobes interact with the main language system (Mesulam, 1990). The cerebellum is associated primarily with the balance and co-ordination of movements, but it has lately also been associated with language functions, particularly with the modulation of linguistic and other cognitive abilities and with motor speech planning (Paquier, 2007).
Epilepsy in childhood

Prevalence, definition and manifestations
Epilepsy is found in approximately 0.45-0.5% of all children and the yearly rate of new cases is 70/100,000 (Forsgren et al., 2005). Epilepsy is defined as two unprovoked epileptic seizures, due to abnormal electrical discharges in the brain. The seizures can be manifested in a variety of ways – from major motor seizures to attacks of inattention – and they result in both conscious and unconscious states. Subclinical (interictal) discharges are often found between seizures. Seizures are caused by hyperactivity in excitatory synapses or hypoactivity in inhibitory synapses of the brain, or hypersynchronisation of neuronal activity. Repeated and prolonged seizures have negative long-term consequences when it comes to cognition in both children and adults (Olsson et al., 1997, Engman et al., 2001). In children, they are likely to result in the disrupted consolidation of cerebral networks. There is an association between how long the individual has had epilepsy and the degree of neuropsychological disorder, especially in childhood-onset epilepsy (Sutula et al., 2003). Epilepsy affects children in a different way than adults, as their brains are developing. The effects are different at different ages, depending on the degree of maturation of different cerebral functions (Sutula et al., 2003).

Association with other developmental conditions
Epilepsy is one of several symptoms in a number of different developmental syndromes in children (Kyllerman et al., 1999). In children with epilepsy, 30-40% have MR (Steffenburg, 1997). Different studies have found autism in 7-42% (Tuchman, 1994). Among children with autism, 33% have epilepsy (Danielsson et al., 2005) and, in children with ASD, 40% have epilepsy (Olsson et al., 1988). In a population-based study, 38% of children with cerebral palsy (CP) were found to have epilepsy (Carlsson et al., 2003). Attention problems are common in children with epilepsy, but they do not always resemble the inattention in ADHD (Svoboda, 2004). According to Aldenkamp and co-workers, hyperactivity is uncommon, while inattentiveness is common in children with epilepsy (Aldenkamp et al., 2005). Epilepsy is also found in combination with ADHD and is 3-7 times more common in children with ADHD than in typical children (Aldenkamp et al., 2005). In another study, the incidence of epilepsy in the inattentive subtype of ADHD was no higher than in a control population (Holtman et al., 2003). According to Deonna, ADHD and epilepsy can co-occur in the same child but without a clear link (Deonna and Roulet-Perez, 2005).

Epilepsy and cognitive function
Besag reports on several studies showing that, in children with epilepsy, both FSIQ and PIQ are lower than in healthy children (Besag, 2002). Inattention in children with epilepsy may be due to a direct effect of the bioelectric dysfunction, a side-effect of anti-epileptic drugs (AEDs) or a basic feature of the brain dysfunction responsible for the epilepsy (Deonna and Roulet-Perez, 2005). There are few studies dealing specifically with memory disorders and epilepsy in children. Nolan et al. compared the memory function in children with different epilepsy syndromes. They found that children with temporal lobe epilepsy displayed more memory dysfunction than children with other types of epilepsy and, in frontal lobe epilepsy and absence epilepsy, there was a memory dysfunction of a lesser degree (Nolan et al., 2004).
Studies of children who have had temporal lobe resection for intractable epilepsy have shown a decline in memory function, but the plasticity of memory functions is also possible in some children (Lah, 2004, Deonna and Roulet-Perez, 2005). Language disorder and epilepsy can be concomitant but unrelated phenomena, but they can also be separate consequences of the same underlying brain pathology. Epilepsy can also be the direct cause of the language disorder (Deonna and Roulet-Perez, 2005). The extent to which seizure activity affects cognitive function is not known. Age at the onset of epilepsy, the duration of the epilepsy, the seizure frequency and the number of anti-epileptic drugs (AEDs) that the child receives are all thought to affect cognition (Elger et al., 2004, Bulteau et al., 2000). According to Besag, the child is also affected after a seizure (post-ictal status) and this phenomenon is probably underestimated, particularly after frequent nocturnal seizures which affect the child directly and indirectly during the daytime as a result of disturbed sleep (Besag, 2002).

Epileptiform EEG activity
Subclinical (interictal) discharges, registered on the EEG as epileptiform activity (EPFA), are present in 50% of patients with epilepsy (Binnie, 2003, Svoboda, 2004). Subclinical discharges are also found in persons without epilepsy; they occur in 10% of children without seizures (Eeg-Olofsson et al., 1971). Transient cortical effects of these discharges, so-called transitory cognitive impairments (TCI), have been reported and they are found to affect a number of cognitive functions (Binnie, 2001, Binnie, 2003). Subclinical discharges can be transient or repeated. The effect of EPFA is greater with more frequent activity, repeated discharges and bilateral and symmetrical discharges. Subclinical discharges alone, without seizures, are usually not treated medically, but this issue has been the subject of debate (Binnie, 2003).

Neuroimaging
Several techniques are available for the study of brain morphology and brain activity. Computed tomography (CT) and magnetic resonance imaging (MRI) are used for studying brain morphology. Brain function can be studied using functional magnetic resonance imaging (fMRI) during the performance of an activity, while single photon emission computed tomography (SPECT) measures the blood flow in various parts of the brain. The blood flow within a brain area indicates the possibility of activity and shows lower-than-normal activity as hypoperfusion and higher-than-normal activity as hyperperfusion. Positron emission tomography (PET) scan is another, more cumbersome, functional technique which displays the metabolic energy activity of brain areas.

Neurophysiological investigation
The electrical potentials in the live brain can be recorded in an electroencephalogram (EEG). Twenty to twenty-two electrodes are placed on the surface of the skull and the electrical activity is registered in the electroencephalograph to which the electrodes are connected. The rhythmic pattern of the electrical potentials is assessed. This is the main instrument for assessing the abnormal electrical activity associated with epilepsy. Discharges are registered as patterns of spikes and waves and low-frequency or high-frequency activity (Figure 2). Recordings are made during wakefulness, drowsiness or sleep, and recordings taken in the sleeping state are preferable. As the electrodes are placed on the surface of the skull, electrical activity originating from deeper brain structures cannot be recorded. Invasive recordings with
electrodes placed on the surface of the brain or in the brain tissue may be applied in potential epilepsy surgery cases as part of a pre-surgical investigation.

**Figure 2.** EEG-recording showing independent spike and wave activity from both hemispheres during sleep. (Picture: A. Hedström)

**Classification of epileptic seizures**

The International League Against Epilepsy (ILAE) has created a system for the classification of different types of epileptic seizures and epileptic syndromes (ILAE, 1981, ILAE, 1989), shown in Table 1. The main types are generalised and partial (focal) epilepsy. In generalised epilepsy, the whole brain is involved, while in partial epilepsy the seizure starts in one part of the brain. There are also a number of epileptic syndromes in children with specific symptoms and courses.

**Generalised seizures**

Generalised seizures can be primary or secondary. Primary generalised seizures involve the whole brain from the start. In secondary generalised epilepsy, the seizure starts in a certain part of the brain and spreads to other brain regions. In status epilepticus, the seizure activity continues for more than 30 minutes and this condition has harmful effects on the brain. The effect on cognition in generalised seizures is unclear. It may be associated with major cognitive or behavioural problems in one child and mild or no problems in another (Deonna and Roulet-Perez, 2005).
Partial seizures
Partial seizures originate from a localised epileptic focus in the brain. It can be simple or complex. In simple partial seizures (SPS), the child is conscious. In complex partial seizures (CPS), consciousness is disturbed. Symptoms follow the localisation of discharges in brain areas (Paquier et al., 2009). Paquier and co-workers found various cognitive dysfunctions which could be directly associated with focal spiking activity in children.

Table 1. Classification of epileptic seizures and syndromes according to the ILAE (1981, 1989)

<table>
<thead>
<tr>
<th>Epileptic seizures</th>
<th>Seizure types</th>
</tr>
</thead>
<tbody>
<tr>
<td>Generalised seizures</td>
<td>Absence</td>
</tr>
<tr>
<td>Partial (focal) seizures</td>
<td>Simple</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Epileptic syndromes</th>
<th>Subgroups</th>
</tr>
</thead>
<tbody>
<tr>
<td>Localisation related (partial, focal)</td>
<td>Idiopathic</td>
</tr>
<tr>
<td>Generalised</td>
<td>Idiopathic</td>
</tr>
<tr>
<td>Unclassifiable</td>
<td></td>
</tr>
</tbody>
</table>

Anti-epileptic treatment
A number of different anti-epileptic drugs are used in clinical practice. Most children become free from seizures with AED treatment. However, drugs may have different negative side-effects. In particular, attention and motor abilities can be affected (Svoboda, 2004). In children with intractable epilepsy, other treatments may be needed. A ketogenic diet, rich in fatty acids and free from carbohydrates, has been shown to be helpful in some cases. A vagus nerve stimulator is sometimes used in children with difficult-to-treat epilepsy. The effects have not always been very promising (Danielsson et al., 2008). Epilepsy surgery may be a good treatment alternative in certain selected cases with a clear epileptogenic focus. In children with abundant sleep-activated EPFA, such as in the Landau Kleffner syndrome, corticosteroid treatment can be used and is often the preferred drug. Immunoglobulin is also sometimes used.
Epilepsy, epileptiform activity and language disorder

General studies
In both children and adults, language function can be disturbed in some forms of epilepsy. According to Svoboda, speech and language difficulties in children with epilepsy are an overlooked problem (Svoboda, 2004). One study of children with epilepsy has reported a prevalence of speech disorder in 27.6% (Sillanpää, 1992), but no other known studies report prevalence rates for speech and language disorders in children with epilepsy. According to Sillanpää, communication disability results in the greatest risk of handicap, following the International Classification of Impairments, Disabilities and Handicaps (ICIDH) (WHO, 1980). There are also indications that epilepsy may be more common in children with language disorder than is generally known and that this is an underestimated problem. However, this condition has not been carefully studied (Tuchman, 1994, Parry-Fielder et al., 1997, Rapin, 1998). In a few studies using different inclusion criteria for the study population, a prevalence of epilepsy in children with language disorder of 8-25% has been found, the highest number in those with the most severe form (Dalby, 1977, Allen and Rapin, 1980, Tuchman et al., 1991, Robinson, 1991). In a survey of the children who had been referred to the SLP at the child habilitation centre of northern Bohuslän, Sweden, because of severe language impairment, 15% of the children received AED treatment for epilepsy (Svensson and Tuominen-Eriksson, 2003). Wheless and co-workers and Elger and co-workers have also reported several studies showing that subclinical discharges affect speech and language, particularly in some childhood epileptic syndromes (Wheless et al., 2002, Elger et al., 2004). EPFA has also been found to affect language in children with language impairment without epilepsy (Echenne et al., 1992, Tuchman, 1994). Subclinical EPFA affecting cognitive function is sometimes labelled “cognitive epilepsy” (Deonna, 1996, Deonna and Roulet-Perez, 2005).

Epileptic conditions specifically affecting speech and language
Speech and language can be affected in all epileptic conditions when brain areas associated with speech and language processing are involved, mostly those of the dominant hemisphere and particularly in Broca’s and Wernicke’s areas, the area around the Sylvian fissure and the Rolandic area (Svoboda, 2004). Language, as well as the motor command of speech, can be affected in epileptic conditions, depending on the location of seizure activity. A particular syndrome with an autosomal dominant speech dyspraxia in Rolandic epilepsy has also been found (Scheffer et al., 1995). Temporal lobe epilepsy with adult onset has negative long-term effects on language function (Engman et al., 2001). There is also a form with childhood onset which runs in families (Pisano et al., 2005). Most research on epilepsy and language disorders in childhood has dealt with the Landau Kleffner syndrome (LKS) (Landau and Kleffner, 1957) and conditions related to LKS. According to Lees, other epileptic aphasias also exist, but the division of different epileptic aphasias poses a number of problems (Lees, 2005).

Landau Kleffner spectrum speech and language disorders
A group of electroclinical epileptic syndromes in childhood share the same characteristics: partial with focal spike and wave activity, EPFA activated during sleep and often overt seizures missing. They are diagnosed on the basis of the EEG pattern, together with various cognitive symptoms. These syndromes have been suggested as a spectrum of related
conditions. Among these syndromes, the following may present with speech and language
dysfunction and form the Landau Kleffner spectrum: the Landau Kleffner syndrome (LKS),
also called acquired epileptic aphasia (AEA), benign childhood epilepsy with centrotemporal
spikes (BCECTS), also called Rolandic epilepsy, and continuous sharp waves during slow

LKS has been considered to be an unusual form of childhood epilepsy, where the main
symptom is the loss or regression of speech and language comprehension and/or expression
(Landau and Kleffner, 1957). The discharges are multifocal and often bilateral. The course is
sometimes dramatic, although epileptic seizures are not always seen. Symptoms which have
been highlighted are auditory agnosia and receptive language disorder, followed by the
regression of expressive ability (Rapin et al., 1977). As new cases have been studied, the
picture of the syndrome has been modified. Other symptoms and courses of the condition
have been reported and it is possible that the syndrome is more common than previously
believed (Deonna et al., 1989, Tharpe and Olson, 1994).

BCECTS is the most common form of childhood focal epilepsy, localised to the temporal
lobes, and it is often accompanied by speech and language dysfunction and oral motor
dysfunction. There are also reports that general cognition may be affected in BCECTS
(Croona et al., 1999). During the last few decades, the speech and language dysfunction in
children with BCECTS has also been studied (Staden et al., 1998, Lundberg et al., 2005).

CSWS is a diagnosis based on the high frequency of EPFA during slow sleep, by definition
more than 85% of non-REM sleep. It is sometimes found in children with LKS (Deonna and
Roulet-Perez, 2005) or BCECTS (Kramer, 2008) and is reported to affect cognitive ability
more generally (Deonna and Roulet-Perez, 2005).

Subclinical EPFA, similar to that found in these epilepsy syndromes, is sometimes found in
children with language disorder. In a few studies, a higher percentage of children with
language disorder were found to have epilepsy and EPFA (Robinson, 1991, Parry-Fielder et
al., 1997, Rapin, 1998). From a clinical perspective, a clear differential diagnosis between
language disorder with EPFA and LKS-related syndromes is often difficult to make.

A number of long-term follow-up studies of patients within the LKS spectrum have been
performed (Bishop, 1985, Paquier et al., 1992, Carlsson et al., 2000, Robinson et al., 2001,
Debiais et al., 2007, Duran et al., 2009). There is still lack of knowledge about the cause, the
symptoms, the course of the condition and treatment effects. Sometimes, the clinical
symptoms in children with LKS do not resemble those usually reported (Mariën et al., 1993,
Deonna and Roulet, 1995). Some children have been reported to have a language delay
already prior to the onset of LKS, while some children may experience the onset of LKS
before speech has started to develop. In such cases, the diagnosis can be missed. As studies of
LKS and CSWS have seldom included a comprehensive description of speech and language
ability, the symptoms are seldom fully described (Lees, 2005). This is of great importance
when it comes to offering appropriate intervention (Tharpe and Olson, 1994). It is also
important to follow the symptoms over time and investigate various prognostic factors.
Longitudinal case studies have been recommended for this patient group, as this is a rare condition with great variation (Deonna and Roulet-Perez, 2005).

AIMS OF THE STUDY

The main objective of this project was to study how minor neurodevelopmental dysfunctions may be related to speech and language disorder in children and to further investigate the role of epilepsy and EPFA in speech and language disorder, using a multidisciplinary approach. The specific aims were:

- To explore the patterns of speech and language dysfunction in children with severe developmental language disorder without mental retardation and the possible co-occurrence with other neurodevelopmental dysfunctions or medical conditions (Study I)

- To investigate speech, language and auditory function in children with epilepsy who are expected to have an otherwise normal development (Studies II and III)

- To analyse the possible association between dysfunction of speech, language and auditory ability and specific epilepsy variables in children with epilepsy (Studies III and IV)

- To relate the corresponding cognitive and neuropsychological profiles and possible aetiological explanations to language disorder or epileptic conditions (Studies I-IV)

- To investigate the long-term outcome in children with focal EPFA and speech and language disorder in childhood and to see whether differences are found for those with different developmental profiles, or different EEG patterns (Study IV)

- To analyse possible prognostic indicators of a poor prognosis for children with focal EPFA within the LKS spectrum (Study IV)
MATERIALS AND METHODS

This thesis includes four studies. They are all multidisciplinary, descriptive studies, including data from the speech and language pathology, medical and neuropsychological professions, with the emphasis on speech and language pathology data. In the first study, the possible co-occurrence with other neurodevelopmental dysfunctions was investigated in children with severe developmental disorders. One of the results led to further studies of speech and language ability in children with different epilepsy syndromes, first in those with epilepsy in general and additionally also in those with a diagnosis within the Landau Kleffner spectrum. Study I is a retrospective study of individual cases. Studies II and III are based on the same research project, which is population based, and they are cross-sectional studies. Study II is a group comparison and Study III contains both a group comparison and an analysis of the ability of individual cases. Study IV is a retrospective and follow-up study of individual cases (Table 2).

Participants

A total of 90 individuals participated in the studies. Sixty of them were patients with language dysfunction and/or epilepsy and thirty were reference children. Studies II and III included the same study group. In all, assessments of 97 individuals are reported, but seven of the participants in Study IV also participated in another study, four in Study I and three in Studies II and III (Table 2).

Table 2. Design of and participants in the included studies.

<table>
<thead>
<tr>
<th>Study</th>
<th>Design</th>
<th>N of participants</th>
<th>Age years</th>
<th>Gender</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>M</td>
</tr>
<tr>
<td>I</td>
<td>Retrospective, case study</td>
<td>28 patients</td>
<td>4-14</td>
<td>17</td>
</tr>
<tr>
<td>II</td>
<td>Prospective, cross-sectional, group comparison</td>
<td>20 patients,</td>
<td>6</td>
<td>6</td>
</tr>
<tr>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>III</td>
<td>Prospective, cross-sectional, group comparison and case study</td>
<td>30 reference group</td>
<td>6</td>
<td>12</td>
</tr>
<tr>
<td>IV</td>
<td>Retrospective and follow-up, case study</td>
<td>19 patients</td>
<td>8-25</td>
<td>10</td>
</tr>
</tbody>
</table>

N= number, M= male, F= female

Study I

A clinical series of all children with persistent speech and language problems born between 1983 and 1994 and living in the city of Göteborg, who were discussed at a regular multi-professional patient conference on additional neurodevelopmental concerns between 1991 and 2001, a total of 57 children, were originally considered for Study I. Children with primary
concerns about possible ASD were not considered, as they were discussed at another forum. The study focused on the children with normal general development and, as a result, 29 of the children who were originally considered were subsequently excluded because of MR. The remaining 28 children without MR were included in this study. There were 17 boys and 11 girls, 4-14 years of age, and the median age was 8.1 years. The included 28 children were all followed by the SLP unit at the university hospital in Göteborg. The majority of the children had been referred to the unit by the Child Health Care (CHC) service, which reaches almost 100% of the population with health surveillance, including language screening. Subsequently, all the children had been assessed for speech and language ability by an SLP and for medical status by specialists in pediatrics, child psychiatry or phoniatrics. In addition, the majority had been assessed for intelligence and cognitive development by a psychologist and had been followed for several years.

Studies II and III
Epilepsy group
Studies II and III are based on a regional cohort from south-western Sweden comprising all six-year-old children with epilepsy, born in 1998 and 1999. The children were living in the city of Göteborg and eight surrounding municipalities and towns. All the children who are diagnosed with epilepsy in the area have their EEG recordings analysed by a specialist in neurophysiology at the university hospital in Göteborg and can therefore easily be identified. Fifty-three children were originally identified with epilepsy (3.4/1000). Twenty-seven of them were excluded, because of additional diagnoses such as MR, CP and/or autism, three had moved out of the area and three families declined participation. Twenty children were included, 14 girls and six boys. Their mean age was 6.5 years and their age range was 6.0-6.11. None of them had a known history of MR, CP or autism. All the included children were at preschool, apart from two who had spent no more than two months at regular school. Sixteen children were monolingual Swedish speakers and four were bilingual.

Reference group
Thirty children without epilepsy and known MR, CP and autism were included as a reference group. There were 18 girls and 12 boys, their mean age was 6.5 years and their age range 6.0-6.11. They were selected to be as similar as possible in terms of the following variables: age, with birth date ± 1 month, gender, mono- or bilingualism and geographical area. All the available children in the preschool or school next to that of the child with epilepsy who met the criteria were included, rendering one or two reference children for every child with epilepsy. Twenty-three were monolingual and seven bilingual.

Medical history and group characteristics
The epilepsy group and the reference group were compared in terms of gender, mono- or bilingualism and parents’ education, using non-parametric statistics (Test for Trends in Contingency Tables), and the groups were comparable. The medical history of the children with epilepsy was described by one of the authors, a specialist in neuropediatrics (IO). Ten children had partial epilepsy, six had generalised epilepsy, five of these with absence epilepsy, and four had unclassifiable epilepsy. Seven had epilepsy onset before the age of three and 13 after. All the children with epilepsy were receiving AED treatment. Fourteen were being treated with only one drug (monotherapy) and six were on more than one drug
(polytherapy). Thirteen children had been free from seizures for the last three months preceding the assessment. Hearing capacity was assessed in all the children by the author (GRHS). They all had normal hearing at 20 dB, apart from one in the study group and two in the reference group, who had hearing levels at 25 or 30 dB within the frequencies 500-4,000 dB due to temporary infections, but at levels of normal perception of speech sounds.

**Study IV**
The participants in this study came from a clinical series of individuals who had been diagnosed at the regional children’s hospital of south-western Sweden in Göteborg during childhood with EPFA and had previously known speech and language dysfunction. Medical registers were used to search for participants and neuropediatricians in the region reported some of the cases. The inclusion criteria were a minimum of two years of follow-up since the first EPFA was discovered and concern about speech and language dysfunction in childhood. Some of the participants had previously been given a definite diagnosis of LKS, while in others this diagnosis had been suspected. Only two possible participants were not included, one was never invited because of family problems and one did not answer the invitation. The study comprised nineteen individuals with a history of sleep-activated EPFA and speech and language dysfunction in childhood. At follow-up, eight were young adults (19.5-25.7 years) and eleven were school children (8.9-14.8 years), ten were males and nine females.

**Procedure**

**Study I**

*Speech and language records*
Assessment protocols from 3-10 different occasions were reviewed by the author (GRHS). General motor ability and attention problems were reported in the records. Speech and language symptoms were classified as expressive or receptive language dysfunction and the presence or not of oral motor dysfunction and they were grouped into combinations of these types of problem. Gender differences with respect to profiles were analysed.

*Psychological records*
Psychological assessment protocols for 23 of the 28 children were available and they were reviewed by one of the authors, a specialist in neuropsychology (GV). An FSIQ level between 70 and 84 was classified as below average, between 85 and 115 as average and higher than 115 as above average. Psychological profiles were established using a discrepancy criterion of ± 1 SD (15 IQ points) for VIQ compared with PIQ. In addition, general motor ability and attention problems were reported.

*Medical records*
Reports from medical examinations included patient history and medical diagnosis in all the children and were reviewed by one of the authors (MK), a specialist in neuropediatrics. EEG recordings were available in 18 of the children, in four only in the awake state and in the remainder combined with drowsiness and/or sleep. The results were interpreted in terms of low-frequency activity, EPFA and focal features, while the EEG findings were classified as
normal or not normal. Heredity for speech-language problems and dyslexia and pre-/perinatal problems were reported.

**Analysis of co-occurrence**

Speech and language dysfunction was analysed with respect to IQ levels, attention problems, EEG abnormalities and heredity for speech and language disorder. The percentage of diagnoses of epilepsy and motor and attention problems was compared with that of the general population.

**Studies II and III**

*Speech, language and auditory assessments*

All the children were assessed for oral motor ability and articulation, phonology, expressive vocabulary and grammar, narrative ability, emerging literacy and auditory ability by the author (GRHS). The expressive subtests were audio-recorded for subsequent assessment of test reliability. A parental questionnaire was used to assess communicative ability. In Study II, group comparisons were performed for the results for the children with epilepsy and the reference children for the speech and language assessments. In Study III, a group comparison of the auditory assessments was performed between the study and reference groups. In addition, the individual profiles of the children with epilepsy were studied.

*Neuropsychological assessments*

The assessments were performed by an experienced neuropsychologist and related to intelligence, verbal, visuospatial, visuococonstructive and visuomotor functions for all children with epilepsy and for 29 of the reference children, as one child was missing for practical reasons. Group comparisons for these assessments were performed. For memory and attention, only the children with epilepsy were assessed and the results were compared with normative data.

*Assessments in relation to medical data*

For Study II, the epilepsy variables, onset age, freedom from seizures or not during the period before assessment and the number of anti-epileptic drugs that the children received, were related to the results of the assessments. For Study III, the type of seizures/syndrome, partial/generalised/unclassifiable, and the type and site of EPFA for each child were related to the speech and language and neuropsychological assessments.

**Study IV**

*Retrospective investigation*

Medical records were reviewed by the author of this thesis (GRHS) and one of the authors of this study (MK). The reviews related to the age at the first seizure, the seizure type or epileptic syndrome, the drug treatments and their effect, other medical examinations and a family history of speech and language delay or disorder, or seizures or of neuropsychiatric disorder. In addition, records from speech and language assessments and therapy were reviewed by the author of this thesis (GRHS), while records from the psychological assessments were assessed by one of the authors of this study (GV). The course of language development and general development was registered. The recordings of the first EEGs were
read retrospectively by one of the authors, a specialist in neurophysiology (AH). The age at the first EPFA, the type of EPFA, the localisation and amount of EPFA were registered.

**Follow-up assessments**

EEG recordings during sleep were performed in 17 of the 19 available participants at follow-up. In two participants, the recordings were only performed in the awake state. The recordings were read by the same author as above (AH). Speech and language were assessed by the author (GRHS) when it came to oral motor ability, articulation, expressive and receptive lexicon and grammar, phonologically restricted word retrieval and spelling. In addition, auditory ability was assessed in terms of perception of speech in noise, auditory attention and ear preference. Pragmatic ability was rated using a parental questionnaire. Neuropsychological assessments included tests of intelligence, verbal functions, visuospatial and visuoconstructive functions, attention span and working memory, processing speed, learning and memory of words and figures and lateral preference. They were performed by one of the authors (GV).

**The assessment battery**

In all four studies, a number of tests and assessment batteries were used. Tests which have norms for Swedish-speaking individuals were chosen when available; some are Swedish versions of tests originally designed for English-speaking individuals. In each study, a few additional tests were used. For an overview of the test instruments used in the four studies, see Table 3.

**Speech and language assessments**

Tests produced for Swedish-speaking individuals were the Fonemtest (Hellqvist, 1984) and *Nya Lundamaterialet* (Lumat) (Holmberg and Stenkvist, 1978), which are picture naming tests for phonology, the latter also for grammar (Study I). A phonological repetition protocol for all Swedish phonemes in different positions in single words and some consonant combinations in sentences (Jennische and Sedin, 1993) was used in Studies II and III. The Rapid Confrontation Naming Test (RCFN) (Eklund, 1996) (Studies I, II, III) is a Swedish test for fast picture naming. The Språkligt impressivt test (SIT) (Study I) is a Swedish test for sentence comprehension (Hellqvist, 1989). Subtests of the *Nelli*, neurolinguistic assessment battery, (Holmberg and Sahlén, 1986) were used in all four studies. For mixed expressive/receptive/communication assessments of very young children, the KOLTIS assessment battery (Rejnö-Habte Selassie, 1998) was used (Study I). For tests of spelling (Study IV), the DLS-test (Diagnostiskt läs och skrivmaterial) (Järpsten, 1997) was used with younger participants and the LS-test (Läs- och skrivtest för högstadiet och gymnasiet) with the older participants (Johansson, 2004). A letter naming task was also administered to assess emerging literacy (Studies II and III) (Table 3).

The other test instruments were Swedish versions of tests designed for English-speaking individuals: The Illinois Test of Psycholinguistic Abilities (ITPA), (Kirk et al., 2003) (all studies), the Peabody Picture Vocabulary Test (PPVT) (Dunn and Dunn, 2001) (all studies), the Boston Naming Test (Study IV), the Test for Reception of Grammar (TROG) (Bishop,
1998a) (Studies II, III) and the second version TROG 2 (Bishop, 2003) (Study IV) (Table 3). Norms were available for children (Holmberg and Bergström, 1996) for oral motor ability assessed according to the Nelli test battery (Holmberg and Sahlén, 1986) and for adults (Hartelius and Svensson, 1990). The FAS-test for word retrieval within a restricted phonological category (f, a or s) used norms for children from the NEPSY (Korkman et al., 2001) and for adults from Tallberg et al. (Tallberg et al., 2008). Word retrieval under time limit was assessed using the NEPSY for children concerning animals and food (Korkman et al., 2001) and according to the procedure suggested by Tallberg et al. for adults concerning animals (Tallberg et al., 2008) (Table 3).

Test translation
For school-age children and young adults, there is a shortage of available tests for Swedish-speaking individuals and, in particular, a test for expressive grammar was missing for this study. A translation from English was therefore made of a few of the subtests in the Clinical Evaluation of Language Fundamentals 3 (CELF 3), which has norms up to adult age for English-speaking individuals (Semel et al., 2000). The test items were translated into Swedish and then back-translated into English by a native English speaker familiar with both Swedish and English vocabulary and culture, in order to assure a correct and meaningful translation. The Sentence Assembly subtest was used to assess syntactic ability in older participants in Study IV (Table 3).

Auditory assessments
In Studies II, III and IV, a computerised Dichotic listening (DL) test of consonant-vowel (CV) syllables in two different versions was used, one to assess simultaneous auditory attention, level of perception and auditory discrimination (Hugdahl et al., 1986), the other for forced attention (Hugdahl and Andersson, 1986) and both for language laterality. A laterality index was registered as right ear advantage (REA), left ear advantage (LEA) or no ear advantage (NEA). In Study IV, a speech-in-noise test of 50 phoneme-based single syllable words and a frequency-weighted unmodulated random noise was performed in order to assess the perception of speech against a background noise (Magnusson, 1995) (Table 3). Norms for adults were already available and were produced for children for this study by students of audiology (Granström and Ilstedt, 2009).

Neuropsychological assessments
For an overview of the neuropsychological tests used in the four studies, see Table 3. Griffiths’ Developmental Scales (Alin-Åkerman and Norberg, 1991) had been used in Study I and the Wechsler scales for different ages were used in all four studies (WPPSI-R, WISC-III, WISC-IV, WAIS-III) (Wechsler, 1999, Wechsel, 1999, Wechsler, 2007, Wechsler, 2003) for assessments of intelligence, verbal, visuospatial and visuoconstructive functions, attention span, working memory and processing speed. In Studies II and III, additional visuomotor functions were assessed. The results were given as FSIQ, VIQ and PIQ scores and, in Study IV, also as a Working Memory Index (WMI) and Processing Speed Index (PSI). For memory, attention and executive function, the memory subtests and the attention and executive subtests from the NEPSY neuropsychological test battery (Korkman et al., 2001) were used in Studies II and III. In Study IV, learning and memory of words and figures was assessed using the Rey-Osterreith Complex Figure (Rey, 1941) and the Luria verbal learning test.
Table 3. Test instruments used in the four studies.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Tests</th>
<th>Study</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral motor function:</td>
<td>Nelli, I, II, III, IV</td>
<td></td>
</tr>
<tr>
<td>Articulation:</td>
<td>Nelli, I, II, III, IV</td>
<td></td>
</tr>
<tr>
<td>Phonology:</td>
<td>Koltis, Fonemtest, Nya Lundamaterialet Protocol for word/sentence repetition FAS-test</td>
<td>I, II, III, IV</td>
</tr>
<tr>
<td>Grammar:</td>
<td>Koltis, ITPA: phoneme blending, TROG 2</td>
<td>I, II, III, IV</td>
</tr>
<tr>
<td>Vocabulary:</td>
<td>Koltis, ITPA: phoneme blending, PPVT</td>
<td>I, II, III, IV</td>
</tr>
<tr>
<td>Vocabulary:</td>
<td>Nelli, ITPA: auditory analogy, RCFN, rapid picture naming, Nepsy/Tallberg: word retrieval under time limit BNT: picture naming</td>
<td>I, II, III, IV</td>
</tr>
<tr>
<td>Auditory memory and learning:</td>
<td>Nelli, ITPA: digit span, Word-list learning tasks, Luria: verbal learning (young participants), Claeson-Dahl learning test (older participants)</td>
<td>I, II, III, IV</td>
</tr>
<tr>
<td>Auditory ability:</td>
<td>Dichotic listening: Speech-in-noise perception</td>
<td>II, III, IV</td>
</tr>
<tr>
<td>Cognitive functions:</td>
<td>Griffiths’ Mental Developmental Scales, WPPSI-R, WISC III</td>
<td>I, II, III, IV</td>
</tr>
<tr>
<td></td>
<td>WPPSI-R, WISC III, WISC-IV, WAIS-III</td>
<td>II, III, IV</td>
</tr>
<tr>
<td></td>
<td>Nepsy, Rey Osterreith Complex Figure</td>
<td>II, III, IV</td>
</tr>
</tbody>
</table>

(Christensen, 1974) for the youngest children and the Claeson-Dahl learning test (Nyman, 1999) for the older participants (Table 3). In addition, handedness was assessed.

**Pragmatic ability**

In Studies II and III, pragmatic ability was assessed with the Swedish version of the Children’s Communication Checklist (CCC) parental questionnaire (Bishop, 1998b) and, in Study IV, the Asperger Syndrome Screening Questionnaire (ASSQ) (Ehlers et al., 1999), which aims to investigate signs of pragmatic problems within the autism spectrum, was used (Table 3).
**Statistical methods**

All the studies comprised a relatively small study group which was not normally distributed. As a result, non-parametric methods were used in all the analyses, for both ordinal scale and continuous variables, except when comparing the neuropsychological test results with the normative data (Study II), where the T-test of means was used. The non-parametric tests were the Mann-Whitney U test for group comparisons (Studies II-IV), Fisher’s exact test for dichotomous variables (Studies I and II) and the Test for Trends in Contingency Tables for comparisons between groups of the speech and language symptoms with respect to the FSIQ level (Study I) and to compare parents’ education (Study II). In addition, the Test Based on Binomial Distribution was used to compare the percentage of diagnoses of epilepsy with that of the general population (Study I). A p-value of 0.05 was considered significant and all the tests were two-tailed (Altman, 1991).

**Reliability**

For reliability measures, 21% of the original assessments of expressive subtests of Studies II and III were re-assessed. The intra- and inter-rater agreements between the original assessments and the re-assessments made by the same SLP and an independent SLP were made with randomly ordered audio-recordings of all 50 children. Percentage agreement for each measurement and for all measurements together was registered. Agreement on measures of time spent on the Rapid Confrontation Naming test (RCFN) was evaluated using the Spearman rank-order-correlation coefficient ($r_s$). Percentage agreement ranged from 0.73 to 1.0 and the average inter-rater agreement was 0.85 and intra-rater agreement 0.95. When measuring time in the RCFN test, the correlation for intra-rater agreement was $r_s 0.995$ and for inter-rater agreement $r_s 1.000$.

**Analysis if individual profiles of dysfunction**

**Study III**

An analysis of speech, language and auditory dysfunction in individual children with epilepsy was performed. Low scores for the subtests were identified on the basis of the stanine value 1 or a result corresponding to the 10th percentile value and were defined as low scores. For tests in which no Swedish norms were available, the scores that corresponded to the lowest 10th percentile values of the reference group in the different measures were used as a norm. The scores at this level or lower were defined as low values. Low scores in assessments were related to the type of epilepsy, seizure localisation, IQ levels and ear advantage in each child.

**Study IV**

To define the degree of dysfunction, the test scores were used to classify the results into four categories: normal, a mild, a moderate or a severe deviation from normal. The stanine or percentile values or a z-score based on the mean value for the age group of a test were converted into SD scores. In order to validate the classifications of speech and language measures, possible relationships between the speech and language tests and VIQ were evaluated by the Spearman rank-order-correlation coefficient ($r_s$). In addition, a global speech and language ability scale including eight categories (A-H) was created, based on the median value of all assessments (Svensson, 2001), in order to obtain an overall view of the ability of each individual.
Analysis of prognostic indicators (Study IV)
Possible prognostic indicators were identified by evaluating the relationship between the test scores and various medical, developmental and EEG variables using the Spearman rank-order-correlation coefficient ($r_s$). An $r_s$ of more than 0.46 indicates a statistically significant relationship for the sample size of 19 individuals.

Ethics
All the studies were approved by the Ethics Committee at the Sahlgrenska Academy at the University of Gothenburg.
RESULTS

Study I

Speech and language dysfunction
Four different combinations of speech and language dysfunction were found. In three children, only expressive language problems were found, in seven, a combination of pure expressive language and oral motor problems. In nine, only expressive and receptive language problems were found and, in nine, both expressive/receptive language problems and oral motor problems. When the children were grouped across language subgroups and across oral motor/no oral motor problems, 36% were found to have pure expressive language problems, 64% had combined expressive/receptive language problems and a total of 57% had additional oral motor problems. Gender differences were found, with girls predominating in expressive/receptive problems and boys in oral motor problems, although the differences did not reach statistical significance (Table 4).

Table 4. Patterns of speech and language dysfunction in 28 children with severe DLD.

<table>
<thead>
<tr>
<th>Type of dysfunction</th>
<th>Participants</th>
<th></th>
<th></th>
<th>Overlapping number</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Males</td>
<td>Females</td>
<td>Total number</td>
<td></td>
</tr>
<tr>
<td>Expressive language problems</td>
<td>8</td>
<td>2</td>
<td>10 (36%)</td>
<td>7 with oral motor problems</td>
</tr>
<tr>
<td>Expressive-receptive language problems</td>
<td>9</td>
<td>9</td>
<td>18 (64%)</td>
<td>9 with oral motor problems</td>
</tr>
<tr>
<td>Oral motor problems</td>
<td>12</td>
<td>4</td>
<td>16 (57%)</td>
<td>16, see above</td>
</tr>
<tr>
<td>No oral motor problems</td>
<td>5</td>
<td>7</td>
<td>12 (43%)</td>
<td>3 with expressive language problems, 9 with expressive/receptive language problems</td>
</tr>
<tr>
<td>Total number</td>
<td>17</td>
<td>11</td>
<td>28</td>
<td>28</td>
</tr>
</tbody>
</table>

Cognitive profiles
Sixty per cent of the children had an FSIQ of > 85. Psychological profiles revealed that all patterns of discrepancy between VIQ and PIQ were present. Problems with attention and/or general motor ability was found in 71%, which is significantly higher than in the general population (Gillberg et al., 1982). Motor problems alone were rare, while attention problems dominated.

Epilepsy, EEG and etiological factors
The percentage of EEG abnormalities – 55% – was higher than that found in the general population (2.7%) (Eeg-Olofsson et al., 1971). Two children had EPFA in the left temporal region, two in the left centro-temporal region and two had bilateral EPFA, while four children had low-frequency activity. In 18%, a diagnosis of epilepsy had been established, a significantly higher percentage than in the general population (0.5%) (Forsgren et al., 2005). The diagnosis was LKS in one, two had SPS, one CPS and one infantile seizures. Preterm birth was found in two children. One child was small for gestational age, two had neonatal
seizures and, the mother of one child had eclampsia in pregnancy and the child had neonatal pneumonia

**Co-occurring factors**

Co-occurrence was found between a few or several of the speech, language, psychological and etiological factors in almost all the children. The children with mixed expressive/receptive problems had a lower FSIQ than those with pure expressive problems. The other IQ variables that differed between the groups were: a profile with VIQ < PIQ was more common in those with pure expressive language problems than in those with mixed expressive-receptive problems, a profile with VIQ = PIQ was more common in mixed expressive-receptive problems and a profile of PIQ < VIQ was more common in those with oral motor problems than in those without. Etiological factors differed between the groups in the following pattern. Attention problems were more common in those with expressive-receptive problems than in those with only expressive problems. EEG abnormalities were more common both in those with expressive-receptive problems compared to those with only expressive problems and in those with oral motor problems compared with those without oral motor problems. Additionally, heredity for speech and language disorders was more common in those with oral motor problems than in those without.

**Studies II and III**

**Group comparisons**

*Speech, language and auditory assessments (Studies II and III)*

Statistically significant group differences, lower for the epilepsy group, were found in Oral Motor Positions, Oral Motor Movements, Articulatory Positions, Letter Naming, Phoneme blending and Word retrieval. In the picture naming test (RCFN), the children with epilepsy were significantly slower but did not give more incorrect responses (Table 5). In Articulatory Patterns and Phonology and in Story retelling measured with the Nelli subtest, there were no significant differences between the groups, There were also no group differences in expressive or receptive grammar, receptive vocabulary or auditory analogy measured with ITPA nor in pragmatic measure according to parent ratings. Significant group differences were also found for the ITPA subtest of auditory short-term memory (digit span) and in the attention measure of the DL test (Table 5). In three other measures of the DL test, they obtained significantly lower scores than the reference children: the level of auditory perception of vowels presented to the right ear, the discrimination of consonants presented to the right ear and ear preference for vowels. This indicated a less dominant left hemisphere for the analyses of speech sounds (Table 5).

*Neuropsychological assessments (Study II)*

The children with epilepsy obtained significantly lower scores in FSIQ and PIQ than the reference group, but not in VIQ. Two children in the study group were diagnosed with an FSIQ of < 70. The children with epilepsy were also significantly slower when performing the NEPSY subtests of visual attention, which call for fast performance, and they had more difficulty with impulse control, standing as a statue, and in the Narrative Memory NEPSY.
Table 5. Significant group differences in Study II.

<table>
<thead>
<tr>
<th>Variables</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral motor positions</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Oral motor movements</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Phoneme blending</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Letter naming</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Word retrieval</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Picture naming, time</td>
<td>0.001</td>
</tr>
<tr>
<td>Digit span</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>DL auditory attention</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>DL auditory perception of vowels</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>DL consonant discrimination</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>DL ear preference, vowels</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Visual attention, time</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Impulse control (statue)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Narrative memory, total</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Free recall</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>FSIQ</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>PIQ</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

Individual profiles of dysfunction (Study III)

Speech and language
Low scores, indicating a dysfunction, were found in all speech and language subtests and all the children with epilepsy had low scores in at least one measure. In the domain of oral motor ability and articulation, 95% obtained low scores in at least one of the subtests. In the domain of phonology and literacy, 70% were found to have low scores in one or several tests. In the domain of word retrieval and narrative ability, 60% had low scores in at least one assessment, while, in the domain of grammar and semantics, 40% obtained low scores. In the pragmatic domain, 15% were reported to have difficulty, whereas, in the auditory attention and memory domain, 65% obtained low scores.

Speech and language profiles and IQ levels (Studies II and III)
No particular speech and language profile could be associated with a specific IQ profile. The two children with an FSIQ of < 70 obtained low scores in all the domains. They had previously been assessed as having normal cognitive development, indicating that the epilepsy may have resulted in hampered development. Despite low scores in speech and language measures, 17 of 20 children had a higher VIQ than PIQ, with a VIQ of > 85 in all but two.

Test results in relation to epilepsy variables

Group comparisons (Study II)
Significantly poorer results were obtained by the children who received more than one AED compared with those with only one drug in the following measures: Auditory Analogy, speed in picture naming (RCFN) and also with the Block Design (WPPSI-R) performance subtest (Table 5). No statistically significant group differences were found in the other NEPSY subtests compared with normative data.
and the Design Fluency and Narrative Memory NEPSY subtests. Onset age was only related to the Object assembly and Picture completion NEPSY subtests and there were no differences between children with different types of epilepsy, or between children who were seizure free and those who were not.

*Individual profiles in relation to type of epilepsy (Study III)*

Low scores in speech and language measures were found in partial, generalised and unclassified epilepsy. Children with partial epilepsy with a left-hemispheric focus had the most extensive speech and language dysfunction, in all of them including all the language domains except that of pragmatic ability. In children with partial epilepsy with some other localisation, low scores were found in phonology/emerging literacy in eight of ten, while no dysfunction was found in the domain of grammar and semantics. In children with generalised epilepsy, the dysfunction was less uniform. One child with a suspected LKS had low scores in all expressive measures but not in verbal comprehension. There was no clear pattern of association between epilepsy variables and ear preference. Both LEA and NEA were found in all types of epilepsy, reflecting undeveloped language laterality (Table 6).

*Table 6. Dysfunction within different domains of speech, language, communication, auditory attention and memory and left ear advantage or no ear advantage in children with different types of epilepsy and different localisations of epileptiform activity in Study III.*

| EEG type/site of EPFA | Oral motor ability/articulation | Phonology/emerging literacy | Grammar/semantics | Word retrieval/narrative ability | Pragmatic ability | Auditory attention/memory | Left ear advantage | No ear advantage |
|-----------------------|---------------------------------|-----------------------------|-------------------|---------------------------------|------------------|---------------------------|------------------|----------------|}
| Partial/frontal | 1/1/1/1 | 1/1/1/1 | 1/1/1/1 | 1/1/1/1 | 1/1/1/1 | 1/1/1/1 | 1/1/1/1 | 1/1/1/1 |
| Partial/EEG normal | 2/2/2/2 | 2/2/2/2 | 2/2/2/2 | 2/2/2/2 | 2/2/2/2 | 2/2/2/2 | 2/2/2/2 | 2/2/2/2 |
| Generalised/myoclonic/astatic | 1/1/1/1 | 1/1/1/1 | 1/1/1/1 | 1/1/1/1 | 1/1/1/1 | 1/1/1/1 | 1/1/1/1 | 1/1/1/1 |
| Unclassifiable/LKS? | 1/1/1/1 | 1/1/1/1 | 1/1/1/1 | 1/1/1/1 | 1/1/1/1 | 1/1/1/1 | 1/1/1/1 | 1/1/1/1 |

N=number of children, LKS=Landau Kleffner syndrome

**Study IV**

**Medical history and EEG features**

Seizures had not been observed in four of the participants and were rare in the majority of the remaining fifteen. All the participants but two had been treated with AEDs or corticosteroids and a positive effect was reported with corticosteroid treatment in the majority of those that
were treated for speech, language, behaviour or sleep patterns. Normal brain morphology was present in all but one of the 14 who had been investigated with CT or MRI. A family history of either speech delay or reading and writing disability, of seizures or of ADHD or autism spectrum disorders was found in the majority. All the participants had a history of spike or spike-and-wave activity. Temporal lobe EPFA was found in twelve and the activity was extended over wide brain areas in all of them. The remaining seven participants had EPFA only in brain areas other than the temporal lobe. Fourteen participants had abundant EPFA of non-REM sleep. In the other participants, the amount of EPFA varied. At follow-up, the EEGs were normal in ten participants, while nine participants still had EPFA, although it was not abundant.

**Developmental characteristics**

General developmental milestones were normal in fourteen of the participants, while they were delayed in five. Early speech and language development was normal in six participants, while 13 were delayed when it came to early language milestones. Later deterioration in language was seen in nine participants. Consequently, three different patterns of language development were discussed:

1. Normal initial language development and later stagnation or deterioration of language – definite LKS
2. Late initial language development and later stagnation or deterioration of language – probable LKS
3. Late initial language development and continued slow language development – possible LKS or epileptic language disorder – ELD

**Results of follow-up assessments**

*Speech, language, communication and auditory ability*

Only three participants were evaluated as normal (A) on the global language scale, with dysfunctions that were only minor or found in a few of the assessments. The other participants showed dysfunction in several of the assessments. Both expressive and receptive language dysfunction was found in fourteen participants. A higher percentage had dysfunction of expressive rather than receptive grammar. On the other hand, a higher percentage had dysfunction of receptive rather than expressive vocabulary. A spelling dysfunction was found in half the participants. In addition, oral motor dysfunction was found in half the participants, while stuttering was observed in four. Nearly half the participants had results in the ASSQ questionnaire indicating a pragmatic dysfunction. Dysfunction of auditory perception of speech in noise was found in the majority. Moreover, all the participants had poor auditory attention ability measured with the dichotic listening (DL) test. The DL test also indicated a right or no hemispheric dominance for language in almost half the participants.

*Cognitive ability*

Seven participants had normal intelligence (IQ>85), four had borderline intelligence (IQ 70-84), six had a mild mental retardation (IQ 50-69) and two a severe mental retardation (IQ<50). An uneven profile of a lower VIQ than PIQ with a large difference in IQ points was found in six participants. Variations were found between the probands in the Processing Speed Index (PSI) and the Working Memory Index (WMI) and in figurative and verbal learning, as well as in figurative and verbal memory.
Follow-up assessments in relation to developmental profiles
Diverse outcomes were seen at follow-up. Participants were found at all IQ levels and all language levels with different combinations. When comparing the results of the follow-up assessments for the children with the three different patterns of language development, no obvious differences could be detected between them.

Prognostic indicators
The main prognostic indicator of a poor prognosis was the amount of EPFA, which correlated with speech and language measures and with neuropsychological measures. Furthermore, a family history of seizures correlated with a few of the test results.

Summary of results from the four studies
Study I was a retrospective study in which earlier assessments were investigated. In Studies II-IV, comprehensive assessment batteries were used for investigating speech, language, auditory and communicative ability, together with neuropsychological investigations. The main results of the assessments of the four studies are shown in Table 7.

Table 7. Main results of the assessment of the four studies.

<table>
<thead>
<tr>
<th>Study I</th>
<th>Study II</th>
<th>Study III</th>
<th>Study IV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Epilepsy and EPFA more common in children with language disorder than in the normal population</td>
<td>Language dysfunction more common in children with epilepsy than those without</td>
<td>Language dysfunction found in all types of epilepsy</td>
<td>Language dysfunction in both LKS and ELD at follow-up</td>
</tr>
<tr>
<td>Both pure expressive language dysfunction and mixed expressive-receptive language dysfunction</td>
<td>Mainly expressive language dysfunction</td>
<td>Mainly expressive language dysfunction</td>
<td>Mainly mixed expressive-receptive language dysfunction</td>
</tr>
<tr>
<td>Oral motor dysfunction common</td>
<td>Oral motor dysfunction common</td>
<td>Oral motor dysfunction common</td>
<td>Oral motor dysfunction in a few</td>
</tr>
<tr>
<td>Auditory attention difficult in many</td>
<td>Auditory attention affected</td>
<td>Auditory attention and perception affected</td>
<td>Auditory attention affected</td>
</tr>
<tr>
<td>No pragmatic dysfunction</td>
<td>No pragmatic dysfunction</td>
<td>No pragmatic dysfunction</td>
<td>Pragmatic dysfunction in some participants</td>
</tr>
<tr>
<td>No MR but borderline IQ in many</td>
<td>MR found in two of twenty participants</td>
<td>MR found in two of twenty participants</td>
<td>Participants both with and without MR</td>
</tr>
<tr>
<td>All patterns of discrepancy between VIQ and PIQ</td>
<td>PIQ&lt;VIQ</td>
<td>PIQ&lt;VIQ</td>
<td>VIQ&lt;PIQ in some participants</td>
</tr>
</tbody>
</table>
DISCUSSION

The main findings in the four studies will be discussed in the first three sections and a general discussion of the findings from different angles will then follow.

Epilepsy and EPFA in language disorders

Some authors have previously pointed out that subclinical epilepsy in children with language disorder is often ignored and that the lack of controlled studies of children with speech and language disorders may deny them medication as a treatment strategy (Parry-Fielder et al., 1997, Rapin, 1998). Our results from Study I, revealing a higher percentage of diagnoses of epilepsy among children with developmental language disorder, also indicate that this is often a neglected problem in children with language disorder. In some of the children in our study, the epileptic problem had not been detected before they had an EEG registration for suspected EPFA as an important factor contributing to their language disorder. Picard and co-workers also found paroxysmal EEG in 50% of children with language disorder, particularly in those with a receptive language disorder (Picard et al., 1998). Two-thirds of the children in our study had mixed expressive-receptive problems and they had more EEG abnormalities than those with a pure expressive dysfunction. A developmental defect in neural organisation may be concealed behind both the EEG abnormalities and the speech and language dysfunction. Furthermore, EPFA without seizures was more common in the children with language disorder in Study I than in the general population. Several authors have previously addressed this phenomenon (Gordon, 2000, Balaban-Gil and Tuchman, 2000, Wheless et al., 2002). However, as EPFA is also relatively common in the general population, even in those without clinical symptoms, there is uncertainty regarding the interpretation of this phenomenon and treatment is usually not recommended. However, our findings highlight the importance of being more observant of possible epilepsy and EPFA in children with language disorder.

Speech and language dysfunction in childhood epilepsy

Few previous studies have addressed the question of whether children with epileptic syndromes other than those within the Landau Kleffner spectrum might run the risk of developing speech and language disorders. Expressive language and oral motor difficulties were found in the study group in Studies II and III, consisting of children with various epileptic syndromes and no previously known additional developmental dysfunctions. However, receptive language and verbal intelligence were not affected. It was not surprising to find speech and language dysfunction in children with epilepsy, as our results from Study I pointed towards possible speech and language difficulties in children with epilepsy. Moreover, Parkinson found a high incidence of language disorder in children with focal epilepsies (Parkinson, 2002) and our results are also confirmed by a recent study by Caplan and co-workers (Caplan et al., 2009). They found more problems in all language areas in children with CPS and absence epilepsy than in a matched control group. The analysis of individual profiles in our study group also revealed that dysfunction was present in all speech and language domains to a varying degree, but pragmatic ability was only affected in a few.
However, contrary to the findings of Caplan and co-workers, oral motor ability/articulation was the most affected domain in our study.

**Diagnostic boundaries or a continuum of LKS-related disorders?**

A history of sleep-activated EPFA and language disorder in childhood was common to all the participants in Study IV. Three different developmental patterns were found, which, according to the prevailing diagnostic constructs, would result in different clinical diagnoses, such as LKS and developmental language disorder (DLD). However, in clinical practice, a differential diagnosis is not always easily obtained when sleep-activated EPFA is present. One variant was clearly compatible with a diagnosis of LKS, as the participants had experienced deterioration and some even a loss of language, against a background of normal initial language development. The other two patterns of language development were more difficult to map onto a recognised diagnostic entity. In both patterns, initial language development was delayed, in one of them with a clear deterioration of language, designated as probable LKS, and in the other with a continued slow development, here designated as possible LKS or epileptic language disorder, ELD. Accordingly, in earlier studies, the idea has been put forward that these conditions may be related, regardless of the developmental pattern (Mariën et al., 1993, Deonna and Roulet-Perez, 2005). Mariën suggested a developmental, an acquired and a mixed variant of LKS.

Furthermore, there was no obvious difference in our study between participants with the different developmental patterns relating to the speech and language profile or the long-term outcome for speech, language or other cognitive variables. It has been suggested that the onset age of LKS occurs after the first period of language acquisition. However, if the onset age is very early, the clinical symptom of language loss or deterioration is never seen and early language delay will be the result. Instead, the loss of language functions in late onset is clear evidence of the way EPFA may affect language, but the possibility that similar effects may be present in cases of early onset should not be overlooked. A diagnosis based on the developmental pattern is therefore an artificial construct that may obscure rather than clarify our understanding of these groups of related conditions. The suggested designation of epileptic language disorder (ELD) for the variant with very early onset may therefore be helpful in clarifying the relationship to an LKS spectrum of disorders. Seven of the participants in Study IV were also included in Studies I, II or III, with a dysfunction in all expressive and some receptive language measures, and they are examples of the variability of developmental patterns in LKS-related epilepsy conditions. It is reasonable to assume that variables other than developmental patterns may influence speech and language ability and long-term outcome to form a diagnostic entity and that they may be epilepsy variables or other variables of brain function or morphology. Moreover, other risk factors, such as heredity and perinatal events, may play a role.

The following sections contain a general discussion of the findings from different angles.
Epilepsy variables and speech and language dysfunction

The epilepsy variables that influenced some results of speech, language and other cognitive ability in Study II were AED polytherapy and age at epilepsy onset, which is in line with previous studies (Bulteau et al., 2000, Elger et al., 2004). However, contrary to the findings of Bulteau and co-workers, we were unable to find any influence of epilepsy variables on IQ levels. This may be due to the fact that our study group consisted mainly of children within the normal range of cognitive level. Several authors have found language problems in children with partial epilepsies (Cohen and Le Normand, 1998, Parkinson, 2002, Caplan et al., 2009). However, in the recent study by Caplan and co-workers, language problems were also found in generalised epilepsies, particularly in absence epilepsy. This confirms our findings of language dysfunction even in generalised, including absence epilepsy, although they were less specific than in partial epilepsy. Language dysfunction in absence epilepsy is therefore probably an underestimated problem. It is reasonable to believe that the children who received more than one anti-epileptic drug were those with a more serious form of epilepsy and this could explain the poorer performance in these children.

In Study II, more obvious dysfunctions were found in children with partial epilepsy, particularly of the left hemisphere. The same pattern was seen in Study I, as left-hemispheric involvement was present in all but one of the children with seizures, in the majority in the temporal lobe, indicating that the EEG abnormalities may have had some impact on the speech-language symptoms. In Study III, it was found that partial epilepsy was associated with dysfunction in phonology and emerging literacy, while left-hemispheric epileptiform activity was associated with more widespread language dysfunction. This was expected, since focal seizures in areas subserving speech and language are expected to have consequences for speech and language (Deonna and Roulet-Perez, 2005). In particular, verbal memory is thought to be affected in temporal lobe epilepsy (Besag, 2002) and, according to Cohen and Le Normand, seizures of a left frontal focus may affect expressive language functions (Cohen and Le Normand, 1998).

For children with disorders within the LKS spectrum, Halász and co-workers pointed out in their study that the epilepsy variables which influenced language most were the localisation of EPFA to left temporal regions and the amount of EPFA (Halász et al., 2005). Accordingly, in our Study IV, the amount of EPFA affected the outcome most, but we were unable to find a correlation with localisation, as the EPFA extended over wider brain areas in the majority. The typical trait in this patient group was abundant sleep-activated EPFA, but few seizures. It is obvious that this pattern of seizure and epileptiform activity – little and silent but often – acts like the continuously falling drops of water on a stone to create a carving. (cf. the Latin proverb: *gutta cavat lapidem, non vi sed saepe cadendo*, “The drop hollows out the stone by frequent dropping, not by force”). The silent and often unnoticed EPFA prohibits cerebral networks from consolidating, particularly when it is abundant. Remedial effects of reorganisation by brain plasticity cannot occur in cases where there is intermittent disturbance and EPFA may therefore be more harmful to highly differentiated functions than brain injury.
**Heredity**

Many researchers have demonstrated that heredity is an important factor behind language disorder. This was also found in our study of children with language disorder (Study I) and, according to our tentative findings, this may be particularly true for those with oral motor problems and for those with EEG abnormalities or epilepsy. According to Bishop, there may be some general motor immaturity behind this heredity (Bishop, 2002). However, as stated by Grigorenko, the details of the way genetic factors exert their influence on speech and language acquisition are yet to be determined, as many different genes are involved and may be linked to various manifestations of a language disorder (Grigorenko, 2009). In our study of children with LKS-related conditions (Study IV), a family history of language disorder, of seizures or neuropsychiatric disorder was found in the majority. This clearly points towards the concept of LKS as a genetically based dysfunction, presented by a number of authors (Deonna and Roulet, 1995, Deonna and Roulet-Perez, 2005, Halász et al., 2005, Rudolf et al., 2009). According to Rudolf and co-workers, genetic factors may play a role in cell migration during cerebral maturation, causing polymicrogyria in perisylvian regions (Rudolf et al., 2009). Heredity for epilepsy, in particular, has been suggested as an important factor behind the focal sharp-wave activity in LKS (Doose et al., 1997). Our findings confirm this suggestion, as some of our results were related to a family history of seizures.

**Cognitive function**

Language disorder can be found in children, regardless of their intelligence levels. Studies of childhood language disorder are, however, frequently performed on children without MR, in order to investigate the language disorder without the influences of additional intellectual dysfunction. This was also done in our Studies I-III. Although the study group in these studies was made up of children without MR, several participants in Study I had borderline intelligence. This is in line with Westerlund and co-workers, who found different cognitive levels among children with language disorder (Westerlund et al., 2002), and with Kamhi, who argued that the general IQ level is not important when determining whether or not a language disorder is present (Kamhi, 1998). The LKS-spectrum group in Study IV, on the other hand, also included participants with MR and different IQ levels were found in both the LKS and the ELD patterns of language development.

The expected pattern in children with language disorder with a lower VIQ than PIQ was found in some participants in Study I and in one-third of the participants in Study IV with a pronounced discrepancy. However, some children in Study I also displayed other profiles. A low PIQ is generally associated with perceptual and motor problems and, in children with a lower PIQ, oral motor problems were also common. The lower PIQ than VIQ, found in children with epilepsy in Study II, is in line with the results presented by Aldenkamp and co-workers in a series of studies of children with epilepsy (Aldenkamp et al., 1998, Aldenkamp et al., 1999). Moreover, processing speed was affected in the children with epilepsy in Studies II and IV, which points towards a general effect of EPFA on processing speed. This is in line with Svoboda, who suggested that children with epilepsy may have delayed reaction times (Svoboda, 2004).
Attention and motor ability

In all four studies, attention problems were common: in the children with severe developmental language disorder (Study I), in those with various epileptic syndromes (Studies II and III) and to an even greater extent in those with sleep-activated EPFA (Study IV). This points towards a general effect of seizure activity on auditory attention. Some of the children with EPFA in Studies II and III also experienced minor absence seizures. According to Aldenkamp and co-workers, hyperactivity is uncommon in children with epilepsy, while inattentiveness is common (Aldenkamp et al., 2005). Attention problems have also been found by several authors to be common in children with language disorder (Westerlund et al., 2002, Miniscalco et al., 2006, Bruce et al., 2006). They were more common than general motor problems in the children with language disorder in Study I, which corresponds with the findings of Gillberg and co-workers concerning children with a different, but probably related, developmental dysfunction – minimal brain dysfunction (MBD, referred to today as ADHD) (Gillberg et al., 1982).

Difficulty with oral motor ability has not usually been reported in children with language disorder or epilepsy. These problems were prominent in the participants in all four studies. The question remains as to whether the children in Study I had CAS or general immature oral motor behaviour and whether these are different entities or just different degrees of the same condition. Dysfunction of oral motor ability and articulation, which was found in the children with epilepsy in Studies II and III, has been reported for children with BCECTS (Lundberg, 2004), but our findings indicate that these problems may be associated with epilepsy in general and not only linked to a specific syndrome. Negative side-effects of medication on oral motor ability could be the cause of these difficulties (Svoboda, 2004). Our findings of such difficulties also in some of the children within the LKS spectrum indicate an effect of the EPFA on oral motor ability and the activity may be related to localisation.

Stuttering was an additional observation in some participants in all the study groups. Stuttering has previously been reported both in children with LKS and in those with other epilepsy syndromes (Tütüncüoglu et al., 2002, Smith et al., 2006). As a result, in some children with severe and persistent stuttering, the possibility of an EEG abnormality as an underlying cause should be considered.

Auditory ability and language laterality

A central auditory processing disorder due to seizure activity in the auditory cortex has been suggested as the cause of the symptoms of LKS. Auditory agnosia is thought to be the extreme variant of this disorder (Rapin et al., 1977). The auditory dysfunction in our study group was shown to be more general, affecting auditory attention and perception of speech against background noise. This is in line with Svoboda, who reported difficulty with auditory discrimination against a noisy background in 24% of the children referred to the Kansas City Epilepsy Center for different types of epilepsy (Svoboda, 2004). However, language laterality, as measured with a dichotic listening test, was different or not developed in nearly half our participants in Study IV, suggesting a disturbance in the consolidation of cerebral networks subserving language and auditory ability. This was also true of the participants in
Studies II and III. Three of the dichotic listening measures indicated reduced laterality for the analysis of speech sounds. This is in agreement with Pisano and co-workers, who found a lack of hemispheric specialisation for speech sounds and impaired access to stored lexical knowledge in individuals with familial temporal lobe epilepsy (Pisano et al., 2005). Our children displayed difficulty with both the analysis of speech sounds and access to lexical store. Furthermore, in children with language disorder, particularly with the expressive subtype, Pecini and co-workers found the same pattern (Pecini et al., 2005), indicating similar mechanisms in children with language disorder without seizure activity.

**Word retrieval and memory**

According to Montgomery, both a deficient phonological working memory and a deficient functional working memory may play a role in poor word retrieval (Montgomery, 2003). Functional working memory refers to the capacity for the simultaneous storage and processing of information. Difficulty with expressive vocabulary was found in the majority of the children in Study I, more than with receptive vocabulary, which indicates difficulty retrieving the words from the mental lexicon. However, difficulty with word retrieval found in our study group of children with epilepsy (Studies II and III) indicated a slow speed for this cognitive computation in particular. Difficulty with narrative memory agrees with the findings of poor performance in the auditory short-term memory, which was also found in this study group. This is in agreement with Svoboda, who reported difficulty with short-term memory in 61% of children referred to the Kansas City Epilepsy Center (Svoboda, 2004). In Study IV, the participants performed better on word retrieval than on receptive vocabulary. The LKS group did not display a particular dysfunction of word retrieval but had a more general dysfunction of the stored lexicon. As adults and adolescents, they had mastered a certain vocabulary and, even if it was small, they had no problems using their long-term memory to retrieve the words from the mental lexicon.

**Phonology and literacy**

A dysfunction of phonology and emerging literacy found in the majority of the children in Studies II and III indicated a potential risk of subsequent difficulty learning to read and write. This is in line with previous studies, which have shown that children with epilepsy may encounter dysfunction with both reading and writing (Papavasilou et al., 2005, Chaix et al., 2005). Particularly those with an epileptic focus originating from the temporal lobe have shown such dysfunctions. However, even the visuoperceptual difficulty that was found in our study group may have affected the results for letter naming and we found a dysfunction in children with a variety of epilepsy syndromes and localisations of seizure activity. A spelling dysfunction was also present in our study group in terms of LKS-spectrum disorders (Study IV). The results from both these study groups highlight the importance of careful assessments of reading and writing ability in children with epileptic conditions.

**Pragmatics**

Pragmatic dysfunction was not found in the majority of children from our Studies II and III. Moreover, the test of story retelling did not reveal any difficulty in narrative ability.
However, the obtained measure was the number of events that the participants remembered and re-told, often used in measuring narrative ability, but this type of measure may not reveal the true ability to construct a narrative. In another study, the results of the same assessment were re-analysed in terms of the macrostructure and the grammar of the story, according to Applebee and Stein and Glenn respectively (Applebee, 1978, Stein and Glenn, 1979). These analyses produced results that were consistent with those from our study, in that no group differences between the children with and without epilepsy were found (Dahlström and Mäki, 2009). On the other hand, as some of the children with epilepsy had a poor memory of the story, maybe due to minor absence seizures, a more detailed analysis of the story was difficult to perform. In contrast to our findings, pragmatic difficulties were found by Caplan and co-workers in children with both CPS and primary generalised epilepsy (Caplan et al., 2001). However, some of the participants in the LKS-spectrum group in Study IV displayed a dysfunction in the pragmatic domain, indicating a suspected ASD. This was expected, as other studies have found an increased risk of autism in LKS-spectrum disorders, particularly in those with CSWS (Tuchman, 2009).

**Prognosis**

Previous follow-up studies of children with LKS have indicated a variable outcome (Deonna et al., 1989, Paquier et al., 1992, Bølling and Sørensen, 2005). Some individuals are reported with total remission of the disorder, some with partial remission and some with continued aphasia (Duran et al., 2009). We also found a variable outcome, both in clear LKS cases and in those with the developmental variant of ELD. Particularly those with CSWS are reported to have a poor outcome (Robinson et al., 2001, Praline et al., 2003). The amount of EPFA was also the prognostic factor that was mostly related to a poor outcome in speech and language ability in our study. For the study group for language disorder (Study I), no long-term follow-up was performed. However, all the participants had a persistent and severe disorder at the time of inclusion. Some of them had EPFA and were followed up in Study IV, with a continued poor outcome.

**Treatment**

Speech and language intervention in children with severe language disorder is often intense. Special programmes, such as augmentative communication (Rejnō-Habte Selassie, 2000) and special school units (Conti-Ramdsen et al., 2001), are sometimes offered. However, in those with abundant EPFA, medication may be helpful as a treatment in addition to the speech and language intervention (Gordon, 2000, Binnie, 2003). This is particularly important, as the disruption of cerebral networks subserving speech and language functions due to abundant EPFA may lead to a permanent dysfunction in adulthood. Additional treatment with AEDs or corticosteroids may help to improve the result of speech and language intervention. However, as language has to be learnt gradually, no immediate result of the drug treatment should be expected. There are indications that medical treatment may aid the development of speech and language and also other cognitive functions (Buzatu et al., 2009), but no safe conclusions can be drawn from our study. Clinical practice is usually restrictive in terms of medication, as negative side-effects cannot be ruled out. In Study II, we found a poorer outcome for those participants with epilepsy who received more than one drug compared with those who
received only one drug. This may be an effect of the fact that those with more severe seizure activity received polytherapy.

**Gender aspects**

A predominance of boys compared with girls in language disorder is expected (Law et al., 2000). This also holds true for several other developmental disorders. A slight predominance of boys was also found in our study group for severe language disorder (Study I) and there was an even greater predominance of boys in terms of oral motor problems. This may be due to later general motor development in boys than in girls, while the predominance of girls in terms of receptive problems may be due to the earlier lateralisation of brain functions in girls that could make them more vulnerable to different kinds of exposure to harmful factors at an early age (Carlsson, 1994). These gender differences in symptoms are intriguing and require further study. In our study group for epilepsy (Studies II and III), the gender ratio was the opposite, with a predominance of girls found in those in the region-derived age cohort who were included in the study. This was surprising, but the fact that around half of all children in the cohort with epilepsy were excluded due to other developmental disorders may explain the unexpected gender ratio. Other developmental disorders may have been present in more boys than girls and, as a result, they were excluded from our study. In the LKS-spectrum group in Study IV, the gender ratio was equal. The severe forms of language disorder may therefore be more evenly distributed between the genders, particularly when seizure activity is present.

**Limitations**

All four studies contained small sample sizes, which calls for caution when interpreting the results. This resulted in a lack of statistical significance for many observed tendencies and possible correlations. The results therefore need to be replicated in studies of larger series of children. Two of the studies were also based on clinical case series, but the participants were recruited in such a way that most children with the studied disorders were reached. Furthermore, two of the studies contained retrospective data which were not uniform. Data of this kind are not possible to control and this has particularly affected Study I, which was only based on retrospective data. However, in this study, we did not make any calculations relating to details. The different ages of the children included in the study resulted in different manifestations of symptoms. However, the fact that the children were followed over repeated observations also revealed that clinical symptoms varied with age. Studies II and III were based on clinical series and the available medical data did not allow a more precise definition of the epilepsy syndromes and, as a result, a more precise analysis was not possible to perform. Furthermore, we studied the ability in preschool children, but the possible long-term consequences of epilepsy for speech and language and subsequent school achievements are still unknown. In Study III, we used a measure of simultaneous attention in dichotic listening that has previously not been tested and the results should therefore be interpreted with caution. In Study IV, the study group was heterogeneous in terms of age at follow-up and, as a result, the follow-up time varied. The participants were also heterogeneous in terms of the original diagnoses given and, due to the retrospective nature of the study, a more detailed analysis of their original diagnoses was not possible to perform.
SUMMARY AND CONCLUDING REMARKS

Language disorder in childhood is a complex phenomenon and its co-occurrence with other developmental conditions has not been fully described. This thesis presents four studies in which the relationship between speech, language and different epileptic conditions was studied. There is a lack of knowledge about the nature of this relationship and it is therefore important to obtain this knowledge in order to improve diagnostic procedures and intervention.

The main findings in the present thesis were:

- Epilepsy and epileptiform EEG activity is more common in children with severe developmental language disorder than in the normal child population

- In children with epilepsy but normal levels of intellectual ability, expressive language dysfunction is common

- A continuum of LKS-spectrum conditions with different onset ages is suggested, as no obvious or specific differences in speech and language profiles or long-term outcomes were found between children with sleep-activated epileptiform EEG activity, who had slow language development and those who had experienced a loss of already acquired language abilities.

Additional findings were:

- Speech and language dysfunctions in children with severe language disorder are seldom uniform. Both pure expressive and combined expressive-receptive disorder may be found, even in those with a persistent disorder

- Oral motor disability is often found both in children with language disorder and in children with epilepsy

- Language laterality is less developed in children with epilepsy or EPFA in language areas than in those without these conditions and auditory attention and perception are affected

- Language can be affected in children with all types of epilepsy, but those with focal features from the left hemisphere and temporal lobe or an LKS-spectrum condition have more pronounced difficulty than those with other types of epilepsy

- Epilepsy in children also affects other cognitive functions, particularly visuoperceptual ability, processing speed and working memory

- A permanent dysfunction of language and other cognitive abilities remains in some children with LKS-spectrum disorders, regardless of onset age
- The amount of epileptiform EEG activity and a family history of seizures affect the long-term outcome.

**CLINICAL IMPLICATIONS AND FUTURE RESEARCH**

The planning of intervention strategies for children with severe speech and language disorder, who display slow progress with speech and language intervention, is dependent on a clear understanding of the mechanisms behind the disorder. An EEG during sleep could add important information and should be considered in such cases, as a diagnosis within the LKS-spectrum could otherwise be missed. This would also create the chance for AED treatment for those who could benefit from medication. Speech and language intervention may lead to a better outcome when assisted by AED or corticosteroid treatment. Moreover, in children with other types of epilepsy, a thorough speech and language assessment should be performed when a dysfunction in speech and language areas is suspected. Assessments should include tests of oral motor ability, speech, language and auditory ability. For school children, assessments of literacy should also be performed. Speech and language intervention and extra support at school for reading and writing acquisition may be needed.

The gender differences in speech and language disorders, which were found in Study I, are intriguing and require further study. Further research on the role of epilepsy and EPFA in language disorder is also needed, as well as research focusing on speech and language ability in larger series of children with epilepsy and the long-term consequences for subsequent school performance. Research is also needed on speech and language ability in absence epilepsy. In LKS-related disorders, the effect on speech and language of corticosteroid and other drug treatments requires further study.
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REFERENCES


Den andra studien undersökte tal, språk och kognition hos 20 6-åringar med epilepsy, från en regional kohort i Göteborgsregionen, och jämförde deras resultat med resultaten från en referensgrupp bestående av 30 barn utan epilepsy. Barnen hade inga andra kända utvecklingsavvikelser. Syftet med studien var att undersöka om förskolebarn med epilepsy men utan andra kända utvecklingsavvikelser ändå har svårigheter som kan ge framtid problem med skolframgång. De bedömdes med ett omfattande testbatteri av både logoped och neuropsykolog, och deras medicinska journaler granskades för att möjliggöra en klassificering av epilepsisyndrom eller typ av anfall. Studien visade, att barnen med epilepsy hade sämre resultat på test av oralmotorik, artikulation, begynnande läsförmåga, snabb ordmobilisering, auditivt minne och uppmärksamhet, samt visuo-perceptuellt förmåga än barnen i referensgruppen, men inte vad gäller verbal förståelse, verbal begävning eller kommunikativ förmåga. De var också långsammare i uppgifter som mätte processhastighet och hade sämre verbalt minne än barnen i kontrollgruppen. De barn som fick flera epilepsimediciner hade sämre förmåga på några av tal- och språktesten, liksom på flera av de neuropsykologiska testen, vilket indikerar en sämre anfallssituation, och de som fått epilepsy före tre års ålder presterade sämre på ett par av de neuropsykologiska testen.


Slutsatser

Avhandlingen visar, att epilepsi och epileptiform aktivitet är vanligare hos barn med språkstörning än hos barn i allmänhet. Samtidigt visas, att barn med epilepsi, men normal allmän utveckling, oftare har svårigheter med expressiv språklig förmåga och med visuo-
perceptuell förmåga än barn utan epilepsi. För barn med sömnaktiverad epileptiform aktivitet och språkliga svårigheter under barndomen varierar språkförmågan på sikt. Vissa får ett normaliserat språk, medan andra har stora kvarstående språkliga och kognitiva svårigheter.


I flera av studierna visades, att epilepsi och epileptiform EEG-aktivitet hos barn ofta påverkar flera kognitiva funktioner. Även hos dem med i övrigt normal utveckling finns en påverkan på såväl språk som andra kognitiva funktioner. Språkläkladen är inte lika välutvecklad som hos barn utan epilepsi och den auditiva förmågan är påverkad. Framför allt syns svårigheter med oral motorik, och hereditet för språkliga avvikelser är särskilt vanlig hos dessa. De språkliga symptomen är sällan enhetliga. En störning som består upp i skolaldern kan röra sig både om renodlat expressiva språkliga svårigheter och om en kombination av expressiva och receptiva språkliga svårigheter, men den kombinerade typen överväger.


Kunskap om mekanismer som påverkar tal- och språkutvecklingen hos barn och som kan leda till en störning är viktig för såväl diagnostik som behandling. EEG-undersökning under sömn kan vara ett hjälpmedel för att förklara några av dessa mekanismer, och bör användas oftare än vad som är brukligt idag, då misstanke om tilläggsproblem hos barnet finns. Då epileptiform aktivitet upptäcks bör man överväga möjligheten till att förbättra inlärningsförmågan med hjälp av antiepileptisk behandling, men fler studier av behandlingseffekter behövs.

Tal- och språkförmågan hos barn med epilepsi bör noggrant undersökas, oftare än vad som hittills varit fallet, så att svårigheter kan upptäckas i tid och behandlingsinsatser erbjudas. Hos skolbarn är det viktigt att också undersöka läs- och skrivförmågan, eftersom barnen riskerar svårigheter med läs- och skrivinlärningen.