



**COGNITIVE DEVELOPMENT OF CHILDREN
WITH NON-PROGRESSIVE UNILATERAL
BRAIN LESION**

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DISSERTATIONES PSYCHOLOGIAE UNIVERSITATIS TARTUENSIS

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*To my husband Juhan, and
my children Tanel, Toomas, Berit*

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LIST OF ORIGINAL PUBLICATIONS

- I **Kolk, A., & Talvik T. (1998).** Cognitive development of children with hemiparesis. In: M. V. Perat (Ed.), *New developments in child neurology* (pp. 689–693). VIII International Child Neurology Congress, Ljubljana, Slovenia, 13–17 September, Bologna: Monduzzi.
- II **Kolk, A., & Talvik T. (2000).** Cognitive outcome of children with early-onset hemiparesis. *Journal of Child Neurology*, 9, 581–587.
- III **Kolk, A., Beilmann, A., Tomberg, T., Napa, A., & Talvik, T. (2001).** Neurocognitive development of children with congenital unilateral brain lesion and Epilepsy. *Brain & Development*, 23, 88–96.
- IV **Kolk, A., & Talvik, T. (2001).** Cerebral lateralization, handedness and cognitive decline following congenital hemiparesis in children. *European Journal of Paediatric Neurology* (Manuscript submitted for publication).

I. INTRODUCTION

In the new millennium, there will be many individuals with compromised cognitive reserve, as an increasing number of factors can affect the cognitive development in children and adults. Medical advances will create a new cohort of survivors of formerly lethal or cognitively devastating brain disorders who will move from childhood to adulthood. The survival rate for children with low birth weight, perinatal conditions, strokes and severe brain traumas will improve. The challenge of understanding central nervous system (CNS) insults across a patient's lifespan may answer many new questions of broader relevance for the brain and cognition. Understanding the biological and cognitive consequences of deviant brain development in survivors of childhood brain insult will enhance our understanding of the risks and buffers of cognitive impairment not only for these disabled children, but will also enable us to use this data as a model for normally developing individuals who may encounter a brain insult or other brain damage at any point in life. At the same time, learning disabilities have become a problem because of heightened academic demands, and the increasing survival rate of neurologically compromised infants whose cognitive capacity does not meet the requirements of modern society (Korkman, 1999). However, a systematic assessment of neuropsychological functions can also reveal a subtle cognitive deficit in the early predictors of later specific disorders in complex cognitive skills and improve the planning of rehabilitation and educational services.

Thus, predicting the emergence of a specific neuropsychological pattern of dysfunction and defining an early intervention program in children with unilateral brain lesion is one of the main tasks in our research, using the childhood insult as a useful model for understanding human cognitive impairment and also the possible recovery processes across the patient's entire lifetime.

II. HISTORICAL BACKGROUND

The evolutions of the concepts of the cerebral localization of cognitive functions in the child's brain have a long and rather complicated history. In 1868 Jules Cotard was the first to report that cerebral organization in children was not the same as in adults, as children with a congenital or early-acquired left hemisphere lesion were not aphasic. The period between the two world wars raised the questions of an incomplete establishment of the hemispheric specialization of cognitive functions as a matter of developmental dyslexia, as well as other disorders according to Orton (1925). In addition, another important finding of the plasticity of the immature brain was revealed, based on the research of Kennard (1938, 1942) performed on infant monkeys who did not show the motor deficit that followed focal brain lesions as adult animals did. The advances in the 1960s demonstrated the morphological differences between the left and right hemispheres (Geschwind & Levitsky, 1968), and by this time investigators reconsidered the possibility that functional asymmetries between hemispheres might have a physical basis on an anatomical level and that the cerebral hemispheres are programmed at the time of birth to function asymmetrically. The detected morphological asymmetries were centered primarily on the language areas such as a larger planum temporale and longer Sylvian fissure in the left hemisphere, doubling of Heschl's gyrus and a larger area of the convexity of the frontal operculum on the right side. However, some researchers have claimed that observed anatomical differences were too small to explain the differences in hemispheric function (von Bonin, 1962). One method of investigating hemispheric specialization has been to study neurological patients with unilateral brain lesions and to infer the function of the area from behavioral deficits. However, in order to conclude that an area has a special or lateralized function, it is also necessary to show that lesions in other areas of the brain do not produce similar deficits; practically, this method is a relatively indirect measure and is not the ideal tool. The studies by Sperry (1971; Sperry, Gazzaniga & Bogen, 1969) of "split-brain" patients became the cornerstone of lateralization methodology, providing clear evidence of the complementary specialization of the two cerebral hemispheres. Furthermore, cerebral site is at least as important in understanding brain function as cerebral side, a fact that is often overlooked (Kolb & Whishaw, 2000 p. 210). The right-shift theory (Annett & Alexander, 1996) proposed the action of a single "right-shift" gene as the explanation of anomalous cerebral organization, which falls into two main types: natural and pathological, as natural is based on the individual variants of mechanisms that induce typical asymmetries. The authors also suggested that the expression of the rs+ gene is more effective in females than males. Finally, the measures of regional blood flow and glucose uptake hold great promise for the identification of asymmetries in cerebral functioning. The investigative works of recent decades

based on neuroimaging techniques such as structural (CT, MRI), and functional neuroimaging in the developing nervous system: single photon emission computed tomography (SPECT), positron emission tomography (PET) and the magnetic resonance (MR)- based modalities such as -fMRI have made it possible to study anatomical asymmetries in the living brain. These new methods have given us the opportunity to enhance our understanding of brain-behavior relationships. Unfortunately neuroimaging findings are not always quite the “gold standards” that they should be, because of a wide variety of individual basis of lateralized abnormalities and the nonspecificity of functional disorders in children with cognitive and/or behavioral disorders.

Several neuropsychological studies have reported that the frequency of cognitive disabilities in children began a remarkable increase since the 1970s. One explanation for this growth is the increased survival rate of very low birth-weight preterm babies (Rapp & Torres, 2000); but as has been discovered, the cognitive decline occurred across all age groups and is also great in older persons and among those with less formal education (Lyketsos, Chen & Anthony, 1999). Results were consistent with the hypothesis that adverse perinatal conditions were associated with severe educational disabilities, whereas less favorable outcomes are influenced also by inappropriate sociodemographic factors. In sum: cognitive outcome is significantly influenced by both perinatal and sociodemographic factors (Resnick *et al.*, 1999). At present it is clear that investigators have only begun the process of studying how anatomical and functional asymmetries are related to cognitive abilities in children. Contemporary brain research proceeds along two main lines: a “microlevel” approach explores the behavior of single neurons and subcellular elements, while “macrolevel” studies deal with more complex cerebral functions such as the assessment of behavior and neurocognitive development.

III. STATING THE PROBLEM

An increasing trend in the prevalence of cerebral palsy (CP) has been reported from several countries over the last twenty years, varying between 1.93 and 2.27 per 1000 births (MacGillivray & Campbell, 1995). The last report of the changing epidemiology of CP also indicated an increasing incidence of hemiplegias, rising from 30% to 37% of all CP cases (Pharoah, Platt & Cooke, 1996), and being the most common type of cerebral palsy in children in term and in second place among preterm babies. Incidence is estimated at about 0.41–0.79 per 1000 live births in Western countries (Aicardi & Bax, 1998) and about 0.7 per 1000 in the region of Tartu City and County in Estonia (Stelmach *et al.*, 2001).

Hemiplegic cerebral palsy is characterized by unilateral motor impairment due to prenatal, perinatal or postnatal brain damage. Childhood hemiparesis is often more than a physical problem; it is usually accompanied by a variety of behavioral, emotional, cognitive and educational disabilities. Despite the apparent similarity of the main clinical features observed in these patients, the cognitive impairments that account for this type of cerebral lesion vary considerably.

The present research was designed for the comprehensive assessment of primary deficits of cognitive functions such as scanning and the evaluation of the strengths and weaknesses of developmental domains, moreover by specifying the nature and mechanisms of cognitive disorders in children with unilateral non-progressive brain damage. Eighty-six children (60 hemiparetics, 12 newly diagnosed epileptics, and 14 controls) aged 4 to 9 years participated in this research. The patients were selected at random among children with a mild or moderate degree of congenital or acquired hemiparesis and from among children with newly diagnosed active focal epilepsy prior to anti-epileptic treatment at the Unit of Pediatric Neurology at the Department of Pediatrics of the Tartu University Clinics between 1 January 1995 and 1 June 2000. The statistical analysis in all studies was performed using the program S-PLUS for Windows (Mathsoft Inc.). Profile analysis methods were used to compare the profiles of specific categories of test results between different groups of children. Continuous and normally distributed variables were compared using ANOVA.

Accordingly, most of the studies reported in this dissertation have been conducted to answer some of these crucial questions. More specifically, the dissertation concentrates on four issues:

- the range and type of the cognitive dysfunctions in the hemiparetic children (Studies **I**, **II**, **III**);
- the nature of the association between unilateral brain lesion, cerebral lateralization and handedness in the child population (Studies **II**, **IV**);
- the manner in which the different etiology of unilateral brain damage i.e. congenital versus acquired hemiparesis and epilepsy, influence neurocognitive performance in children (Studies **II**, **III**);
- the association between gender and cognitive development in children with nonprogressive focal brain lesion (Studies **I**, **II**, **IV**).

IV. RANGE AND TYPE OF COGNITIVE DYSFUNCTIONS IN HEMIPARETIC CHILDREN

Cognitive function is the capacity of the human brain to process information and to program adaptive behavior. It involves the ability to solve problems, to focus attention and to memorize information (Rapin, 1988). Among the major causes of brain damage in children are early hypoxic events, head traumas and encephalitis (Mattis, 1992). Perinatal anoxic events are among the most common risk factors for cognitive disorders. In general such anoxic damage tends to compromise those systems that are metabolically most active, i.e. Betz and Purkinje cells, and in addition to cognitive disorders it is not surprising to observe some aspects of motor disabilities, and this is indeed a prevalent finding in these patient populations. Moreover, one possibility is that damage in early childhood may occur to neurons that have not as yet fully myelinated and undergone dendritic arborization, thus being incompletely incorporated in higher cortical functions. As a result, such damage may not be detected at the time of insult or for some time thereafter (Mattis, 1992). Also, the different sets of impaired neuropsychological processes after unilateral brain lesion in children can manifest as the same clinical phenomenon and make it difficult to predict further cognitive and academic achievement in these patients. In sum, it may be concluded that underlying brain pathology cannot be drawn only from neurological examination and neurophysiological and neuroimaging findings but must also be supported by the neuropsychological assessment of impaired cognitive functions (Korkman, 1999; Studies I, II, III, IV).

In addition, the risk of becoming cognitively impaired after a CNS insult is not the same as the risk of such an insult taking place; the difference lies in the buffering effect of the two reserves: as a biological reserve, which involves plasticity, and a cognitive reserve, which involves the capacity for adaptive, efficient, and flexible problem solving. Some brain regions show little plasticity at any age, such as the frontal eye fields, the colliculi, and part of the cerebellum, so that early and late brain lesions in these regions show similar, immediate, long-lasting deficits (Dennis, Hetherington, Spiegler & Barnes, 1999). Plasticity in brain regions with a more protracted developmental course, for example the frontal association cortex, gradually diminishes as functions become established throughout development, or reorganize in response to a brain insult.

It must be emphasized that a prior brain insult reduces the options for biological plasticity, whether this occurs congenitally, in childhood, or during adult life. Cognitive reserve refers to intelligence, which is used here to mean the capacity for adaptive problem solving across various domains of knowledge, arising from the sum of endowment, education, and experience. In children too, cognitive reserve moderates the effect of pathological factors affecting the CNS (Dennis, 1999). Normal cognitive development may require more biological

plasticity than the maintenance of cognitive structures once these have developed. For the child with a brain insult, however, biological plasticity must be shared between the normal task of cognitive development and the abnormal task of formulating a strategic, adaptive response to the insult. Usually it is insufficient for both tasks, which is why most children with brain lesions solve problems in a suboptimal manner, and why many forms of early brain insult compromise later intelligence (Dennis, Spiegler & Hetherington, 2000). In other words, Studies I, II, III, IV were conducted to investigate the problems of depleted cognitive reserve associated with unilateral brain lesions in children.

The aim of neuropsychological assessment is to specify primary deficits, clarify the nature of cognitive disabilities as also the areas in which a child's cognitive performance is relatively strong, provide a basis for planning rehabilitation as well as for the child's ability to cope with his or her problems. The modern brain imaging technique unfortunately does not in every case help to understand a child's neurocognitive decline, as brain abnormalities, whether developmental disorders or postasphyxial damages, tend to be multifocal or diffuse, sometimes affecting merely the microstructural and cellular level (Duane, 1991; Truwit, Barkovich, Koch, & Ferriero, 1992; Volpe, 1992). Attempts to relate neurocognitive findings to underlying brain pathology are therefore not likely to be successful in every case. In other words, to detect and specify all cognitive deficits in a detailed manner, it is important to use the sensitive neuropsychological subtests appropriate to the children's developmental age.

The neuropsychological examination in this research was performed with the aid of a test-battery called NEPSY developed by Korkman (1988), standardized in Estonia in 1995 and intended for young developmentally disabled children. The NEPSY test-battery is based on Luria's view of cognitive and visuopraxic functions as being complex functional systems composed of various subcomponents. In the assessment a complex function, such as reading or visuomotor production, the important subcomponents of these complex functions are assessed on an individual basis, so that the deficient link(s) in the chain of subprocesses may be determined (Korkman, 1999). The NEPSY has been adapted for the assessment of congenital or acquired brain dysfunctions, as well as in the quantitative description of a patient's cognitive status in numerous types of brain-dependent cognitive abilities. In children, however, the tendency towards the comorbidity of cognitive disorders emphasizes the importance of a thorough investigation of all domains, after which an in-depth analysis of affected domains may be performed to further analyze the nature of the problem. NEPSY is normed for children aged 4 to 9 years. It consists of 37 subtests subdivided into five areas: attention and executive functions, language, sensorimotor and visuospatial functions, memory and learning.

In sum: on the basis of the comprehensive and systematic scanning of functional components, the NEPSY may aid in specifying the mechanisms of cognitive dysfunction and also the processes of normal cognitive development. In addition, using neuropsychological batteries in children with focal brain lesion,

one may measure not only the cognitive deficits at the time of the insult, but also detect a variety of future cognitive events, including abilities to meet routine cognitive or physical challenges, stresses, fatigues, multitasking; reliance on effortful as well as automatized processing, such as adopting strategies and organizational approaches, and remembering and solving problems. The findings of Bates *et al.* (1997) showed that at later ages brain damaged children usually perform more poorly than control children, whereas a different pattern of impairment results from left versus right hemisphere damage (Vargha-Khadem, Isaacs, & Muter, 1994; Vargha-Khadem, Isaacs, van der Werf, Robb, & Wilson, 1992; Aram & Ekelman, 1988; Studies I, II, IV). On the basis of the above-mentioned studies it was clearly demonstrated that whichever hemisphere was lesioned, the children with hemiparesis scored at a below-average cognitive rate compared to controls matching their age and gender. In addition, it must be emphasized that the cognitive impairment of focal brain-damaged children frequently tends to be diffuse, especially with accompanying seizure disorders, but essentially depends on the side of the hemispheric lesion.

Right-side brain injury was associated above all with impaired visuospatial ($p < 0.05$, compared to left-sided lesion), attention and language comprehensive abilities; left-side brain injury was associated mainly with impaired phonological and expressive language abilities, and also with visuomotor and verbal memory dysfunctions (Studies I, II, III, IV; Isaacs, Christie, Vargha-Khadem, & Mishkin, 1996). Following these findings and contrary to the claims that due to brain plasticity most children with left-hemisphere injury develop within the normal range (Stiles & Martinez, 2000), my data and that of other authors demonstrated that children who fall outside the normal range encounter complications in many cognitive realms in addition to their focal brain lesion (Vargha-Khadem & Polkey, 1992). Carlsson *et al.* (1994) reported that deficits in linguistic abilities of pre- or perinatal unilateral origin could result in persistent selective deficits, especially when children face new linguistic challenges. Eisele, Lust & Aram (1998) reported that language functions were affected differently depending on whether either the left or right hemisphere was damaged, and the same was revealed in Studies II and IV. Left hemisphere lesions appear to cause grammatical deficits, whereas right hemisphere damage appears more likely to result in semantic and comprehensive deficits. One explanation of this finding is offered by Voeller (1991), who proposed that dysfunction of the right hemisphere results in abnormalities in the mediation of the sensory-attentional, motor-intentional, and arousal-activation systems. In addition, both children with left hemisphere damage and also normal children were more successful in implication tasks than in presupposition tasks. On the bases of Studies II and IV, the author is able to conclude that childhood unilateral brain lesion selectively impaired cognitive functions. The comparison of verbal performances between left versus right hemisphere lesion (when lesion was confirmed by neuroradiological findings) showed clearly that the children with left-sided cortical and subcortical lesions had more severe impairments in language and speech

production abilities. In their SPECT study of children with developmental dysphasia, Chiron *et al.* (1999) found a lack of regional cerebral blood flow predominance in the left hemisphere at rest, and these children also showed a lack of hemispheric asymmetry and impaired functional specialization of both hemispheres. The hypothesis of the side-specific type of cognitive impairment in hemiparetic children is also supported by the findings that attention functions are significantly more impaired in children with right hemisphere lesions than left side lesions ($p < 0.001$). Other neuropsychological parameters such as inefficiency, slowness, and the inability to cope with changes and novelty were also revealed in children with developmental right-hemisphere syndrome (Studies II, IV).

In sum: our data showed deterioration in many neurocognitive functions in children with hemiparesis, but one important finding is a side-specific type of cognitive deficit that was detected. The selective type of impairment was better revealed in those children whose clinical findings were confirmed through CT or MRI findings, whereas overall intellectual development in these children was within the normal range.

V. LATERALIZATION OF BRAIN FUNCTIONS AND HANDEDNESS IN CHILDREN WITH HEMIPARESIS

The discovery of hemispheric asymmetry or lateralization, i.e. the degree to which each side of the brain is dominant (or specialized) for a cognitive process, represents one of the most challenging goals of neuropsychology. Previous studies of the lateralization of cerebral functions in children with unilateral brain lesions have generated conflicting findings and theories. There are two different theoretical conclusions of the development of brain asymmetries in children. The authors of the first conclusion of equipotentiality argued that any area of the brain could assume responsibility for any behavioral function, as the two hemispheres have the same cognitive potential at birth, and that lateral specialization only develops slowly throughout childhood (Lenneberg 1967; Vargha-Khadem, Isaacs, & Muter, 1994). A second conclusion proposes that asymmetries between the left and right hemispheres exist already at birth. The young brain has a tremendous ability to reorganize itself in the face of damage to specific regions, although this plasticity decreases with age. The authors of the second hypothesis (Aicardi & Bax, 1998) ruled out the adult pattern of side-specificity for lesions acquired in childhood. This evidence originates from morphological studies that show the neuroanatomical asymmetries in the adult cerebrum as well as the similar asymmetries in the neonatal cerebrum (Geschwind & Levitsky, 1968; Geschwind & Galaburda, 1985). Functional asymmetries have been proven by Chiron *et al.* (1997), measuring the cerebral blood flow during rest using SPECT. They found that the blood flow shows a right hemispheric predominance between 1 and 3 years of age, whereas dominance shifts to the left side after 3 years. These findings support the idea that in newborns the right hemisphere develops its functions earlier than the left, because the right hemisphere sustains the functions necessary for the survival of the species, such as visuospatial and emotional abilities. Developmental studies have shown a right ear advantage for verbal material across cultural studies (Nagafuchi, 1970) in children as young as 3 years of age (Hiscock & Decter, 1988), and it was also accepted that consistent hand preference typically develops at around the same age. According to this conclusion, the period of vulnerability must be more prolonged for the left hemisphere, being associated with more frequent left hemisphere lesion. The same was confirmed by current studies; such as, for example, the ratio between left and right hemisphere lesions was 23 to 14 in Study II and 32 to 23 in Study IV respectively. The above-mentioned views appear to be a clear indication that the human cerebral hemispheres became specialized even at a very early age. According to Bates (1993) there are some initial biases in the human brain, which under normal circumstances lead to the familiar adult patterns of brain organization. However, when these default conditions apply the infant brain can find alternative neural and behavioral solutions resulting in forms of brain organization that are not usually seen in normal children or brain-damaged adults. Explanations of anomalous

cerebral organization in adults fall into two main types: natural and pathological; natural being based on the individual variants of mechanisms that induce typical asymmetries and could, as mentioned previously, be genetic, and pathological organization due to various pathologies such as cerebral palsy, epilepsy and traumas which distort brain modality.

In sum, the question is whether variations in anatomical and functional organization are related in any meaningful way to factors such as handedness and gender. To date, however, the existing literature provides no definite interpretation of the relationship between unilateral brain damage, non-right handedness and cognitive deficits in children with unilateral brain damage. Previous data suggest that stressful birth and perinatal complications are significant factors contributing to the development of left-handedness and the lack of right-hand preference (Bakan, 1973), and that left-handedness (and presumably all cases of right-hemisphere or bilateral control of speech) is a result of brain injury, however subtle (Obrzut & Hynd, 1981), as there is a greater incidence of left-handedness among mentally defective children and children with various neurological disorders than in the general population (Kolb & Whishaw, 2000). Several studies have linked left-handedness with speech defects, emotional instability, alcoholism, epilepsy, learning disabilities and malfunctions in many areas (Bakan, 1973; Sunseri, 1982). Yet little evidence has been found to support the argument that cerebral organization in left-handers with speech representation in the left hemisphere differs from the cerebral organization of right-handers, in addition to the fact that handedness is not an absolute, since some people are completely left- or right-handed, whereas others are ambidextrous. Satz (1973; Satz, Strauss, & Whitaker, 1990) subdivided left-handers in the child population into two types differing in cerebral organization as natural and pathological left-handers. Following these findings and based on the idea proposed by Isaacs, Christie, Vargha-Khadem, & Mishkin (1996), my Study IV was conducted to test the hypothesis that cerebral lateralization in hemiparetic children may be demonstrated using measures of handedness. In any case, there are no particularly good methods accepted to demonstrate cerebral lateralization in children. It turns out, however, that handedness is indeed a reliable tool to help detect cerebral asymmetries. First the excess of left-handedness among children with focal brain lesion was obtained, which was about 41% among all children and rose to 71.9% due to pathological not to familial cases of left-handedness in the children with left hemisphere lesion (Study IV). This is not surprising, because if the dominant hemisphere is injured at an early age, handedness as other cognitive functions can shift under the control of the hemisphere being normally non-dominant. Taken together, it is therefore quite plausible that left hemisphere injury increases the overall rate of non-right handedness in high-risk populations by increasing the number of cases of pathological left-handedness (Study II, IV; Satz, Strauss & Whitaker, 1990).

Thereafter Satz, Strauss & Whitaker (1990) divided the shifts in lateral preference after unilateral brain lesion into the following two types: bimodal, involving the reorganization of speech and handedness, and unimodal, with speech reorganized but hand preference maintained. More specifically, the

author of this study suggests that other still unreported types of cerebral organizations could also be found, like a non-shifted hand control associated with non-reorganized speech and/or other cognitive functions. Which type of shift occurs is related to many factors, although younger children more frequently show the bimodal type of functional reorganization (Goodman, 1989), and such type of cerebral reorganization significantly decreases after the age of 5 years (Rasmussen & Milner, 1977). It has been shown that, due to better brain plasticity, children who have sustained left hemisphere damage early in life demonstrated favorable language function reorganization, because the language functions began to be mediated by the right hemisphere (Studies II, IV; Isaacs, Christie, Vargha-Khadem, & Mishkin, 1996; Chiron *et al.*, 1997). Some authors have found that seizure disorders may enhance the dysfunction of the damaged sensorimotor area, leading to a shift of hand control to the opposite hemisphere (Isaacs, Christie, Vargha-Khadem, & Mishkin, 1996). This statement does not correlate directly with our findings, as only 35% of children with seizure disorders were left-handers compared to 41% of all hemiparetic children.

As mentioned above, it is rather difficult to examine the processes of cerebral lateralization and functional reorganization in children with brain lesion, but using the handedness measure as an indicator of typical or atypical cerebral lateralization, more information may be obtained about the cognitive status of children with congenital hemiparesis, who are exposed to the dual risk of factors that cause academic problems in the general population and an extra risk due to unilateral brain lesion. According to this view the pattern of cognitive deficit in hemiparetic children depends in addition to the side and size of the brain lesion, also on the type of cerebral lateralization, i.e. typical or atypical. It was assessed that the profile of cognitive impairment was different in children with shifted and non-shifted hand preference after unilateral brain lesion. The children with shifted handedness, i.e. the left-handers with left-hemisphere lesion (LHL), and right-handers with right-hemisphere lesion (RHL) (Studies II, IV) demonstrated a relatively well-preserved language function. The right-hemisphere lesion group (right-handed children) displayed a slightly below average score in language comprehension abilities, which could be explained by the failure of right hemisphere functions to integrate sensory information, thereby causing the dysfunction in the initial stage of language comprehension abilities. Again, the children with left-hemisphere lesion showed impairment mainly in receptive language abilities, although they were also impaired in visuomotor abilities. Within this overall dysfunction we found an interesting and unexpected malfunction of the non-paretic hand in motor and sensory integration tasks, i.e. they scored below the controls' level when using their healthy left or right hand. The revealed dysfunction in the sensorimotor area opposite the damaged side may be explained by the greater amount of parallel processing of information in the motor and sensory systems. In sum, the children with the bimodal type of cerebral reorganization after brain lesion when both speech and hand controls are shifted to the opposite hemisphere displayed a better overall cognitive outcome. But the crucial finding was that children who did not undergo a shift in hand preference after brain damage, such as right-handed chil-

dren with left-hemisphere lesions, displayed diffuse impairment in cognitive performance. Their cognitive deficit was almost severe: the language measures, both phonological and speech production functions, were impaired, besides they performed poorly in visuomotor and narrative memory domains even though they had only a mild motor deficit (hemiparesis). This relatively well-preserved motor function can be explained on the one hand by limited damage area in the motor cortex, and on the other hand also by well organized rehabilitation work. The overall decline of cognitive abilities might be explained by the assumption that the damaged left hemisphere could not reorganize its impaired manual, complex visuomotor and language functions to the right hemisphere capable of supporting them, and this incomplete brain lateralization may disturb further cognitive development. It was found that if language control was bilateral or otherwise more extensive in the impaired left hemisphere, this atypical lateralization caused greater dysfunctions in language and other cognitive areas. These findings are clinically important, pointing to inappropriate functional overlap between brain systems and also to reduced brain plasticity. These children require, in addition to careful medical attention, an assessment of their major cognitive functions to prevent later-life neuropsychological decline.

Some critiques and scepticism of the usefulness of laterality researches have been published in a provocative book by Efron (1990), who claimed that the apparent right-left differences in laterality studies could be explained only by the way the brain “scans” sensory input. In addition, he stressed that the researchers of hemispheric specialization should remember that a functional deficit after brain damage is usually more general and does not imply only this function, related to that damage area or even hemisphere, because the neural substrate remains as yet unknown.

At present researchers are far from having definitive answers to all questions regarding the development of asymmetries, and further investigations involving the tools of cognitive neuroscience are clearly required. Again, in hemiparetic children neurocognitive development is strategically and temporally aberrant, suggesting that cerebral lateralization and functional reorganization is not equivalent to normal development. Consequently, the typical pattern of cerebral reorganization, when both speech and hand control are reorganized after unilateral brain damage, showed a favorable cognitive outcome compared to the incomplete type of reorganization, demonstrating mostly a diffuse cognitive decline.

In sum, the author of the present study would like to emphasize that these children, who demonstrated an anomalous pattern of cerebral lateralization, require special medical attention, neuropsychological examination and individual neurorehabilitation and educational measures in order to prevent later-life cognitive difficulties.

VI. HOW DOES THE ETIOLOGY OF UNILATERAL BRAIN DAMAGE, I.E. CONGENITAL VERSUS ACQUIRED HEMIPARESIS AND EPILEPSY, INFLUENCE NEUROCOGNITIVE PERFORMANCE IN CHILDREN?

1. Relationship of age of brain damage to cognitive performance in children

This section deals with cognitive disorders in children with congenital versus acquired hemiparesis to study the effect of age at onset of brain lesion.

There are many works supporting the hypothesis of greater neural plasticity in infant-age, giving more favorable cognitive recovery in the case of early brain lesion, regardless of which hemisphere is impaired (Bates *et al.*, 1997; Goodman & Yude, 1996; Woods, 1987; Basser, 1962). For a time this widely accepted idea that early brain injury has milder and more short-lived effects on cognitive development, gradually demonstrated that earlier may not always be better. A series of studies suggest greater neuropsychological deficits in children with congenital and early postnatal brain lesions compared to lesions occurring later, arguing that early brain lesions may reduce overall intelligence (Riva & Cazzaniga, 1986; Müller *et al.*, 1999). Vargha-Khadem, Isaacs & Muter (1994) indicated a period of reduced compensatory plasticity for lesions occurring between six months and four years of age and better average outcome for congenital lesions and those occurring between four and ten years of age. Since the processes of human development are sustained and individual variability of responses are great, the author of the present studies proposes that the time-relationship may be an oversimplification, and that cognitive outcome is not directly predicted by the age at onset of brain lesion. It is on this hypothesis that Studies I, II were conducted. It has been shown that the age of injury was indeed a less important factor in predicting cognitive disorders in children than the side and size of brain damage. Cognitive abilities were significantly reduced in children with congenital or acquired hemiparesis compared to controls, and moreover, the profile of impairment was not directly related to the time at injury but more clearly to the side of the brain lesion, as mentioned above, and the study of Isaacs, Christie, Vargha-Khadem & Mishkin (1996) supports this view. No relevant differences were obtained in the performance of the verbal domain between the congenital or acquired brain lesions. The children with acquired hemiparesis scored slightly worse on motor, tactile, attention and short-term memory tasks, but the small differences between groups were not significant. One explanation of this finding is that a unilateral brain lesion occurring at

whatever time induces delay in neurocognitive outcome, besides their cerebral lateralization is not equivalent to normal development.

2. Relationship of epileptic disorders to neurocognitive development

Studies II and III were designed to investigate the effect of seizure disorders on cognitive development. At present a considerable number of researchers have addressed the question of the cognitive outcome of children with seizure disorders and epilepsy, since these children appear to run a high risk. It is accepted that children with epilepsy are frequently affected by cognitive and learning disorders, but it is as yet unknown which factors contribute to the development of such problems, and our current knowledge does not allow the prediction of prospective educational delay in each individual case of a child with epilepsy. It may be caused by the interaction of a multiplicity of factors such as the type, frequency and duration of seizures, age at onset of the first seizures, electrical characteristics, the localization and site of discharges, their persistence, as well the etiopathogenesis of the disease and the adopted antiepileptic therapy (Aldenkamp *et al*, 1996). Some forms of childhood epilepsy also have a direct impact on cognition, as the normal pattern of cerebral dominance is altered by the presence of epileptic foci, and the epileptic hemisphere may lose some of its special cognitive functions (Riva, Pantaleoni, Milani & Giorgi, 1993; Deonna, 1995). The study by Aldenkamp, Wouterina, Overweg-Plandsoen & Arends (1999) has shown that heterogeneity of cognitive impairment is responsible for learning problems in epileptic children.

More specifically, it was proposed that children with seizure disorders are exposed to the risk of diffuse or multiple types of cognitive impairment rather than specific dysfunction (Studies II, III). In these studies it was discovered that the children with congenital hemiparesis combined with epilepsy demonstrated a more severe cognitive deficit than the seizure-free hemiparetic children ($p < 0.05$). This relatively widespread dysfunction in neuropsychological development does not reflect only the more extensive brain lesion in these children, as the same diffuse type of cognitive impairment was revealed in children with newly diagnosed yet non-medicated focal epilepsy. It is more likely that it is above all due to epileptic discharges. On the one hand it is possible to conclude that seizure disorders may adversely influence the maturation and maintenance of normal brain function, as epileptic foci may change the normal pattern of cerebral dominance with successive cerebral lateralization, and the epileptic hemisphere may thereby lose some of its special cognitive functions. On the other hand it is important to emphasize that the epileptiform activity as an anti-epileptic treatment interferes not only with the functions of the damaged hemi-

sphere, but also with the otherwise normal functions of the intact hemisphere, thus affecting bilateral dysfunctions. In the analysis of the profile of cognitive difficulties it was discovered that the children with seizures indeed displayed a diffuse deficit, as three or five main cognitive domains were impaired. They displayed below average scores in attention, language, especially receptive language skills but also in the capacity for repeating words, non-words, and rapid naming, as well as in visuomotor processing and memory functions. In addition, after damage of the left hemisphere right-handed children with seizure disorders demonstrated an equivalent decline in both verbal as well as non-verbal performance, showing altogether the most severe cognitive decline (Study IV).

Another main question is the cognitive outcome of children with different types of epilepsy. Characteristic findings include more severe attention dysfunctions in children with epileptic discharges in the right hemisphere (epileptic discharges were detected by EEG) compared to children having epileptic discharges in the left hemisphere ($p < 0.05$). Moreover, attention dysfunction was associated with both seizure types: primarily generalized and partial epilepsy. Language and short-term memory dysfunctions were more extensive in children with generalized epilepsy. In addition, language dysfunction associated most clearly with paroxysmal epileptic discharges in the left hemisphere (epileptic discharges were detected by EEG). Interestingly, in some instances language dysfunction was also associated with paroxysmal activity in the right hemisphere. Moreover, epileptic children with congenital hemiparesis attained lower scores in language tasks than children with epilepsy alone ($p < 0.05$), and children with primarily generalized epilepsy attained lower scores than children with partial epilepsy ($p < 0.05$). In short-term memory tasks the children with generalized epilepsy scored lower than those with partial epilepsy ($p < 0.05$). The comprehensive study (Study III) of neuropsychological impairment in children with focal brain lesion manifested as congenital hemiparesis with epilepsy and epilepsy alone demonstrated the profile of diffuse neurocognitive dysfunctions in both types of focal brain damage accompanied by epilepsy. It was quite notable that the children with newly diagnosed partial epilepsy prior to antiepileptic medication demonstrated, contrary to expectations, a high rate of neurocognitive disability. These children scored poorly compared to controls in four main cognitive domains, especially in the areas of attention and language, but also in visuo-perceptual and short-term memory. It is also interesting that in some cognitive domains they scored at nearly as low a level as children with congenital hemiparesis accompanied with epilepsy. One should observe that these children were free of the possible depressive side effect of antiepileptic therapy. Taken together, the findings given above show that the profile of cognitive deficit appeared to be diffuse in the presence of seizure disorders, and in addition, these children demonstrated overall cognitive delay. The same was found by Spreen (1995). Cioni *et al.* (1999) suggested a strong connection between mental retardation and epilepsy in hemiplegic children, as epilepsy might indicate a more diffuse neurological dysfunction interfering with the re-organization capacity of

the young damaged brain. Intellectual deterioration was once thought to be common with epilepsy. It is now known to be uncommon, and usually associated with specific causes such as concomitant brain disease and specific epileptic syndromes (Brown, 1999). Note that all the children of my studies were of normal intellect (Studies II, III). Once again, it is possible that seizure disorder may adversely influence the maturation and maintenance of normal brain function, giving a picture of diffuse cognitive impairment, as there is evidence that seizures are associated with neuronal damage (Rabinowicz, Correale, Boutros, Couldwell & Henderson, 1996). Despite a favorable medical prognosis nowadays, children with childhood onset epilepsy are at increased risk for unfavorable cognitive development, as demonstrated above.

VII. THE ASSOCIATION BETWEEN GENDER AND COGNITIVE DEVELOPMENT IN CHILDREN WITH NON-PROGRESSIVE FOCAL BRAIN LESION

Brain development is highly dependent on the quantity and types of steroid hormones available during brain formation. Numerous investigators have hypothesized that handedness, an indicator of brain organization, is correlated with the same tests of cognitive abilities that typically show sex differences, the underlying idea being that brain laterality and sex differences in cognition are in part controlled by the same prenatal sex hormones. There is also evidence for structural differences in the corpus callosum (and other brain mechanisms involved in cognition) that vary as a function of sex and handedness, supporting the idea that males and females and left- and right-handers differ in the hemispheric organization of cognition, which is caused at least in part by the actions of steroid hormones (Innocenti, 1994; McEwen, Gould, Orchinik, Weiland & Wooley, 1995; Halpern, Haviland & Killian, 1998). In addition, a large body of studies documents typical sex-related patterns of cognitive abilities as females on average score higher on tests of verbal fluency, many types of memory tasks, and fine motor skills. Males on average score higher on tests that require transformation in visual-spatial working memory, such as mentally rotating objects to determine what they would look like in a different orientation, and in some tests of mechanical and mathematical reasoning (Halpern, 1992; 1997). The clearest evidence of the effects of sex and handedness on cognition was found in the high and low-ability end of the distribution of intelligence test scores. There are more males and more left-handed men among individuals with several types of mental retardation and with delayed or poor verbal abilities, including several reading disabilities (Bathoja & McManus, 1985; Pipe, 1990). Furthermore, the proportion of left-handed males in the group of gifted people was also approximately double what would have been expected from the proportion of left-handers reported in the population study of Halpern, Haviland & Killian (1998). My research on gender differences has shown that there were no great differences in left-handedness between boys and girls, as left-handedness was about 48% among boys and 44% among girls (Study II, IV). The clearest evidence of the interaction between sex and handedness was found in the right-handed boys with LHL who demonstrated the highest risk for the development of language and verbal memory dysfunctions, as right-handed girls with LHL suffer more often and severely from visuomotor deficiencies that might be explained also by the effect of androgens, which may delay left hemisphere maturation in boys and lead to a left-to-right shifting of verbal functions resulting in a mixed dominance of cognitive abilities (Eviatar, Hellige & Zaidel, 1997). In a comparison of the performance of left-handed boys and girls (non-paretic hand groups) in attention tasks, we found typical sex differences, as boys performed

more poorly, but in the case of right hemisphere lesions the right-handed boys and girls had equally poor attention scores, which might explain why a side-specific pattern of impairment of the right hemisphere is more expressive than a gender effect. The comparison of the language domain between left-handed boys and girls with LHL showed that receptive language was the most severely affected verbal function, but no significant differences were recorded between boys and girls, although the boys performed less successfully. In addition, we determined significant gender differences ($p < 0.01$) between left-handed boys and girls (LHL) in short-term memory measures; the boys performed less successfully than the girls, especially in verbal memory tasks. Again, the girls with congenital hemiparesis outperformed boys in the areas of attention, language, and short-term memory, and the boys outperformed girls in visuospatial skills, which may be due to sex differences in intrahemispheric organization, as hypothesized by Crucian & Berenbaum (1998).

In sum, converging evidence across studies of sex differences, laterality and cognitive development suggests that organizational differences of boys and girls and right- and left-handers are related to different patterns of cognitive abilities, and the same typical pattern of sexual differences in cognitive performances was also revealed in children with early-onset unilateral brain lesion. (Studies I, II, IV).

VIII. CONCLUSIONS

Taken together, the main conclusions of this dissertation are the following:

- In hemiparetic children neurocognitive development is strategically and temporally aberrant, pointing to depleted cognitive reserve and the fact that cerebral lateralization and functional reorganization is not equivalent to normal development. Children with unilateral brain damage clearly demonstrate impairment in attention, language, visuospatial, tactile and memory functions compared to age and gender matched controls, regardless of which hemisphere is lesioned. In addition, a different pattern of cognitive decline results from left versus right-hemisphere damage, but frequently the cognitive impairment of focal brain-damaged children tends to be diffuse (Studies **I, II, III**).
- The side-specific type of cognitive deficit was mostly obtained after childhood unilateral brain lesion and was supported by the findings that attention and visuospatial functions are more impaired in children with right hemisphere lesion, and language, visuomotor and verbal memory functions in children with left hemisphere lesion. Consequently, the side of damage is an important factor in predicting the profile of cognitive disorders in children (Studies **I, II, III**).
- In addition to the side and size of the hemispheric lesion, the cognitive outcome of focal brain damage depends also on whether the type of cerebral lateralization is of a typical or atypical pattern. The typical, i.e. complete pattern of cerebral reorganization displayed a favorable cognitive outcome, associating with specific cognitive impairment contrary to the atypical i.e. incomplete pattern of reorganization, which displayed multiple disorders. Children who did not undergo a shift in hand and speech preference after brain damage had a high risk of cognitive disabilities, as right-handed children with left-hemisphere lesion displaying impairment of the language measures in phonological as well as speech production abilities, in addition to visuomotor, verbal and narrative memory domains. Moreover, it must be kept in mind that cerebral lateralization and functional reorganization may also be affected by seizure disorders. (Studies **I, II, III, IV**).
- Using the handedness measure as one of the possible tools for examining typical or atypical cerebral lateralization could provide more information on the cognitive status of children with unilateral brain damage (Studies **II, IV**).
- Cognitive abilities were significantly reduced in children with congenital or acquired hemiparesis, and also the profile of cognitive impairment was not directly related to the time of the injury, as there were not significant differ-

ences between the outcome of children with congenital and acquired hemiparesis. Children with both injury groups obtained low scores in cognitive domains such as attention, phonological analysis, tactile and visuomotor precision and short-term memory (Studies I, II).

- Children with congenital hemiparesis associated with epilepsy have severe and children with newly diagnosed partial epilepsy moderate cognitive deficit. The profile of cognitive weakness appears to be quite similar in both groups, which is a novel finding. Epilepsy in children with congenital hemiparesis means a high additional risk for developing attention, phonological, visuo-perceptual, memory, and learning deficits, as children with newly diagnosed epilepsy develop impairment in attention, visuo-perceptual and short-term memory skills, and also obtain below averages scores on language abilities, especially in auditory perception, lexical skills and speech comprehension function. Consequently, the children with seizure disorders have a diffuse or multiple pattern of cognitive disorders rather than specific cognitive impairment (Studies I, II, III).
- Boys and girls have different patterns of neurocognitive outcome: girls with congenital hemiparesis outperformed boys in attention, language, and short-term memory domains, and boys outperformed girls in visuospatial skills (Studies I, II, IV).
- Early evaluation of the structure of cognitive dysfunction in children with focal brain lesion is extremely important for appropriate intervention, including individual training and support for neurorehabilitation and educational programs, in order to prevent later-life cognitive and academic failures.

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SUMMARY IN ESTONIAN

Ühepoolse mitteprogresseeruva ajukahjustusega laste kognitiivne areng

Uuel aastatuhandel on jätkuvalt suurenemas kognitiivsete häiretega inimeste arv. Selle põhjuseks võib pidada üldist eluea pikenemist ja meditsiini edusamme (Dennis, 1999; Dennis, Spiegler & Hetherington, 2000). Uute ravimeetodite tõttu kasvab sügavalt enneaegsete laste elulemus ning paranevad varem letaalselt lõppenud haiguste ja ajutraumade ravitulemused, millega seoses jõuab täiskasvanuikka järjest suurem hulk inimesi, kelle kognitiivne võimekus ei vasta moodsa ühiskonna pidevalt kasvavatele hariduslikele nõuetele (Korkman, 1999; Rapp & Torres, 2000).

Neuropsühholoogilised uurimismeetodid võimaldavad avastada kognitiivsete funktsioonide häireid juba subkliinilises staadiumis ning peale primaarse defitsiidi kindlaks teha ka inimese kognitiivse võimekuse tugevad küljed, mille põhjal saab prognoosida nii lapse edasist kognitiivset arengut kui ka kasutada õigeaegselt sobivaid arendusravi- ja parandusõppeprogramme vältimaks ebaõnnestumisi edaspidises akadeemilises ja sotsiaalses karjääris.

Väga sobivaks mudeliks, et mõista ajukahjustuse ja mõtlemise ning tunnetusega seotud kõrgemate vaimsete protsesside, s.o. kognitiivsete funktsioonide seost, samuti inimese bioloogilise ja kognitiivse reservi võimalusi ajukahjustusest taastumiseks, on uurida kaasasündinud insuldi juhtumeid. Kaasasündinud ajuinsuldi kui ühepoolse ajukahjustuse mudeli kasutamine annab vastuse paljudele küsimustele nii ajukahjustuse riskifaktorite kui puhversüsteemide kohta mitte ainult nendel lastel, vaid ka täiskasvanutel, kellel võib tekkida ajukahjustus ükskõik millisel eluetapil.

Käesolevas dissertatsioonis keskendutakse kognitiivse defitsiidi uurimisele tserebraalparalüüsi (*PCI*) hemipareetilise vormi korral. Epidemioloogilised uuringud annavad *PCI* esinemissageduseks lastel 1,93–2,27 1000 sünni kohta (MacGillivray & Campbell, 1995). Lisaks näitavad viimased uuringud *PCI* hemipareetilise vormi sagenemist, kus tõusuks antakse 7% (30%→37%). Hemiparees on ühtlasi ka kõige levinum *PCI* vorm ajaliste laste populatsioonis (Pharoah, Platt & Cooke, 1996). Lääneriikides antakse hemipareesi esinemissageduseks 0,41–0,79 iga 1000 elusalt sündinud lapse kohta (Aicardi & Bax, 1998), Tartu linnas ja maakonnas on see arv 0,7 (Stelmach, Rein, Tali, Kinkar, Talvik & Ilves, 2001). Prenataalne, perinataalne või postnataalne hemiparees on komplitseeritud probleem, kuna sageli lisandub motoorsele puudele veel rida emotsionaalseid, kognitiivseid, käitumis- või õppimishäireid. Õppimishäiretega inimesi on Põhja-Ameerikas ja Euroopas juba 10–15% kogu õpiealisest elanikkonnast (Lyketsos, Chen & Anthony, 1999; Resnick *et al.*, 1999). Oluline on veel rõhutada, et vaatamata küllalt sarnasele kliinilisele leiule hemipareeside

korral, varieerub kognitiivse kahjustuse ulatus igal individuaalsel juhul suurtes piirides, mistõttu nende laste täpne neuropsühholoogiline uurimine on väga oluline.

Käesolev dissertatsioon on pühendatud primaarse kognitiivse defitsiidi uurimisele, samuti kognitiivse arengu nõrkade ja tugevate külgede kindlakstegemisele mitteprogressseeruva ühepoolse ajukahjustusega lastel, et täpsustada kognitiivsete häirete olemust ja mehhanisme. Uurimisgrupi moodustasid 60 last kaasasündinud või omandatud hemipareesiga ja 12 last fokaalse epilepsiaga (enne antiepileptilise ravi alustamist). Kontrollgruppi kuulus 14 tervet last vanuses 4–9. a. Neuropsühholoogiline uuring teostati NEPSY-testipatareid kasutades (Korkman, 1988), mis andis võimaluse uurida viit põhilist kognitiivset valdkonda: tähelepanu ja täidesaatvaid funktsioone, kõnet, sensomotoorseid funktsioone, ruumitaju ja orientatsiooni ning mälu funktsioone. Dissertatsioon põhineb neljal uurimisel, kus keskendutakse täpsemalt järgmistele küsimustele:

- hemipareesidega laste kognitiivse arengu profiil (**I, II, III** uurimus);
- varase fokaalse ajukahjustuse toime ajufunktsioonide lateralisatsiooni ja käelisuse väljakujunemisele (**II, IV** uurimus);
- fokaalse ajukahjustuse erinevate etioloogiliste faktorite nagu kaasasündinud vs. omandatud kahjustuse ja epilepsia mõjust lapse neurokognitiivsele arengule (**II, III** uurimus);
- soo ja kognitiivse arengu seosed ühepoolse ajukahjustusega lastel (**I, II, IV** uurimus).

Tuginedes esitatud uurimustele, on väitekirja põhiseisukohad järgmised.

- Hemipareesiga laste kognitiivne areng erineb tervete laste arengust nii ajalise kulu kui ka funktsioonide küpsemise seisukohast, viidates nende laste puudulikule kognitiivsele reservile. See omakorda takistab vajalike kompensatoorsete mehhanismide väljakujunemist, olenemata sellest, kumb ajupoolkera on kahjustatud. Neil lastel oli sageli häireid tähelepanu, kõne, visuaalruumilise ja taktilise taju ning mälu funktsioonide valdkonnas. Kuigi ühepoolse ajukahjustuse korral esines ka difuusset tüüpi kognitiivset häiret, olid üldjuhul vasaku ja parema ajupoolkera kahjustusest tingitud kognitiivse düsfunktsiooni mudelid erisugused (**I, II, III** uurimus).
- Tähelepanu ja ruumiline orientatsioon olid rohkem häiritud parema ajupoolkera kahjustusega lastel; kõne, visuomotoorne võimekus ja sõnamälu aga vasaku ajupoolkera kahjustusega lastel. Võib kinnitada, et ajukahjustuse poolel on laste kognitiivsete häirete profiili määratlemisel oluline tähtsus (**I, II, III** uurimus).
- Peale kahjustatud ajupoolkera ja kahjustuse suuruse on lapse kognitiivses arengus oluline tähtsus ka ajufunktsioonide lateralisatsiooni tüübil, s.t. kas on tegemist tüüpilise või atüüpilise lateralisatsiooniga. Tüüpilisele e. täielikule ajufunktsioonide lateralisatsioonile kaasub spetsiifilist tüüpi kognitiivne häire, mis annab hea prognoosi lapse edasise kognitiivse arengu suhtes erin-

evalt atüüpilisest e. mittetäielikust ajufunktsioonide lateralisatsioonist, millele kaasub sageli difuusset tüüpi kognitiivne kahjustus. Lapsed, kellel pärast ühepoolset ajukahjustust ei kujunenud välja kompensatoorset käelisuse või kõnekeskuse reorganisatsiooni kahjustamata ajupoolkera poolt (nii nagu paremakäelistel lastel pärast vasaku ajupoolkera kahjustust), olid rohkem dispooneeritud kognitiivsele düsfunktsioonile, eriti kõne (nii fonoloogilise kõne kui kõne produktiooni), visuomotoorse ja sõnamälu valdkonnas. Selgus veel, et ajufunktsioonide lateralisatsiooni- ja reorganisatsiooniprotsessid olid häiritud krampide korral (**I, II, III, IV** uurimus).

- Laste käelisuse uurimine on oluliseks abivahendiks hindamaks tüüpiliselt või atüüpiliselt kulgevat tserebraalset lateralisatsiooni, see omakorda võimaldab täpsemalt prognoosida ühepoolse ajukahjustuse läbiteinud laste edasist kognitiivset arengut (**I, IV** uurimus).
- Kognitiivne võimekus oli tervete lastega võrreldes oluliselt madalam nii kaasasündinud kui ka omandatud hemipareesidega laste grupis, kusjuures kognitiivse defitsiidi struktuur ei olenenud otseselt ajukahjustuse tekke ajast. Mõlema grupi lastel oli normist madalamaid tulemusi nii tähelepanu, kõne fonoloogilise analüüsi, taktiilse taju, visuomotoorse võimekuse kui lühimälu valdkonnas, kusjuures kahjustuse profiil ei erinenud oluliselt kaasasündinud ega omandatud kahjustusega laste gruppides (**I, II** uurimus).
- Hemipareesiga lastel, kellel kaasnes epilepsia, olid kognitiivsed häired raskemad kui hiljuti diagnoositud fokaalse epilepsiaga lastel, kellel oli mõõdukas kognitiivne defitsiit. Kognitiivsete häirete profiil nendes kahes grupis oli sarnane, mis on oluline ja uus leid. Seega tähendab epilepsia lisariski hemipareesidega laste tähelepanu, fonoloogilise ja visuomotoorse võimekuse ning mälu funktsioonide arengule, kusjuures ainult epilepsiaga lastel olid kahjustunud samad kognitiivsed funktsioonid. Kokkuvõtteks võib öelda, et difuusset tüüpi kognitiivse kahjustuse profiil kaasneb epilepsiaga sagedamini kui spetsiifilist tüüpi kognitiivse kahjustuse mudel (**I, II, III** uurimus).
- Poistel ja tüdrukutel oli erinevat tüüpi kognitiivse arengu profiil: hemipareesidega tüdrukud edestasid poisse tähelepanu, kõne ja lühimälu funktsioonide osas, kusjuures poisid ületasid tüdrukuid visuaal-ruumilise taju osas (**I, II, IV** uurimus).
- Kognitiivsete häirete struktuuri kindlakstegemine fokaalse ajukahjustuse läbiteinud lastel on väga oluline, et võimalikult vara sekkuda individuaalselt sobiliku treeningu- ja õppeprogrammiga, ennetamaks nii edaspidise elu käigus ettetulevaid kognitiivseid ja akadeemilisi ebaõnnestumisi.

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Cognitive development of children with hemiparesis

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SUMMARY

Cognitive disorders (CD) affect perceptual processes, thinking and the acquisition of new information. This impairment of CD may manifest itself when the children have to complete complex academic skills. The aim of the following study was to investigate the effect of unilateral brain injury on the cognitive functions (CF) in hemiparetic (HP) children using the neuropsychological test-battery NEPSY (Korkman '85). 23 patients with left-hemisphere lesion (LHL) and 14 with right hemisphere lesion (RHL) as 13 normal controls were examined in 4-8 yr. age group. The patient was divided into two groups: congenital hemiparesis (CHP) 31 and acquired hemiparesis (AHP) 6. Neuropsychological (NP) assessment revealed, accepting the findings of MRI and CT scans, that the side of brain lesion was important factor for predicting CD in HP children. The LHL group demonstrated significant impairment on phonological and language tests, the RHL group was worse in visual and spatial skills. CD in children with unilateral brain damage tends to be multiple, impairment more than one CF confirmed by the individual test profiles.

INTRODUCTION

An increasing trend in the prevalence of cerebral palsy (CP) has been reported from several countries over the last 20 years. The increase is directly proportional to decreasing birthweights and short gestations, rising

from approx. 1 per 1000 live births among infants weighing over 2500 g at birth to approx. 80 per 1000 in infants weighing 1500g or less at birth (Pharoah et al. 1990). The overall rate of CP varying between 1,93 and 2,27 per 1000 births (MacGillivray et al, 1995). The last reports of the changing epidemiology of CP also indicated an increase in incidence of hemiplegias, rising from 30% to 37% of all CP cases (Pharoah et al, 1996). Due to the increasing number of specific learning disabilities, changes besides medical care need to be made to improve planning for a better special education. Childhood HP is often more than a physical problem, it is usually accompanied by a variety of the cognitive, educational, behavioral and emotional disabilities. Some of the psychological accompaniments of hemiplegia are direct consequences of the brain damage, and many reflect the complex interplay of these organic and reactive pathways of developing the brain. Unlike adults, it is difficult in many cases, to localize the lesion and predict later development, with cognitive and academic achievement. The problem becomes more evident because brain injury often does not manifest itself until these children are challenged by more complex preacademic or academic skills. Thereby, the development of CF remains an important but yet unsatisfactorily studied problem in HP children though in many cases the minor or moderate cognitive sequelae occur even in the absence of relevant motor disability (Shankaran et al, 1991). The studies of the cognitive outcome of HP in children has shown that the side of the injury is a dominant factor in determining which cognitive and behavioral functions will become reorganized after early brain damage (Isaacs et al, 1996). Whether or not specific patterns of neuropsychological deficiencies occur after CHP or AHP is the main question of the present study. We also think that cognitive assessment in HP children is a good model to find the pattern of lateralization of brain function in developing individuals. Our study was designed to assess the patterns of cognitive impairment after left or right hemisphere damage, congenital or acquired, taking CT or MRI findings into account.

MATERIAL AND METHODS

Fifty children, thirty-seven hemiparetic and thirteen controls at the age of 4 to 9 year were included into our study. The patients were selected from the children treated at neurological department on the basis of a measurable degree of hemiparesis resulting from a unilateral brain insult. The hemiparesis was determined by clinical history, neurological examination and confirmed by neuroimaging-computerized tomography (CT) scan or magnetic resonance scan (MRI) and by electroencephalography (EEG). Criteria for inclusion into the study were as follows:

- 1) Slight or moderate degree of HP, congenital or acquired
- 2) Absence of mental retardation
- 3) Use of Estonian language as maternal tongue.

In the study group, there were 22 boys (59,6%) and 15 girls (40,5%), in control group 7: 6 (53,9%: 46,1%) respectively. The patient group with right and left hemispheric injury was divided into congenital (31) and acquired (6) groups (see Tab.).

Study Group			
Children with HP	No. of children		
	Total	Boys	Girls
Congenital HP	31	18	13
Right-Side	20	9	11
Left-Side	11	9	2
Acquired HP	6		
Right-Side	3	2	1
Left-Side	3	2	1
Controls	13	7	6

Birth asphyxia was diagnosed in 22 (59,5%) cases, resuscitation at birth was needed in 7 (18,9%) children of hemiparetic group.

Language disorders (LD) was found in 23 hemiparetic children, 15 children (40,5%) with expressive LD, 5 children (13,5%) with both expressive and receptive LD, 3 children (8%) with combined LD. Dysarthria was diagnosed in 25 cases (67,5%).

Epilepsy was found in 14 cases (37,8%) of hemiparetic group (in 13 cases of children with CHP and in 1 case in AHP).

There were 27 right-handed, 7 left-handed and 3 ambidextrous children in the study group. CT or MRI images of the brain revealed pathological findings in 67% (20 cases) of the group with CHP and in 83,3 % (5 cases) of AHP group respectively.

Neuropsychological assessment.

The neuropsychological examination was performed with the aid of diagnostic

test-battery for young developmentally disabled children - called NEPSY, worked out by M. Korkman (Helsinki 1988) and adapted into the Estonian language in 1995. NEPSY test battery consists of 37 tests that tap various aspects of attention, language, learning, memory, visual perception and visual constructive function, fine motor and coordination and sensory functions. Each subject was tested individually.

Design, scoring of data and statistical analysis.

The raw scores for each test was converted into zero scored (z) and thus the mean z score for the verbal and nonverbal functions was calculated. All test scores are reported as standard deviation (SD) scores based on the distribution of a norm group of corresponding age. The test results were related to the control subjects through scoring as 0 corresponded to the mean and 1 to one SD from mean of normal subjects. These procedures permitted to not only evaluate the mean group characteristics, but also to obtain individual diagnosis and to determine the corresponding age of development of each child.

The statistical analysis (means and SD) was made by using SAS system. Comparing the means we used t-test or Wilcoxon signed rank test. The variables with abnormal distribution were tested with the chi-squared or ANOVA test. The degree of significance was set at 0,05 or 0,01.

The sum score of the NEPSY tests were also calculated. The author (AK) performed the assessment.

RESULTS AND CONCLUSIONS

In order to clarify what deficiencies were characteristic of the study group, the means on the separate NEPSY tests were compared with controls. Significant group differences ($p < 0,01$) were found for 20 tests: the Inhibition and Control (mean $-1,29 \pm 1,3$ SD versus $0,35 \pm 0,5$ SD), Sustained Concentration (mean $-1,3 \pm 1,4$ versus 0), Auditory Analysis (mean $-1,62 \pm 1,3$ SD versus $0,69 \pm 0,6$), the Relative Concepts A (mean $-1,8 \pm 1,3$ SD versus $0,15 \pm 0,8$ SD), the Relative Concepts B (mean $-1,2 \pm 1,2$ SD versus $0,3 \pm 0,4$), Naming Token errors (mean $-0,9 \pm 1,4$ SD versus $0 \pm 0,2$ SD), Reading Readiness (mean $-1 \pm 1,4$ SD versus $0,23 \pm 0,4$ SD), the Kinesthetic Praxis (mean $-0,86 \pm 1,1$ SD versus 0 ± 0 SD), the Dynamic Praxis (mean $-0,3 \pm 1,0$ SD versus $0,85 \pm 0,3$ SD), Kinesthetic Feedback from Forms (mean $-0,3 \pm 0,8$ SD versus $0,23 \pm 0,4$ SD), Kinesthetic Feedback from Movements (mean $-1,26 \pm 1,4$ SD versus $0,31 \pm 0,4$ SD), Tactile Perception of Forms (mean $-0,8 \pm 1,1$ SD versus $0,15 \pm 0,3$ SD), Discrimination of Slopes (mean $-0,28 \pm 0,5$ SD versus $0,07 \pm 0,2$ SD), the Block Construction (mean $-0,5 \pm 0,004$ SD versus $0,54 \pm 0,5$ SD), the Left-Right Discrimination (mean $-0,249 \pm 0,5$ SD versus $0,08 \pm 0,2$ SD), Digit Span (mean $-0,8 \pm 1,4$ SD versus $0,75 \pm 0,45$ SD), Word Span (mean $-0,27 \pm 0,8$ SD versus $0,23 \pm 0,4$ SD), Memory For Faces (mean $-0,8 \pm 1,1$ SD versus $0,08 \pm 0,4$ SD), Logical Learning (mean $-1,0 \pm 1,28$ SD versus $0,17 \pm 0,5$ SD) and Name Learning tasks (mean $-0,8 \pm 0,8$ SD versus $0,46 \pm 0,5$ SD). Comparing the cognitive outcome of CHP to AHP group attention deficit was registered in both groups. There were no significant differences in language functions, although, the CHP group scored slightly worse and the AHP group was worse in motor and tactile skills. This trend probably reflects the fact that the AHP group included more severe forms of hemiparesis. The delay of the visuospatial functions was registered in both groups. The memory abilities were more impaired in CHP group, but no statistical difference was established.

The results of cognitive outcome in HP children was also studied in regard to the side of MRI or CT scan findings. 14 children with HP had a unilateral parenchymal lesion (6 in right and in 8 left hemisphere), and bilateral lesions were seen in eight children. The neuropsychological test profiles showed significantly poorer scores in left hemisphere lesion group on Auditory Analysis of Speech, Relative Concepts, Naming Colors, Oral Kinesthetic Praxis and in right hemisphere lesion group on Block Construction, Venger's Test of Strategy, Neglect, Digit Span, Memory for Faces and Name Learning. There was a significant relationship between hemispheric side of injury and shifts in cerebral lateralization of CF in our study. The LHL group delayed mainly in language tasks, as RHL scored poorer in spatial functions and memory for faces and digits span.

In conclusion, the results suggest that cognitive impairment in children with unilateral brain damage tends to be multiple and essentially depends on the side of the hemispheric lesion rather than age at injury. This view was also supported by other studies (Isaacs et al, 1996, Koelfen et al, 1993, Satz et al, 1988). The poor scores on phonological analysis (78,4% of HP children can't perform it), language and attention tests frequently accompanied by deficiencies on visuo-motor production (impaired in 63

%), logical learning and immediate memory. The individual test profile indicated a noticeable impairment in more than one CF in a child with HP. In addition, the NP tests are aimed to detect some specific, narrow ability and appear to be more informative with respect of diagnosing the types of neurodevelopmental impairments. The latter results also reinforce the findings of Korkman et al. (1996). The hemiparetic children with seizure disorders performed all tests below the normal score, but especially impaired were immediate memory, logical learning and attention capacities.

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Cognitive Outcome of Children With Early-Onset Hemiparesis

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ABSTRACT

The aim of this study was to examine the cognitive outcome of children with congenital and acquired early-onset unilateral brain lesions associated with hemiparesis. The neuropsychologic evaluation was done using the NEPSY test battery on 37 children with hemiparesis and 13 sex- and age-matched healthy controls. Compared to the controls, children with left-sided brain lesions had significant delay in phonologic and language functions, while children with right-sided brain lesions performed more poorly in visual and spatial skills and in somatosensory functions. There were more left-handed children in the former (6 of 23) than in the latter (1 of 14) group. There was no significant difference in cognitive outcome between children with congenital and acquired lesions. The cognitive outcome of boys and that of children with active epilepsy was more affected. Overall, the patients showed impairment in many cortical functions and diffuse cognitive delay compared to controls and the side of lesion, active epilepsy, and male gender were significant factors in predicting cognitive outcome. (*J Child Neurol* 2000;15:581-587).

Cognition is an integral part of both innate and adaptive behavior and thus constitutes the basis of successful learning. Cognitive disorders affect perceptual processes, thinking, and the acquisition of knowledge and new information. Complex cognitive skills, such as calculating, language, reading, and spelling require the simultaneous integrated activity of many brain systems. Thus, children with brain lesions often have a disorder affecting more than one cognitive function.¹ Although considerable new knowledge has been obtained on the brain-behavior relationship in adults, very little information is available on these aspects in children. A focal brain lesion in childhood similar to one that invariably results in specific disorders in adulthood does not necessarily result in a persistent deficit of specific cognitive function.²⁻⁴ One explanation for that is the better recovery of younger brain because of its greater neuronal plasticity.⁵ The plasticity of the central nervous system depends on experience and the anatomic and physiologic characteristics of the central nervous system; recovery might occur where functional overlap between systems is possible or

where systems can be duplicated.⁶ Early damage in childhood might occur in neurons that have not yet fully myelinated and undergone dendritic arborization, and are thus not fully incorporated into higher cortical functions. The cognitive deficits of early trauma might not be detected at the time of insult, but instead at adolescence or when affected children are challenged by more complex academic skills.⁷

Previous studies of the cognitive outcome of early unilateral brain lesions have generated conflicting findings. The findings of Vargha-Khadem⁸ suggest that the side of lesion does not affect verbal or visuospatial discrepancies, except in children with seizures. Aicardi and Bax⁹ supported the adult pattern of side-specificity in the case of lesions acquired in later childhood. Nass¹⁰ found that children with left-sided lesions had reading difficulties and more problems with language-based academic skills.

It has been argued that the hemispheres have the same cognitive potential at birth and that lateral specialization of cognitive functions develops slowly throughout childhood.^{8,11} It also has been shown that neuroanatomic asymmetries in the adult brain are matched by similar asymmetries in the neonatal brain^{12,13} and that functional asymmetry between the left and right cerebral hemispheres already exists at birth.¹⁴ Blood flow is predominantly in the right hemisphere between 1 and 3 years of age, whereas asymmetry shifts to the left hemisphere after 3 years of age. Accordingly, the period of vulnerability would be more prolonged in the left hemisphere, accounting for the greater occurrence of left

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sided over right-sided lesions. Some authors have argued that the left hemisphere develops earlier, particularly the language areas.¹⁵ It is thought that during maturation the hemispheres can fail to become specialized at the usual rate, therefore leading to cognitive disorders.¹⁶ The age of a child when he or she develops cerebral injury is an important factor for predicting cognitive disorders, as early damage can reduce overall intelligence.¹⁷

It is known that hemispheric brain lesions in adults determine cognitive functioning later in life. However, it is not known if the situation is the same in children. Therefore, the present study was commenced using a diagnostic neuropsychologic test battery developed especially for disabled children. The aim of this study was to discover the answers to the following questions concerning children with early-onset nonprogressive unilateral brain lesions associated with hemiparesis:

1. What is the overall cognitive outcome?
2. What is the association between the side of the unilateral brain lesion and cognitive outcome?
3. How does the etiology of unilateral brain lesion (ie, congenital versus acquired lesion) influence cognitive performance?
4. What is the association between gender and cognitive outcome?
5. What is the association between epilepsy and cognitive outcome?

METHODS

Subjects

The study was performed at the Children's Hospital of the University of Tartu. Fifty children (37 hemiparetics and 13 controls) aged 4 to 9 years participated in our study. The patients were selected consecutively from among the children with a measurable degree of congenital or acquired hemiparesis treated at the neurologic department from January 1, 1995 to December 31, 1998. Most of these children came from southern Estonia. The methods included a clinical history, physical neurologic examination, and confirmation by computed tomography (CT) or magnetic resonance imaging (MRI) and electroencephalography (EEG). The following were criteria for inclusion in the study: (1) slight or moderate hemiparesis, either congenital or acquired, (2) normal intellectual development determined by clinical examination related to the age norms of the Developmental Scale Battery developed by Talvik et al,¹⁸ (3) use of the Estonian language as mother tongue, and (4) age from 4 to 9 years.

The study group had a history of normal mental development in the first year of life. The school-aged children in our study group were attending a normal school in classes appropriate for their age. There were 22 boys (59.5%) and 15 girls (40.5%) in the study group (mean birthweight, 3248 g; mean age, 6.2 years). The number of preterm births (less than 34 weeks' gestation) was four: three boys and one girl. The average birthweight of premature infants was 1950 g.

The patient groups with right- and left-hemisphere injury were each divided into congenital (31 patients) and acquired

(6 patients) groups (Table 1). The two congenital groups (right-sided hemiparesis, 20; left-sided hemiparesis, 11) had sustained injuries either prenatally or neonatally. In three cases strokes in newborns manifest with seizures. Their hemiparesis became obvious with the development of gross motor skills during the first year of life. We used the definition of Kotlarek et al¹⁹ for "congenital hemiparesis" as a nonprogressive central nervous system syndrome with spastic hemiparesis, clinically obvious in the first year of life, without any history of acute brain-damaging incidents between the age of 7 days and 1 year.

The two groups with acquired hemiparesis (right-sided hemiparesis, 3; left-sided hemiparesis, 3) consisted of those children in whom the hemiparesis became blatantly apparent after a single well-documented episode in a previously healthy child. The mean age at insult in the acquired group was 35 months. In five cases the lesion was recognized as an ischemic infarct in the region of the medial cerebral artery. One remaining child with acquired hemiparesis had a brain hemorrhage.

In our study the lesion was more often located in the left hemisphere, which was the case in 23 children (11 boys and 12 girls), than in the right hemisphere (11 boys and 3 girls). The side of injury was decided by clinical neurologic and CT or MRI findings. There were seven (18.9%) left-handed children, and left-handedness was more common in cases of left-sided than right-sided lesions (6 of 14 versus 1 of 13; Table 2). Interestingly, right-handedness was recorded in 14 of 23 children with left-hemisphere lesions.

Epilepsy was diagnosed in 14 children (37.8%), 13 in the congenital and 1 in the acquired group. The onset of epilepsy took place before the age of 5 years in 11 patients and after the age of 5 years in 3 patients. Generalized tonic-clonic seizures were the most common form of epilepsy in the study group (occurring in eight children), followed by complex partial seizures (in six children). EEG revealed spike-wave discharges and sharp and slow-wave complexes in the right hemisphere in seven children and in the left hemisphere in four children. Generalized spike-wave complexes were observed in a further three patients. There were eight children with right-sided hemiparesis and six with left-sided hemiparesis in the epilepsy group. All patients with seizures were on anticonvulsant medication (10 children were on monotherapy, including valproate, carbamazepine, or phenytoin, and 4 were on polytherapy); 12 remained seizure free for longer than 1 year.

We selected controls at random from kindergarten and grade school according to age, gender, and socioeconomic status. Parental permission for their children's participation in the neuropsychologic study was obtained. The control group was normal according to neurologic examination and consisted of seven boys and six girls.

Table 1. Study Group

	No. of Children		
	Total	Boys	Girls
Congenital hemiparesis	31	18	13
Right side	20	9	11
Left side	11	9	2
Acquired hemiparesis	6	4	2
Right side	3	2	1
Left side	3	2	1
Controls	13	7	6

Table 2. Preferred Hand

Side of Lesion	Right Handed	Left Handed	Ambidextrous	Total
Left	14	6	3	23
Right	13	1	0	14
Total	27	7	3	37

Computed Tomography and Magnetic Resonance Imaging

All 37 patients underwent neuroradiologic examination; 3 did so twice. There were 33 CT and 4 MRI examinations. For CT examinations, Somatom AR HP or Pfizer 450 equipment was used and for MRI examinations, Acutscan (Instrumentarium Corp, 0.02 Tesla) equipment was used. The standard axial slices were acquired with 5- to 10-mm slice thickness. The type and localization of each lesion was identified according to the side (right, left), depth (cortical, subcortical, deep white matter, capsula interna, or basal ganglia), and lobe where it was located. According to their size, the cerebrospinal fluid spaces (cortical sulci, fissures, cisterns, and ventricular system) were classified as normal or dilated (mild, moderate, or marked dilation) and symmetric or asymmetric. CT or MRI indicated asymmetric periventricular atrophy in 15 (40.5%) patients (10 in the left hemisphere and 5 in the right hemisphere), cortical-subcortical atrophy in 12 (32.4%) patients, maldevelopments in 6 (16.2%) patients, and asymmetric focal lesions in the region of the basal ganglia in 4 (10.8%) patients and in the region of the capsula interna in 2 (5.4%) patients. Findings were normal in 4 (10.8%) cases).

Assessing Handedness

Hand preference was identified on the basis of tasks and a questionnaire (adapted from Korkman et al^{20,21}) in which subjects indicated the hand they normally used to perform each of six special actions. Handedness was determined through the following tasks: throwing a tennis ball, drawing and erasing a cross, making small holes in paper, pretending to light a match, and putting the matches back in their box. Information on handedness was also obtained during the writing of the tasks of the Neuropsychological Assessment for Children (NEPSY). A score of 1 was given for each task performed with the right hand and 2 for a task performed with the left hand. The handedness score was a sum of individual scores. Subjects were classified as right handed (sum, 6 or 7), left handed (sum, 11 or 12), or ambidextrous (sum, 8 to 10).

Neuropsychologic Assessment

The neurocognitive assessment consisted of a comprehensive neuropsychologic test, the NEPSY, a Neuropsychological Assessment for Children, first published in Finnish.^{22,23} The NEPSY is a neuropsychologic assessment normed for children aged 4 to 9 years. It consists of 37 subtests in five domains: attention and executive functions, language, sensorimotor functions, visuospatial functions, memory, and learning. An international version called the NEPSY: A Developmental, Neuropsychological Assessment was recently standardized in the United States.^{20,21} The US NEPSY is equivalent to the 1988 version but is standardized for a larger age range, 3 to 12 years. Validation studies have shown that the NEPSY can discriminate between different types of language disorders,²⁴ for example, between attention disorders and specific learning

disorders.²⁵ It also reflects characteristic neurocognitive strengths and weaknesses of children with congenital hemiplegia.²⁶ Each subject was individually tested by one of the authors (A.K.).

Scoring of Data and Statistical Analyses

The raw scores for each test were converted into Z-scores and the mean Z-score for the verbal and nonverbal functions was calculated. The test results were related to the control subjects through scoring, as 0 corresponded to the mean and 1 to one standard deviation from the mean of normal subjects. This procedure permitted us not only to evaluate the characteristics of the mean group of children with unilateral brain lesions, but also to obtain an individual diagnosis and determine the corresponding age of development.

The program S-PLUS for Windows (Mathsoft Inc) was used for the statistical analyses. Profile analysis methods were used to compare the profiles of specific categories of test results between different groups of children. Since we were unable to reject the hypothesis of parallel profiles (for any of the test categories), it was possible to use analysis of variance for average test results in each category. Individual test results were standardized beforehand.

RESULTS

Comparison of Congenital and Acquired Hemiparetic Groups With Controls

Attention Tests

Results of attention tests (Table 3) indicated that the congenital and acquired hemiparesis groups scored significantly lower ($P < .01$) than control children in General Orientation, Inhibition and Control, and Sustained Concentration tests. The acquired hemiparesis group fared slightly worse in the Attention subtests, but there were no differences between the two hemiparetic groups.

Language Tests

The children with congenital and acquired hemiparesis scored significantly lower ($P < .01$) than controls in Verbal Fluency, Auditory Analysis, Comprehension of Instruction, Relative Concepts, Token Test, Naming Token errors, Naming Token time, Oral Kinesthetic Praxis, and Reading Readiness. No significant differences in verbal skills were recorded between congenital and acquired hemiparesis groups.

Motor and Sensory Test

The children with congenital and acquired hemiparesis were significantly ($P < .01$) more impaired than the control group in Kinesthetic Praxis, Dynamic Praxis, Kinesthetic Feedback From Movements, Tactile Perception of Forms, and Visual-Motor Precision. No significant differences were recorded between congenital and acquired hemiparesis groups, but the children with acquired hemiparesis were somewhat more impaired in their motor and tactile skills.

Visual and Spatial Tests

Compared to the controls, both groups displayed significant differences in all spatial tests. The Block Construction test

Table 3. Comparison of Congenital and Acquired Hemiparesis Groups With Controls

	Subtest Scores*								
	1	2	3	4	5	6	7	8	9
Attention tests									
Controls	0.517	0.621	0.728						
Congenital	-0.196	-0.391	-0.247						
Acquired	-0.245	-0.391	-0.387						
Language tests									
Controls	0.668	1.073	0.415	0.748	1.151	0.804	0.723	0.482	0.479
Congenital	-0.259	-0.394	-0.03	-0.322	-0.434	-0.32	-0.254	-0.266	-0.191
Acquired	-0.228	-0.27	-0.622	0.199	-0.07	0.054	-0.21	0.482	-0.218
Perceptual tests									
Controls	0.652	0.789	0.777	0.627	0.655				
Congenital	-0.146	-0.155	-0.281	-0.173	-0.252				
Acquired	-0.688	-1.12	-0.389	-0.593	-1.106				
Visual and spatial tests									
Controls	0.696	0.872							
Congenital	-0.255	-0.296							
Acquired	-0.283	-0.491							
Memory tests									
Controls	0.819	0.405	0.609	0.825	0.931	0.157	0.044		
Congenital	-0.234	-0.15	-0.166	-0.241	-0.312	-0.177	-0.158		
Acquired	-0.565	-0.119	-0.554	-0.7	-0.548	0.908	0.709		

*Standardized means.

and Venger's Test of Strategy were the most impaired tasks. No significant differences between the two hemiparesis groups were recorded.

Memory Tests

Children with congenital hemiparesis did not differ significantly from children with acquired hemiparesis in memory test results. There were, however, significant differences ($P < .001$) from the control group in immediate memory tests such as Digit Span, Word Span, Memory for Faces, Logical Learning, and Name Learning. Children with acquired hemiparesis scored lower in Digit Span, Memory for Faces, and Name Learning. The acquired hemiparesis group had somewhat more problems with short-term memory than did the congenital hemiparesis group. The long-term memory function was relatively well preserved in both groups.

Association Between Side of Lesion and Cognitive Outcome

Attention Measures

The left- and right-hemisphere lesion groups scored significantly lower ($P < .001$) than control children in attention tests, and the right-hemisphere lesion group had more severe attention problems than did the left-hemisphere lesion group, the differences being significant ($P < .001$) between the groups in the performance of General Orientation, Inhibition and Control, and Sustained Concentration tests (Table 4).

Language Measures

Hemiparetic children underperformed in the language subtests. Both groups differed significantly ($P < .001$) from controls in Auditory Analysis, Relative Concepts, Verbal Fluency, Comprehension of Instructions, Token Test, Oral Kinesthetic Praxis, Reading Readiness, Naming Token time,

Naming Token errors, and Repeating Words and Non-Words. There was a significant difference ($P < .01$) in Verbal Fluency function: the left-hemisphere lesion group scored lower. These children also had lower scores in other language tests, as they had more problems with verbal skills. The comparison of verbal functions, taking into account the CT findings, revealed greater differences for the left-hemisphere lesion group, where the children with subcortical lesions were more impaired than children with right-side lesions in language functions ($P < .01$).

Motor and Sensory Measures

The investigation of motor and sensory functions revealed that the right- and left-hemisphere lesion groups were both significantly more impaired ($P < .001$) than the controls. In general the right-hemisphere lesion group scored lower than the left-hemisphere lesion group, and there was a significant difference ($P < .01$) between groups.

Visual and Spatial Measures

Both the right- and left-hemisphere lesion groups had impaired visuospatial functions; in this respect they differed from the control group ($P < .001$). There was not, however, a notable statistical difference ($P < .19$) between the right- and left-hemisphere lesion groups, although the right-hemisphere lesion group demonstrated lower scores. We revealed a significant ($P < .016$) site-specific visuospatial deficit in patients whose clinical findings we confirmed using CT or MRI. In fact, the children with focal right-hemisphere lesions displayed lower scores than did the left-side focal lesion group.

Memory Measures

The right- and left-hemisphere lesion group scored lower than the controls ($P < .001$) in the short-term memory subtests. Differences between the left- and right-side lesion

Table 4. Comparison of Left- and Right-Hemisphere Lesions

	Subtest Scores*									
	1	2	3	4	5	6	7	8	9	10
Attention tests										
Controls	0.517	0.621	0.728							
Left side	0.21	0.05	-0.112							
Right side	-0.929	-0.709	-0.529							
Language tests										
Controls	0.668	1.073	0.415	0.748	1.151	0.804	0.723	0.482	0.479	0.662
Left side	-0.228	-0.27	-0.622	0.119	-0.01	0.054	-0.21	0.482	-0.218	-0.336
Right side	-0.101	-0.264	0.217	-0.14	-0.338	0.097	-0.134	0.038	0.046	-0.139
Perceptual tests										
Controls	0.652	0.789	0.777	0.627	0.655					
Left side	0.173	0.085	-0.214	-0.126	-0.124					
Right side	-0.894	-0.646	-0.431	-0.431	-0.64					
Visual and spatial tests										
Controls	0.696	0.872								
Left side	-0.08	-0.233								
Right side	-0.561	-0.478								
Memory tests										
Controls	0.819	0.405	0.609	0.825	0.931	0.157	0.044			
Left side	-0.294	0.177	-0.213	-0.057	-0.272	-0.294	0.087			
Right side	-0.259	-0.717	-0.232	-0.728	-0.47	0.271	-0.239			

*Standardized means.

groups existed in the short-term memory function, where the right-hemisphere lesion group performed less well, although the differences were not significant ($P < .11$).

Association Between Gender and Cognitive Function

Attention Measures

According to our findings, boys demonstrated significantly lower ($P < .001$) results in the attention domain than did girls (Table 5). In addition, we established the effect of lateralized brain lesion on the attention function in the boys' and girls' groups separately. Boys with right-hemisphere lesion had significantly lower results on the Orientation test (-1.94 versus 0.6) than boys with left-side lesions; in addition, boys with right-side lesions also underperformed in other attention tests. Hemiparetic girls also had attention problems. Girls with right-hemisphere lesions demonstrated significantly lower scores ($P < .05$) in the Inhibition and Control test (mean, -2.33 versus -0.33) and in the Sustained

Concentration test (mean, -1.5 versus -0.58) than girls with left-hemisphere lesions.

Language Measures

The comparison of the language skills of boys and girls revealed a significant ($P < .01$) deficit in the boys' group, while girls performed these tasks better.

Motor and Sensory Measures and Visual and Spatial Measures

There were no significant differences ($P < .3$), between the performance of boys and girls in either motor or sensory tests or in visual and spatial functions ($P < .3$).

Memory Measures

Significant differences ($P < .05$) between boys and girls were revealed in memory function, where the girls scored higher in Digit Span and Word Span and in long-term memory tests.

Table 5. Effect of Gender on Cognitive Functions

	Subtest Scores*									
	1	2	3	4	5	6	7	8	9	10
Attention tests										
Boys	-0.44	-0.561	-0.555							
Girls	0.21	0.0306	0.197							
Language tests										
Boys	-0.44	-0.571	-0.386	-0.527	-0.455	-0.524	-0.367	-0.405	-0.377	-0.357
Girls	0.083	-0.059	0.308	-0.172	-0.271	0.134	-0.046	0.179	0.072	-0.059
Perceptual tests										
Boys	-0.436	-0.297	-0.311	-0.413	-0.307					
Girls	0.136	-0.287	-0.274	0.072	-0.33					
Visual and spatial tests										
Boys	-0.197	-0.157								
Girls	-0.363	-0.607								
Memory tests										
Boys	-0.487	-0.428	-0.413	-0.319	-0.41	-0.082	0.024			
Girls	0.069	0.298	0.084	-0.163	-0.237	-0.047	-0.096			

*Standardized means.

Association Between Epilepsy and Cognitive Function

Hemiparetic children with seizures differ significantly ($P < .05$) from the seizure-free hemiparetic group in memory function (Table 6); they had more problems performing short-term memory tasks. We found delayed cognitive development in the group with hemiparesis with epilepsy.

In multiple regression analysis we took into account the effect of site, gender, and epilepsy status on cognitive development. We revealed that in the Attention domain the site of the brain lesion (right hemisphere; $P < .001$) and gender (boys; $P < .05$) were significant risk factors predicting further cognitive delay. In the verbal domains, site (left hemisphere; $P < .05$) and male gender ($P < .05$) were factors that predicted more severe cognitive dysfunction. The results revealed that memory function was related to epilepsy ($P < .05$) and male gender ($P < .05$) and that these factors influenced cognitive outcome.

DISCUSSION

The development of cognitive function was investigated in a group of children with congenital or early-onset acquired left- or right-sided nonprogressive brain lesions associated with hemiparesis and compared to the data on sex- and age-matched, randomly selected, healthy controls. Cognitive abilities were significantly reduced in children with congenital or acquired unilateral early-onset hemispheric lesions. In many instances impairment was diffuse, affecting attention, phonologic analysis, logical learning, tactile and visuo-motor precision, and memory functions. Our results are in agreement with some studies,^{27,28} yet contradict some other studies that suggest that after early unilateral brain damage, particularly in the absence of seizures, language and verbal intelligence generally develop well.²⁸⁻³¹ This contradiction is most likely due to differences in the patient populations studied.

The profile of cognitive impairment was not directly related to the time of the injury, as was also demonstrated by Isaacs et al.³¹ We believe that the less-intensive impairment of cognitive function after early brain injury is due to improved brain plasticity at this stage of development. The left hemisphere undergoes a rapid maturation process after birth and is thereby more frequently affected.¹⁵ Our results support the hypothesis that the human cerebral hemispheres are already specialized at an early stage of development and that the period of vulnerability is more prolonged for the left

than for the right hemisphere. Like many other authors,^{9,28,31-33} we also emphasize an adult pattern of side specificity for brain lesions in children with hemiparesis.

Our observations that verbal function was relatively well preserved after left-hemisphere lesion and that children with right-sided injury performed on language tests below normal scores are in line with the suggestion that language has priority during development, regardless of the side of lesion.³⁴ Our findings indicate diffuse depression of cognitive functions in hemiparetic children. These results do not contradict the side specialization of brain functions in early childhood, since this functional reorganization of verbal skills in children with unilateral brain lesions is due to the plasticity of the developing brain rather than to the non-specificity of brain functions.

The significant negative effect of right-sided brain lesion on visuospatial functions also has been reported elsewhere.³³ The observation that children with right-hemisphere lesions had impaired visuospatial functions and impaired processing of complex functions might be explained by the assumption that the intact left hemisphere could not reorganize the complex visuospatial skills, as reported by Kohn and Dennis.³⁵

The greater impairment of memory function in hemiparetic boys than in girls could be associated with a more severe attention-deficit in boys. It is quite understandable that active epilepsy also had a depressive effect on memory functions.

It has been demonstrated that early left-hemisphere lesions are associated with pathologic left-handedness, impaired language function, and a shift of language to the right hemisphere.^{27,28,36-38} The prevalence of left-handedness is about 8% in the normal population.³⁹ In our study this figure was greater (20% in the whole group and even more in children with left-hemisphere injury). It is peculiar that there were 15 children with same-sided handedness and hemiparesis (14 right-sided and 1 left-sided). This might be explained by the phenomenon of shifting some central functions to the contralateral hemisphere, as presented above.

We conclude that (1) diffuse cognitive delay in comparison with controls is associated with unilateral brain damage in children, (2) the side of damage is an important factor in predicting the profile of cognitive disorders: left-sided brain injury is associated with significant impairment in phonologic and language tests and right-sided injury is associated with impaired attention, visuospatial, and language functions, (3) there were no significant differences between the cognitive outcome of children with congenital

Table 6. Memory Tests in Children with Epilepsy

	Subtest Scores*						
	1	2	3	4	5	6	7
Controls	0.819	0.405	0.609	0.825	0.931	0.157	0.044
No seizures	0.061	0.071	-0.174	-0.308	-0.364	0.193	0.287
Seizures	-0.86	-0.53	-0.302	-0.304	-0.315	-0.52	-0.502

*Standardized means.

and acquired hemiparesis, (4) the cognitive outcome of girls was less strongly influenced than that of boys, and (5) the cognitive outcome of children with active epilepsy was more strongly affected than that of children without epilepsy.

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Neurocognitive development of children with congenital unilateral brain lesion and epilepsy

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Abstract

The aim of this study was to specify the neuropsychological deficits characteristic of children with unilateral non-progressive brain lesion. In order to assess these specific functions, we used a comprehensive model of congenital hemiparesis with partial epilepsy and newly diagnosed partial epilepsy without hemiparesis. The neuropsychological examination was performed using the NEPSY test battery on 44 children aged from 4 to 9 years. The children were divided into three groups: 18 children suffering from congenital hemiparesis with chronic partial epilepsy, 12 children with newly diagnosed partial epilepsy prior to anti-epileptic treatment, and 14 healthy controls matched by sex, age, and socioeconomic status. Children with congenital hemiparesis and epilepsy had a more clearly expressed cognitive dysfunction, especially in language, visuo-perceptual and memory tasks, than children with newly diagnosed partial epilepsy. The profile of cognitive weakness appears to be diffuse and quite similar in both groups, and it did not demonstrate a clear effect of lateralization, according to the side of epileptic electroencephalogram discharges. Children within both groups are likely to have a high risk of developing attention, phonological, visuo-perceptual, and memory deficits in their life. Especially interesting and surprising was the fact that the newly diagnosed epilepsy group demonstrated impairment not only in attention, visuo-perceptual and short-term memory skills, but also in auditory perception, lexical function, and the comprehension of speech. Therefore, it is recommended that children with epilepsy would undergo neuropsychological examination in order to assess their cognitive abilities. © 2001 Elsevier Science B.V. All rights reserved.

Keywords: Cognition; Hemiparesis; Epilepsy; Cerebral palsy; Unilateral brain lesion; Neuropsychological testing; Children

1. Introduction

Unilateral focal brain lesions may cause specific long-lasting deficiencies in the cognitive functions processed by the injured hemisphere [1–4]. Some forms of childhood epilepsy have a direct impact on cognition. The normal pattern of cerebral dominance is altered by the presence of epileptic foci, and the epileptic hemisphere may lose some of its special functions [5,6].

Several studies have shown that the hemispheres of the human brain are already asymmetrical at birth, and reach complete functional asymmetry during adolescence [4,7,8]. Yet a related question is why children with congenital lateralized brain damage do not typically demonstrate clear effects of lateralization and cognitive dysfunctions according to the damaged side [1,2,5].

Though clinicians are confronted daily with these problems, this relationship in children remains poorly understood. According to this background and based on

our recent research [9,10] we wish to find answers to the following questions:

1. What differences would occur in the degree and pattern of cognitive impairment between the two groups representing different types of focal brain lesion, such as congenital hemiparesis combined with epilepsy and newly diagnosed partial epilepsy prior to anti-epileptic medication?
2. What is the relationship between partial epilepsy and cognitive outcome in children with congenital hemiparesis?
3. What is the relationship between newly diagnosed non-medicated partial epilepsy and cognitive development in children?

2. Methods

2.1. Subjects

Forty-four children aged from 4 to 9 years were investi-

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gated: 18 children had congenital hemiparesis associated with partial epilepsy, 12 children had newly diagnosed partial epilepsy, and 14 healthy children were the controls. Patients were selected at random among children with a mild or moderate degree of congenital hemiparesis and from among children with newly diagnosed active partial epilepsy prior to anti-epileptic treatment at the Department of Pediatric Neurology at the Children's Clinic of Tartu University Clinics between 1 January 1995 and 1 June 1999.

The criteria for inclusion in the study were the following:

1. A mild or moderate degree of congenital hemiparesis with epileptic seizures of focal origin.
2. Newly diagnosed partial epilepsy prior to anti-epileptic treatment.
3. Normal psychometric intelligence determined by psychological examination using the Developmental Scale Battery developed by Talvik et al. [11] and the Kaufman Assessment Battery for Children [12]; thus, intellectually disabled children were excluded.
4. Use of the Estonian language as mother tongue.

In the study groups there were 15 boys and 15 girls. The mean age of the hemiparetic group during the study was 6 years 8 months, in the newly diagnosed epilepsy group 6 years 7 months and in the controls 6 years 5 months, whereas the mean birth weight was 3110.6 (± 556), 3556.8 (± 327), and 3450.0 (± 300) g, respectively (Table 1).

Eighteen children with congenital hemiparesis fulfilled the diagnostic criteria for 'congenital hemiparesis' established by Kotlarek et al. [13]. The hemiparesis was determined on the basis of physical neurological examination, and unilateral brain lesion was confirmed using computerized tomography (CT) or magnetic resonance imaging (MRI). In this group we had eight children with right-hemisphere lesion and ten children with left-hemisphere lesion.

The International League Against Epilepsy 1981 classification of epileptic seizures was used for definitions and the principles for diagnosis. A seizure was classified as partial when there was evidence of a clinical partial onset and characteristic focal electroencephalogram (EEG) findings. Children with partial active epilepsy (including simple partial seizures, complex partial, and partial with secondary generalization) were included in the study. The epileptic

focus of the children was determined using awake and/or sleep EEG recorded in every case during the interictal state. Electrodes were applied according to the 10–20 systems. Four montages, bipolar and referential, were used for visual analysis. The recording included eye opening, hyperventilation for 3 min plus 2 min follow-up, and intermittent photic stimulation. EEG was analyzed by one of the authors (neurophysiologist A.B.).

In the group of hemiparetic children complex partial seizures were diagnosed in 17 children, and a remaining child had simple partial seizures. In this group (12 boys and six girls) the mean age at onset of epilepsy was 3 years 10 months. All hemiparetic children with epilepsy were on anti-convulsant medication: 17 children were undergoing monotherapy, including valproate (seven cases), carbamazepine (nine cases), and phenytoin (one case), and one child was receiving valproate combined with carbamazepine.

Twelve children (three boys and nine girls) with newly diagnosed active partial epilepsy formed the second group. There were seven children with epileptic EEG discharges in the left and five children with such discharges in the right hemisphere. These children had not previously used anti-epileptic drugs. The mean age at onset of epilepsy in this group was 4 years 3 months.

The etiology of brain lesion in the study groups did not include any infections, or vascular or other acquired causative factors. Thus, the etiology was congenital in all children with hemiparesis and in six children with newly diagnosed epilepsy, and remained unknown in six further children in the latter group.

The study group had a history of normal first-year development, evaluated by the Developmental Scale Battery, and the psychometric intelligence according to the Kaufman Assessment Battery for Children was over 80. In addition, the school-aged children were attending a normal school in a class appropriate for their age.

The control group of 14 children (seven boys and seven girls) was selected at random from kindergartens and schools on the basis of sex, age and socioeconomic status. Clinical and neurological examinations of these children showed normal findings, and they were also otherwise healthy. Their parents' oral permission was required for neuropsychological study.

Table 1
Main characteristics of the study groups

	Children with hemiparesis and epilepsy (n = 18)	Children with newly diagnosed epilepsy (n = 12)	Control group (n = 14)
No. of boys	12	3	7
No. of girls	6	9	7
Birth weight (g) (mean \pm SD)	3110.6 \pm 556	3556.8 \pm 327	3450.0 \pm 300
Mean age during the study (years/months)	6/8	6/7	6/5
Mean age at onset of seizures (years/months)	3/10	4/3	
Right-side hemiparesis (n)	10		
Left-side hemiparesis (n)	8		

2.2. Neuropsychological assessment

In order to detect and specify the primary and secondary cognitive deficits in a detailed manner, it is important to use the sensitive neuropsychological subtests appropriate for the children's developmental age. The neuropsychological examination was performed with the aid of a test battery called NEPSY, intended for young developmentally disabled children and developed by Korkman [14,15] and translated into Estonian in 1995. The NEPSY test battery is based on Luria's methods, and has been adapted for the assessment of congenital or acquired brain dysfunctions, as in the quantitative description of a patient's cognitive status in numerous types of brain-dependent cognitive abilities.

NEPSY is intended for children aged from 4 to 9 years. It consists of 37 subtests subdivided into five areas: attention and executive functions, language, sensorimotor functions, visuo-spatial functions, and memory and learning. An international version called NEPSY: A Developmental Neuropsychological Assessment was recently standardized in the United States [16,17]. Validation studies have shown that NEPSY can discriminate between different types of language disorders, i.e. between attention disorders and specific learning disorders.

Each subject in the present study was tested individually by one of the authors (A.K.).

The following 24 subtests were administered within the present study:

1. General Orientation – a test of knowledge of personal and environmental data.
2. Inhibition and Control – a test evaluating control impulses.
3. Sustained Concentration – the time the subject is able to keep working during the test sessions.
4. Verbal Fluency – naming as many animals as possible in 1 min and, similarly, things to eat or drink.
5. Auditory Analysis of Speech – a test that demands recognition of words that are pronounced by the examiner as separate parts ('g-itl').
6. Comprehension of Instructions – measures the ability to follow complex instructions in paper-and-pencil tasks.
7. Relative Concepts – comprehension of concepts such as 'between', 'forward', etc.
8. The Token Test, the subject points out or manipulates tokens according to spoken instructions.
9. Naming Tokens, the child is to name size, color, and shape of the tokens from the Token Test as quickly as possible; the score used in this context consists of the number of correct answers rather than a time score.
10. Naming Token, time.
11. Repeating Words and Non-Words, for example 'screw-driver' and 'pylobity'.
12. Reading Readiness – a test that demands recognition of the letters in a child's name or written on paper (A, E, U, I, P, M), and also reading words such as CAR...
13. Storytelling – a story is read out to the child, who is then asked to retell it.
14. Kinesthetic Praxis – the subject imitates complex positions of fingers.
15. Dynamic Praxis – the subject has to produce motor series with both hands simultaneously.
16. Visual-Motor Precision – is assessed by having the subject draw lines along given intricate shapes.
17. Venger's Test of Strategy – the task is to find the right path using maps (picture book, six tasks).
18. Digit Span – the child has to continue series of digits.
19. Word span – the child has to continue series of words.
20. Memory for Faces – the task is to find eight pictures of faces previously presented among other pictures.
21. Logical Learning – the subject first listens to a story and then answers questions concerning the content.
22. Name Learning – learning the names of seven children on photographs.
23. Delayed Recall for Faces – the task is to find eight pictures with faces half an hour after their first presentation (test 30).
24. Delayed Recall of Name Learning – the same photos and names as in test 22 to be remembered after 30 min.

2.3. Electroencephalographic examination

The EEG was evaluated visually. EEG did not show a normal background in any of our patients (Table 2), while general background slowing (polymorphic theta, delta activity) was detected in seven patients with congenital hemiparesis and in two patients with newly diagnosed epilepsy. Focal background slowing (lateralized poly-

Table 2
EEG background activity findings in patients with epilepsy and hemiparesis

	Normal		General slowing			Focal slowing		
			Left hemisphere			Right hemisphere		
	Frontal	Temporal	Frontal	Temporal	Temporo-parietal	Frontal	Temporal	Temporo-parietal
New cases (n = 12)	0	2	1	0	4	0	2	3
Cases with congenital hemiparesis (n = 18)	0	7	0	0	6	2	1	2

Table 3
Epileptiform discharges in EEG of patients with epilepsy and hemiparesis

	No. of discharges	Bilateral discharges	Focal discharges					
			Left hemisphere			Right hemisphere		
			Frontal	Temporal	Temporo-parietal	Frontal	Temporal	Temporo-parietal
New cases (<i>n</i> = 12)	0	0	1	0	6	1	2	2
Cases with congenital hemiparesis (<i>n</i> = 18)	0	1	1	0	4	1	3	6

morphic theta–delta activity) was identified in ten cases with newly diagnosed epilepsy and in 11 cases with congenital hemiparesis. Focal background activity was recognized more frequently in the right than in the left temporo-parietal regions (15 vs. 12).

Epileptic discharges were most frequently recognized in the temporo-parietal regions in both groups (Table 3). There were no great differences in the lateralization of epileptic discharges between cases of congenital hemiparesis with epilepsy and those of newly diagnosed epilepsy. Epileptiform activity was recorded in the temporo-parietal regions, with shifting from left to right hemispheres in one child with congenital hemiparesis.

2.4. Neuroimaging

CT or MRI was performed on all the hemiparetic and epileptic children to define the type and extension of the brain lesion. For CT examinations Somatom AR HP or Pfizer 450 equipment, and for MRI examinations BRUKER (TOMIKON S 200 2.0 T) equipment was used. Standard axial slices were performed at a slice thickness of 5–10 mm. A neuroradiologist (T.T.) analyzed the CT and MRI findings. The type of localization of each lesion was identified according to the side (right, left) and depth (cortical, subcortical, deep white matter, basal ganglia, capsula interna). The size of the cerebrospinal fluid spaces (cortical sulci, fissures, cisterns and ventricular system) was classified as normal or dilated, and symmetrical or asymmetrical. Abnormal CT/MRI findings were found in 12/18 hemiparetic children with epilepsy and in 6/12 children with epilepsy

alone (Table 4). We found cortical/subcortical lesions in the left hemisphere in six children, and in the right hemisphere in another six children, while a further two children had bilateral lesions. Ventricular dilatation with periventricular leucomalacia (PVL) was asymmetric in three children and symmetric in one child.

2.5. Design, scoring of data and statistical analysis

Raw scores for each test were converted into zero scores (*z*), and the mean *z* scores for the verbal and non-verbal functions were calculated. The test results were related to the control subjects through scoring, with 0 corresponding to the mean and 1 to one standard deviation (SD) of normal subjects. This procedure permitted not only the evaluation of the mean group characteristics of the children with unilateral brain lesions, but also the determination of the corresponding developmental age.

The statistical analysis (means and SD) was performed using the SAS system. Continuous and normally distributed variables were compared with ANOVA. A Wilcoxon rank test was used for abnormally distributed data. Categorical data were compared using χ^2 analysis. The degree of significance was set at 0.05 or 0.01.

3. Results

3.1. Unilateral brain lesion and cognitive development

The relation of focal brain lesion to cognition was investigated taking into account the degree and duration of brain

Table 4
Description of neuroradiological findings of study groups

CT/MRI findings	Group of children with hemiparesis and epilepsy (<i>n</i> = 18)	Group of children with newly diagnosed epilepsy (<i>n</i> = 12)
Normal findings	6	6
Symmetrical ventricular enlargement	0	1
Asymmetrical ventricular enlargement with PVL	3	0
Bilateral cortical atrophy	0	1
Hemiatrophy or cortical atrophy in left hemisphere	3	0
Hippocampal lesion in right hemisphere	2	2
Hippocampal lesion in left hemisphere	2	1
Hippocampal bilateral lesion	0	1
Atrophic lesion in right hemisphere (reg. capsula interna)	2	0

Table 5
Subtest scores of subgroups on neuropsychological assessment

	Group ^a						Differences by groups (<i>P</i> value)		
	1		2		3		1–2	1–3	2–3
	M	SD	M	SD	M	SD			
General Orientation	0.2	0.67	0.4	0.5	0.86	0.36	0.57	0.0004	0.0002
Inhibition and Control	-1.39	1.5	-0.9	0.88	-0.14	0.86			
Sustained Concentration	-1.39	1.37	-1.6	1.2	0.0	0.0			
Auditory Analysis of Speech	-1.78	1.21	-1.5	1.5	0.62	0.63	0.03	0	0.0004
Verbal Fluency	-0.28	0.46	0.1	0.31	0.21	0.42			
The Token Test	-1.39	1.29	-0.7	0.9	-0.07	0.9			
Relative Concepts A	-1.7	1.49	-1.3	1.25	0.46	0.51			
Reading Readiness	-0.9	1.4	-0.2	0.6	0.21	0.42			
Repeating Words and Non-Words	-0.94	1.14	-0.3	0.67	0.0	0.32			
Naming Tokens, errors	-0.87	1.24	-0.2	0.42	0.07	0.27			
Naming Token, time	-1.47	1.5	-1.8	1.6	-0.07	0.27			
Visuo-Motor Precision	-1.5	1.2	-0.9	1.3	-0.28	0.82	0.2	0.0002	0.0017
Dynamic Praxis	-0.64	1.5	0.02	0.42	0.0	0.0			
Kinesthetic Praxis	-0.38	1.02	-0.4	0.69	0.85	0.36			
Venger's Test	-1.06	1.14	-1.0	0.9	0.21	0.69			
Digit Span	-1.35	1.2	0.3	0.67	0.61	0.65	0.02	0	0.0002
Word span	-0.41	0.79	-0.1	0.31	0.21	0.42			
Logical Learning	-1.13	1.14	-0.8	1.03	-0.15	0.55			
Name Learning	-0.75	1.12	-0.6	0.69	0.43	0.51			
Memory Faces	-0.52	0.94	-0.3	0.67	0.07	0.47			
Storytelling	-1.13	1.14	-0.8	1.03	-0.15	0.55			
Delayed Recall Names	-0.93	1.2	0.22	0.44	-0.23	0.59	0.04	0.018	0.9
Delayed Recall Faces	-0.4	0.85	0.0	0.53	0.14	0.53			

^a 1. Group with hemiparesis and epilepsy; 2. group with focal epilepsy; 3. control group.

dysfunction. Neuropsychological testing was performed in the group of congenital hemiparesis with focal epileptic seizures (controlled by anti-epileptic drugs), in the group with newly diagnosed partial epilepsy prior to anti-epileptic medication, and in the control group. The results of the groups in the neuropsychological testing are shown in Table 5. A comparison of the NEPSY results revealed significant differences between both study groups and the control group in all five cognitive domains. Surprisingly, the profile of cognitive disabilities did not differ specifically between the two epileptic groups. However, there existed differences with respect to the degree of cognitive impairment (see Fig. 1). When the sum score for the domains was considered it was the areas of language, short-term memory and delayed recall that significantly differed between the two groups ($P = 0.03$, 0.02 and 0.04 , respectively): children with hemiparesis and epilepsy showed more severe dysfunction than those with newly diagnosed epilepsy.

3.2. Attention function

The children with focal brain lesion demonstrated a significant attention deficit. In analyses of attention processes between congenital hemiparesis and active epilepsy groups, we found unexpectedly severe impairment of the attention domain also in children with newly diagnosed epilepsy: Selective and Sustained Attention was

impaired in 8/12 and Impulse Inhibition and Control in 7/12 of these children compared to 10/18 and 9/18 of hemiparetic children, respectively. In addition, as shown in Table 5, children with newly diagnosed epilepsy performed the attention tests at a level as low as that of children with congenital brain lesions. Comparing the group of congenital hemiparesis with epilepsy and the control group in the area of attention span, the results among hemiparetic children were significantly lower than the controls ($P = 0.0004$, see Fig. 2). Children with newly diagnosed epilepsy also performed significantly less well than the controls ($P = 0.0002$, see Fig. 3).

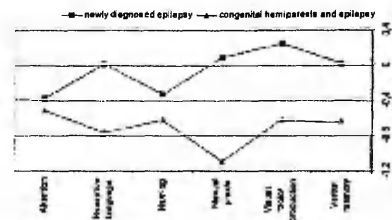


Fig. 1. Significant impairment in composite scores of receptive language, and short-term memory tasks ($P = 0.03$ and 0.02 , respectively), as impairment in manual praxis and visuo-motor precision of hemiparetic children with epilepsy compared to children with newly diagnosed epilepsy.

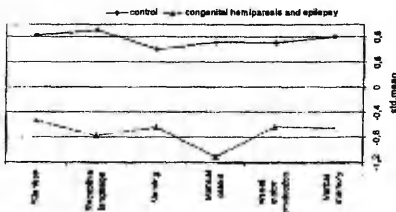


Fig. 2. Significant impairment on composite scores of attention ($P = 0.0004$), language ($P = 0.00$), visuo-motor precision ($P = 0.0002$), and short- ($P = 0.00$) and long-term memory ($P = 0.018$) tasks of children with congenital hemiparesis and epilepsy compared to control children.

3.3. Language function

Children with congenital hemiparesis showed more severe language impairment than children with newly diagnosed epilepsy ($P = 0.03$). The receptive language function was impaired in 14/18 children with congenital brain lesions and in 8/12 children with newly diagnosed active epilepsy. The corresponding test scores of the receptive language domains in children with congenital hemiparesis were lower in both Auditory Analysis of Speech (-1.78 vs. -1.5 , respectively), and in the Token Test (-1.39 vs. -0.5 , respectively) than those of children with newly diagnosed epilepsy.

The capacity of expressive language skills such as repeating words and non-words and rapid naming were impaired in 10/18 children with congenital hemiparesis, and in 2/12 children with newly diagnosed partial epilepsy.

As shown in Table 5, the congenital hemiparetic group, as well as the active partial epilepsy group, differed significantly from the results of the control group in the area of language ($P = 0.00$ and 0.0004 , respectively). The congenital hemiparesis group differed from the controls across all eight language subtests, while children with newly diagnosed partial epilepsy differed across three subtests. Reading Readiness was impaired in 9/18 children with hemiparesis and in 4/12 children with newly diagnosed

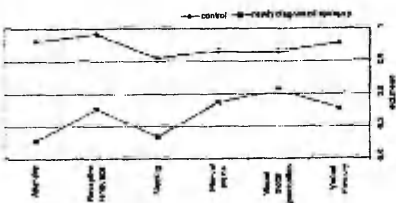


Fig. 3. Significant impairment in composite scores of attention ($P = 0.0002$), language ($P = 0.0004$), visuo-motor precision ($P = 0.0017$) and short-term memory tasks ($P = 0.0002$) of children with newly diagnosed epilepsy compared to control children.

epilepsy. We revealed a close correlation between reading disorders (Reading Readiness function) and impairment of receptive language (Auditory Analysis of Speech, $r = 0.59$) and Relative Concepts ($r = 0.65$) in both groups.

3.4. Motor and sensory function

Relatively less impairment was exhibited in the measures of manual praxis and motor and sensory integration. We found significant differences between the two study groups only in visuo-perceptual functions. Children with congenital hemiparesis underperformed this task in 12/18 cases, and children with newly diagnosed epilepsy underperformed this task in 5/12 cases. In the Visuo-Motor Precision test the children with hemiparesis attained lower scores than the children with newly diagnosed epilepsy (-1.5 vs. -0.9), but group differences did not reach significance ($P = 0.2$). In this task we revealed significant impairment in both groups compared to controls (hemiparesis group, $P = 0.0002$, and newly diagnosed partial epilepsy group, $P = 0.0017$).

3.5. Memory

One of the characteristic neuropsychological findings in the group with congenital hemiparesis was impaired memory function. The results of short-term memory and long-term memory subtests of children with congenital hemiparesis differed significantly from the results of the control group ($P = 0.000$ and 0.018 , respectively). In short-term memory measures children with hemiparesis associated with epilepsy also attained the lowest scores compared to children with newly diagnosed epilepsy (significant group differences were obtained, i.e. $P = 0.02$). They underperformed in the three main short-term memory tasks, and particularly poor results were obtained in the Digit Span (impaired in 12/18 children), Logical Learning (impaired in 10/18 children) and Story Telling (impaired in 11/18 children) tests. On the contrary, a relative strength on memory tasks was obtained in the children with newly diagnosed epilepsy. They performed these tasks on the level of the control group, especially in the case of tests of long-term memory functions, though they scored lower than the controls ($P = 0.0002$) in short-term memory subtests, especially in the Story Telling subtest, in which 6/12 children demonstrated weaknesses. A significant difference existed in long-term memory functions ($P = 0.04$) between children with hemiparesis and those with newly diagnosed epilepsy.

4. Discussion

The first aim of this study was to carry out a comprehensive neuropsychological assessment in children with focal brain lesion as manifested as congenital hemiparesis with epilepsy or epilepsy alone. The observation that the profile

of cognitive deficit appeared to be diffuse in both focal brain damage groups is a novel finding. Children in both groups displayed deficit in three to five main cognitive domains. The children with congenital hemiparesis combined with epilepsy proved to be more severely affected than the children with newly diagnosed partial epilepsy. We emphasize that children with different types of focal epilepsies expressed relatively widespread dysfunction on neuropsychological development [6,18–20]. The significant differences between the study groups and the controls were revealed in all five cognitive domains, including attention and executive, language, visuo-perceptual and short-term memory functions.

Intellectual deterioration was once thought to be common with epilepsy. It is now known to be uncommon, and usually associated with specific causes such as concomitant brain disease and specific epileptic syndromes [21]. Note that all our children had normal intellect. However, it is possible that seizure disorder may adversely influence the maturation and maintenance of normal brain function, giving a picture of cognitive impairment. There is evidence that seizures are associated with neuronal damage [22] due to a number of factors such as hyperactivity of glutamate and oxidative stress [23]. Positron emission tomography (PET) studies suggest enhanced post-lesional plasticity in childhood reflecting individual variability probably due to clinical and demographic factors besides lesion onset [24]. Other methods of studying the patterns of functional recovery of brain lesion include electromyographic responses to focal transcranial magnetic stimulation [25], PET studies [24] and neuropsychological examinations like NEPSY.

Characteristic neuropsychological findings, such as linguistic problems in naming and phonological analysis, difficulties in complex tasks of visuo-perceptual production and problems with short-term memory have also been reported previously [26,27], and seem to predispose learning disabilities, especially verbal learning problems at school. The latter position is also corroborated by the high correlations between reading disorders (Reading Readiness function) and receptive language (Auditory Analysis of Speech, $r = 0.59$) as well as verbal comprehension impairment (Relative Concepts, $r = 0.65$) in our study. The measurement of a reduced amount of peritrigonal white matter with MRI together with the neuropsychological examination is useful for detecting visuo-perceptual impairment in children with spastic diplegia [28]. Of the memory tasks, the group-specific differences were obtained in the present study on the Digit Span, on memory of a story (Logical Learning) and on all long-term memory tasks in children with congenital hemiparesis.

The second aim was to clarify what neuropsychological deficiencies were characteristic of the children with congenital hemiparesis associated with childhood partial epilepsy. The present study showed that for the children with congenital unilateral brain lesion, impairments of attention language, especially the receptive language function and

the capacity for repeating words and non-words, rapid naming, visuo-motor processing and short- and long-term memory functions were very typical.

The third aim was to examine the relationship between newly diagnosed partial epilepsy prior to medication, and cognitive development. Our study demonstrated, contrary to expectations, a high rate of neurocognitive disabilities in these children. It is also interesting that they scored poorly compared to controls in four main cognitive domains, in particular including attention and language, but also visuo-perceptual functions and short-term memory. These children performed in some cognitive domains at nearly the same low level as the children with congenital hemiparesis with epilepsy.

In the analysis of language functions, difficulties in auditory perception, in the production of phonological sequences, and in verbal comprehension tasks would tend to point to a primary and secondary deficit in the chain of cognitive subprocesses [26]. Abnormal electrographic activity, specified as a secondary deficit, was responsible for additional weakness in the language ability of the children in our study. In a study by Roberts et al. [29], adult patients with complex partial seizures prior to medication have demonstrated impaired verbal lateralization, which improved significantly after the commencement of anti-epileptic medication. Based on the latter work and a study by Bishop [30], as with our present results, epileptiform discharges and/or seizures themselves are essential causes of cognitive disability, especially of language dysfunctions. In some instances, underlying neurological structural lesions may cause both epilepsy and cognitive disorders, whereas in others this causal relationship could not be detected by either neuroimaging techniques or other methods [27]. Gordon et al. [31] have also demonstrated that frequent epileptiform discharges affecting cognitive performance may improve with anti-epileptic treatment. It has been emphasized that for the children with epileptic EEG discharges a specific abnormal pattern of cognitive dysfunction includes attention deficit and verbal auditory agnosia [32–35]. Despite a favorable medical prognosis nowadays, children with childhood-onset epilepsy are at increased risk for unfavorable educational and subsequent social outcome [30,36–38].

Our children with newly diagnosed epilepsy are now receiving anti-epileptic treatment. Early appropriate intervention including anti-epileptic drug treatment as training and supporting methods not only improve cognitive performance in children with focal brain lesion, but may also alter the size of the dysfunctional brain area in the processes of brain development. The cerebral plasticity of young individuals makes this optimism realistic [24].

It may be concluded that:

1. Children with congenital hemiparesis associated with epilepsy have severe and children with newly diagnosed partial epilepsy moderate cognitive deficit. The profile of cognitive weakness appears to be quite similar in both groups, which is a novel finding.

2. Epilepsy in children with congenital hemiparesis means a high additional risk for developing attention, phonological, visuo-perceptual, memory, and logical learning deficits later in life.
3. Children with newly diagnosed epilepsy develop impairments in attention, visuo-perceptual and short-term memory skills and they also demonstrate impaired verbal lateralization, which causes the neuropsychological malfunction in auditory perception, lexical skills and the comprehension of speech.
4. In addition to clinical neurological examination and modern neuroimaging techniques, specifying the neurodevelopmental impairments in children after focal brain lesion also requires neuropsychological assessment as a functional tool to determine subtle but stable cognitive disabilities, as children's brain dysfunctions tend to be diffuse or multifocal rather than focal.

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CEREBRAL LATERALIZATION, HANDEDNESS AND COGNITIVE DECLINE FOLLOWING CONGENITAL HEMIPARESIS IN CHILDREN

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1. INTRODUCTION

The purpose of this paper is to investigate the pattern of atypical lateralization of cognitive functions in the children with congenital focal brain damage. Explanations of anomalous cerebral organization in adults fall into two main types: natural and pathological, as natural is based on the individual variants of mechanisms that induce typical asymmetries and could be genetic¹ (the right shift theory i.e. rs+ gene), and pathological- follows various pathologies such as cerebral palsy, traumas and pathological left-handedness which distort the modal brains, and in addition authors suggest that expression of the rs+ gene is more effective in females than males. Although many authors²⁻⁷ have examined the effect of early hemispheric injury on cerebral lateralization and handedness much has remained unclear and explanations of cases of atypical cerebral lateralization is required. Isaack⁴ has proposed that these processes are demonstrated in children with hemiparesis most clearly in the handedness measures. Another issue is sex-related differences in the lateralization of cognitive functions. Although sex differences have been investigated in adults, little is known about when these gender differences emerge and how they develop, especially in brain-damaged children. Based on this background the aims of the present study were to determine:

- (1) whether and how the handedness is related to cerebral lateralization and cognitive development in children with congenital hemiparesis;
- (2) sex-related differences in cognitive development in children with congenital hemiparesis.

2. METHODS

2.1. Subjects

Fifty-six children aged from 4 to 9 years with congenital hemiparesis were investigated. 32 children had a left hemisphere lesion (LHL) with right-sided congenital hemiparesis; of these 23 were left-handed and 9 were right-handed. A further 24 children had a

right-hemisphere lesion (RHL) associated with left-sided hemiparesis; of these 21 were right-handed and 3 were ambidextrous (Table 1). Patients were selected at random among children with a slight or moderate degree of congenital hemiparesis at the Unit of Pediatric Neurology at the Children's Clinic of the Tartu University Clinics between 1.1.1995 and 1.6.2000. The methods included a clinical history, physical neurological examination, and confirmation by computed tomography (CT) or magnetic resonance imaging (MRI), and also electroencephalography (EEG) and neuropsychological assessment.

The criteria for inclusion in the study were the following:

1. A slight or moderate degree of congenital hemiparesis.
2. Normal psychometric intelligence determined by psychological examination using The Developmental Scale Battery developed by Talvik⁸ and The Kaufman Assessment Battery for Children;⁹ thus intellectually disabled children were excluded.
3. Use of the Estonian language as mother tongue.
4. Age from 4 to 9 years.

In the study groups there were 31 boys and 25 girls. Patient clinical data are presented in Table 2. All children in the study group fulfilled the diagnostic criteria for "congenital hemiparesis" established by Kotlarek¹⁰ as a nonprogressive central nervous system syndrome with spastic hemiparesis, without any history of acute brain-damaging incidents between the age of 7 days and 1 year. The hemiparesis was determined on the basis of physical neurological examination, and unilateral brain lesion was confirmed using computed tomography (CT) or magnetic resonance imaging (MRI). Epilepsy was diagnosed in 25 children (44.6%). Complex partial seizures were the most common form of epilepsy in the study group (13 children), followed by secondary generalized tonic-clonic seizures (11 children) and simple partial seizures (in one child). EEG recordings revealed spike wave discharges and sharp and slow-wave complexes in the right hemisphere in 10 children, and in the left hemisphere in 8 children. Generalized spike-wave complexes were observed in a further seven patients. In the epilepsy group there were 11 children with a right-hemisphere lesion and 14 with a left-hemisphere lesion. All hemiparetic children with epilepsy were receiving antiepileptic medication: 24 children had received monotherapy incl. valproate (10 cases), carbamazepine (13 cases), phenytoin (1 case) and one child was receiving valproate combined with carbamazepine; 18 had been seizure-free for longer than 1 year at the time of the study.

The study group had a history of normal first-year development, evaluated by the Developmental Scale Battery and the psychometric intelligence according to the Kaufman Assessment Battery for Children was over 80. In addition, the school-aged children were attending a normal school in a class appropriate for their age. To compare the processes of hemispheric specialization, which may develop at a usual or non-usual rate we used the data of the children of the control group. A control group of 14 children (7 boys and 7 girls, all right-handed) was selected at random from kindergartens and schools on the basis of age, sex and socio-economic status. Clinical and neurological examinations of these children showed normal findings, and they were also otherwise healthy. Their parents' oral permission was required for neuropsychological study.

2.2. Neuropsychological assessment

The neuropsychological examination was performed with the aid of a test-battery called NEPSY, which is intended for young developmentally disabled children and was developed by M. Korkman^{11, 12} and was standardized in Estonia in 1995. The NEPSY test-battery is based on Luria's methods, and has been adapted for the assessment of congenital or acquired brain dysfunctions, as in the quantitative description of a patient's cognitive status in numerous types of brain-dependent cognitive abilities.

NEPSY is normed for children aged 4 to 9. It consists of 37 subtests subdivided into five areas: attention and executive functions, language, sensorimotor functions, visuospatial functions, memory and learning. An international version called NEPSY: A Developmental Neuropsychological Assessment was standardized in the United States in 1995^{13, 14}. The 24 subtests, used within the present study are presented in the Appendix.

Each subject in the present study was tested individually by one of the authors (A.K.).

2.3. Assessing Handedness

Hand preference was identified on the basis of tasks and a questionnaire (adapted from M. Korkman¹¹) in which patients indicated the hand they normally used to perform each of six special actions. Handedness was determined through the following tasks: throwing a tennis ball, drawing and erasing a cross, making holes in paper, pretending to light a mach, and putting the matches back in their box. Information on handedness was also obtained during the writing of the tasks of the Neuropsychological Assessment for Children (NEPSY). Hand preference was quantified on the basis of tasks and a questionnaire in which subjects indicated the hand; they normally used to perform each of the 6 special actions.

A score of 1 was given for each task performed with the right hand and 2 for a task performed with the left hand. The handedness score was a sum of individual scores. Subjects were classified as right-handed (sum, 6 or 7), left-handed (sum, 11 or 12), or ambidextrous (sum, 8 to 10).

2.4. Neuroimaging

CT or MRI was performed on all the hemiparetic and epileptic children to define the type and extension of the brain lesion. For CT examinations Somatom AR HP or Pfizer 450 equipment, and for MRI examinations BRUKER (TOMIKON S 200 2,0 T) equipment was used. Standard axial slices were performed at a slice thickness of 5–10 mm. The type of localization of each lesion was identified on the basis of side (right, left) and depth (cortical, subcortical, deep white matter, basal ganglia, capsula interna). The size of the cerebrospinal fluid spaces (cortical sulci, fissures, cisterns and ventricular system) was classified as normal or dilated, symmetrical or asymmetrical. Abnormal CT/MRI findings were found in 44 of 56 hemiparetic children (Table 2). We found cortical/subcortical lesions in the left hemisphere in 19 children, and in the right hemisphere in 13 children. Symmetrical ventricular dilatation was found in 7 children with LHL and 5 children with RHL.

2.5. Design, scoring of data and statistical analysis

Raw scores for each test were converted into Z- scores, and the mean Z- scores for the verbal and nonverbal functions were calculated. The test results were related to the control subjects through scoring, as 0 corresponded to the mean and 1 to one standard deviation from the mean of normal subjects. This procedure permitted us not only to evaluate the characteristics of the children with unilateral brain lesions, but also to obtain an individual diagnosis and determine the corresponding age of development.

The program S-PLUS for Windows (Mathsoft Inc) was used for the statistical analyses. Profile analysis methods were used to compare the profiles of specific categories of test results between different groups of children. Since we were unable to reject the hypothesis of parallel profiles (for any of the test categories), it was possible to use analysis of variance for average test results in each category. Individual test results were standardized beforehand.

3. RESULTS

3.1. Cognitive performance and brain function asymmetries in groups with shifted hand preference

The results of cognitive performance in left-handers with a left-hemisphere lesion (LHL) and right-handers with a right-hemisphere lesion (RHL) were represented in Table 3. The neuropsychological assessment of these groups revealed, that right-handed children (RHL) scored significantly lower than left-handed children (LHL) on attention tasks ($P < 0.03$). In addition both groups performed significantly less successfully than the controls ($P < 0.001$ in RHL, and $P < 0.03$ in LHL group). The results showed most impairment in the Sustained Concentration in which 71% of RHL and 54.5% of LHL children had below-average scores. Scores in the executive domain were lower in the RHL group, and 50% of these children had below-average scores on the Token test, in contrast to 39% of the LHL group.

We revealed moderately impaired language function in both groups; they scored significantly ($P < .001$) lower than the controls on several language tasks. Receptive language and phonological processing were more impaired than speech production and verbal fluency abilities. There were no significant differences ($P < 0.14$), between the performance of left-handers and right-handers in language skills, but the right-handers with RHL performed less well in some of the language comprehension tasks, such as the Relative Concepts test that showed below-average scores for 63 % of these children (mean -2.1).

Abnormal motor and sensory integration abilities compared to controls were obtained in both left- and right-handers ($P < 0.001$ in right-handers, $P < 0.0001$ in left-handers), and difficulties were more evident in tactile perception and manual praxis tasks. The impairment was not related to the side of the brain lesion: in contrast, the left-handed children performed motor-perceptual tasks at the same level as right-handed children and differences between groups were not significant ($P < .14$).

Performance on visuomotor precision was poorer in left-handed children and 56% out of these children had below-average scores on this task compared to 44% of right-handed children.

Visual and Spatial measures differed significantly between the study and control groups ($P < .001$). Neuropsychological assessment revealed that right-handers were more impaired in the visuospatial domain than left-handers ($P < .03$). More than 55% of right-handed children obtained low scores on the Route Finding (Verger's) task, reconfirming problems in executive functions.

The investigation of memory and learning functions revealed that left-handers and right-handers were both significantly more impaired ($P < .0001$, $P < .001$ respectively) than the controls. In general, short-term memory functions, especially word span and logical learning were weaker in right-handers (RHL) than left-handers ($P < .04$). Long-term memory function was relatively well preserved in both groups (Figure 1).

3.2. Cognitive performance and brain functional asymmetries in groups with shifted and non-shifted lateral preference

The results of the neuropsychological assessment performed between the shifted and non-shifted hand preference groups are presented in Tables 4 and 5. As shown in Table 4, the children with left-hemisphere lesion (left-handers as well as right-handers) differed significantly ($P < 0.04$ – $P < 0.001$) from the controls. They demonstrated a deficit in all five cognitive realms except for the long-term memory tasks in left-handers, the scores for these being comparable to the normal controls. The same was found for the right-hemisphere lesion groups (Table 5), while ambidextrous children performed the long-term memory tasks almost as well as the controls. Left-handed children with LHL had more problems in attention functions than right-handed children, and 58% out of left-handers underperformed the Sustained Concentration task, though the differences between the two groups did not reach statistical significance. Interesting results were obtained in the language domain: the right-handed children demonstrated more severe and general language impairment than left-handed children ($P < 0.03$). The right-handed children scored more poorly in 11 of 15 language subtests. They performed poorly in both phonological and in speech production tasks. Receptive language abilities were extremely weak, the Auditory analysis test was impaired in 78% and the Token test in 67% out of all right-handers, whereas among left-handers these figures were 50% and 40% respectively. The corresponding test scores of RHL groups also showed impaired receptive language abilities in right-handed children, but as the group of ambidextrous children was too small, statistical analysis was not performed.

Visual-motor production and the sensorimotor test revealed another interesting finding. Tasks demanding motor precision did not differentiate significantly between left (a non-hemiparetic hand) and right hands (a paretic hand), but right-handers demonstrated lower scores in the visuomotor task. In contrast, spatial skills were significantly ($P < .04$) more impaired in left-handed than right-handed children (Verger's test result -1.1 compared to -0.7). Still, the most severe spatial problems were demonstrated by right-handers with RHL (Verger's test -1.6).

We found the verbal and narrative memory function to be weak, especially in the right-handers in the LHL group. Long-term memory abilities were less impaired.

The results indicated that the right-handed children with LHL displayed more cognitive dysfunctions, especially in language, visuomotor and verbal-memory tasks than left-handed children (Figure 2). The right-handed children with RHL had more problems in attention and spatial functions.

3.3. Sex-related differences in cognitive development

In this part we compared the results of cognitive performance in 31 boys to 25 girls with left and right-hemisphere lesions. According to our findings, in the group of children with LHL left-handed boys demonstrated significantly lower results in ($P < .04$) in the attention domains than left-handed girls (Table 3, Figure 3). In the group with RHL these differences were not significant, because the right-handed boys and girls were both severely impaired in the attention tasks (Figure 4). Consequently, the right-handed boys with RHL performed most poorly on attention related tasks as they also demonstrated remarkably low scores in executive tests. The comparison of language domain between left-handed boys and girls with LHL showed that receptive language was the most severely affected verbal function, and the low scores were common to both groups. No significant differences were recorded between boys and girls though the boys performed less successfully. Moreover, the low scores in the language domain were recorded in right-handed boys with LHL. The comparison of language abilities between boys and girls with right-hemisphere lesions indicated that comprehensive abilities were the most frequently affected language measures, but significant gender differences were not revealed, although the boys had more problems than girls. The visuomotor skill was the most impaired function in girls with LHL, and there the right-handed girls performed less successfully than did the left-handed girls. Differences between boys and girls (in the case of left as well right-hemisphere lesion) in the motor and sensory tasks were not significant. The results of the neuropsychological assessment of spatial domains between boys and girls revealed a significant gender difference ($P < 0.03$), the left-handed girls had lower scores than left-handed boys (LHL), and the same gender differences were found between right-handed girls and boys (with RHL), but no notable statistical difference was revealed ($P > 0.12$). In addition we obtained significant gender differences ($P < 0.01$) between left-handed boys and girls (LHL) on short-term memory measures, and the boys performed less successfully than girls, especially in verbal memory tasks. There were no significant sex differences between right-handed (RHL) boys' and girls' results in verbal memory impairment and no significant differences between boys and girls in long-term memory functions.

4. DISCUSSION

In order to detect and specify cognitive deficits in a detailed manner, it is important to use sensitive neuropsychological subtests appropriate to the children's developmental age. In any case, there are no particularly good methods accepted to demonstrate cerebral lateralization in children. The present study, using such a method with the NEPSY test-battery, showed that handedness is an effective and reliable tool to detect the lateralized abnormalities of cerebral functions in hemiparetic children, suggesting also that reorganization of functions is not equivalent to normal neurocognitive development being strategically and temporally aberrant. The results are discussed in the framework of pathological handedness and shifts in hemispheric control of language and other cognitive functions. The findings of this study support our hypothesis that the pattern of cognitive deficit in hemiparetic children depends on the side in which the brain lesion occurs and on the type of cerebral lateralization, i.e typical or atypical. One crucial

finding was that children, who did not undergo a shift in hand preference after unilateral brain damage, such as right-handed children with left-hemisphere lesion displaying atypical cerebral lateralization, showed diffuse cognitive impairment. These findings are clinically important indicating the inappropriate functional overlap between neural systems and reduced brain plasticity. In our opinion these children, who demonstrated an anomalous pattern of cerebral lateralization, require special medical attention, neuropsychological examination of their major cognitive functions and rehabilitation measures, in order to prevent later-life cognitive difficulties. On the contrary- the complete (i.e. typical) pattern of cerebral reorganization was associated with a favorable cognitive outcome in hemiparetic children, especially in the development of language functions. In comparing the cognitive effect of left and right hemisphere impairment, we found a clear side-specific pattern of cognitive deficit in the children without seizure disorders who have undergone a shift in their hand preference after early-onset brain lesion. The right-hemisphere lesion group (right-handed children) demonstrated depression in attention, executive, spatial and short-term memory functions, while their language comprehension abilities were only moderately impaired. The children with left-hemisphere lesions (left-handed) demonstrated moderate receptive language difficulties, and also performed visuomotor tasks less successfully.

The main sex difference in cognition was related to the different pattern of neurocognitive development after unilateral cortical lesion in boys and girls, as in boys handedness was more coherent with language, verbal memory and attention functions, in girls- with visuomotor and spatial functions. The authors of this study believe that gender differences were congenital and became more extensive and complete with age; in addition, the typical cognitive pattern of gender differences and problem — solving strategies may be revealed also in children with early brain lesion.

As mentioned above, the overall findings of this study affirm the different pattern of cognitive impairment in children with shifted and non-shifted hand preference after a unilateral brain lesion. The cognitive deficit was diffuse in children with non-shifted hand control: language abilities both phonological and speech production abilities were impaired, and they also performed poorly in visuomotor and narrative memory processing, even though they had only a mild motor deficit (hemiparesis). This relatively well-preserved motor function can be explained on the one hand by limited damage area in the motor cortex, and on the other hand also by well organized rehabilitation work.

Our findings also support the other hypothesis that seizure disorders might disturb successive cerebral lateralization,^{15, 16} as there were 7 out of 9 children with seizure disorders in this diffuse cognitive impairment group. Our previous studies have also indicated that the profile of cognitive impairment was diffuse in hemiparetic children with seizure disorders as in children with epilepsy alone due to a lack of the typical development of hemispheric specialization.¹⁷⁻¹⁹ Consequently, the present study does not confirm the results of Rugland²⁰ who suggested that academic problems in epileptic children arise only from specific cognitive deficiencies rather than generalized dysfunction.

Satz *et al.*² reported that there might be two types of reorganization of cerebral functions in children after brain damage. We found following types of shifts: bimodal reorganization of both language and hand control in 44 out of 58 children, and unimodal, with hand preference maintenance in 12 of 58 children. In addition, other alternatives of brain reorganization also exist, as the incomplete pattern of brain specialization, when hand preference is not reorganized, as 28.1% of children remained right-handed in spite of left-hemisphere lesion (confirmed by MRI or CT) and the language-related area also

did not transfer essential functions to areas, capable of supporting them in the right hemisphere. It appears that language control is bilateral or otherwise more extensive in an impaired left-hemisphere, which may cause greater dysfunctions in language and other cognitive domains as was detected in present study. Patients with a left-hemisphere lesion showed motor system damage leading to a shift in handedness to the left side in 23 children out of 32, whereas 9 children maintained a right-hand preference; in the case of right-hemisphere lesion, shifts in hand preference to the right side (right-handedness) were detected in 21 cases, whereas 3 children remained ambidextrous. Left-handedness, which was about 11.6 % in the normal population²¹ rose to about 41% of hemiparetic children in our study and to as much as 71.9% in the left-hemisphere lesion group, while it was 35% among the children with seizure disorders and fell to about 0 in a comparable group with right — hemisphere damage. The high incidence of left-handedness can be explained as the result of early brain injury, other words as pathological left-handedness. Within this overall dysfunction we found an interesting and unexpected malfunction of the non-paretic hand in motor and sensory integration tasks, i.e. they scored below the controls' level when using their healthy left or right hand. The revealed dysfunction in the sensorimotor area opposite the damaged side may be explained by the greater amount of parallel processing of information in the motor and sensory systems. As reported by other studies, the patient with damage to the left hemisphere but without paralysis of the right side may have difficulties making hand movements and complex finger positions with either the left or right hand.²²

One important statement that has been made concerning the language profile of children with focal brain damage is the fact that regardless of the lesion site children show initial delay and subsequent development, as multiple areas of the brain can subserve language functions.²³ We believe that relatively well preserved language abilities in left-handed children after LHL were due to altered speech lateralization, i.e. a bimodal type of cerebral reorganization where both, speech and hand control were shifted to the right hemisphere. Our results are in agreement with these of Isaack *et al.*⁴ and Chiron *et al.*,²⁴ that children who have sustained left-hemisphere damage early in life, particularly since plasticity at this age should favor functional reorganization in language functions, had come to be mediated by the right hemisphere. Therefore the speech depression in children with right-hemisphere damage, showing that RHL is associated with delay in language comprehension abilities that play a particularly important role in the integration of sensory information.²⁵⁻²⁷

Comparing the left-handed boys and girls (non-paretic hand groups) in attention tasks, demonstrated a typical sex difference where boys performed less successfully, but in the case of right hemisphere lesion right-handed boys and girls performed equally poorly attention tests, which might be explained as a side-specific pattern of impairment of the right hemisphere. However, a slightly higher proportion of left-handedness was revealed among boys than girls, the ratio being 48%: 44% respectively, there might be a partly genetic influence on these mechanisms as suggested by many authors.^{1, 28, 29} Moreover, girls with congenital hemiparesis outperformed boys on language and short-term memory domains, while boys outperformed girls on visuospatial skills; this may be due to sex differences in intrahemispheric organization^{30, 31} and reported also in our previous studies.^{17, 18} In addition, we found that right-handed boys with LHL had the highest risk for the development of the language and verbal memory dysfunctions, as right-handed girls with LHL suffer more often and severely from visuomotor deficiencies. Androgens may delay left hemisphere maturation in boys and lead to a left-to-right

shifting of verbal functions resulting in a mixed dominance of cognitive abilities,⁷ as these differences are probably due to different hormonal influences that take place in the prenatal period.

5. CONCLUSIONS

Taken together, the main conclusions of this study are following:

1. Cognitive outcome of focal brain damage depends in addition to the side and size of hemispheric lesion also on whether the type of cerebral lateralization is of a typical or atypical pattern. The typical, i.e. complete pattern of cerebral reorganization displayed a favorable cognitive outcome, associating with specific cognitive impairment contrary to the atypical i.e. incomplete pattern of reorganization, which displayed multiple disorders.
2. Using the handedness measure as one of the possible tools for examining typical or atypical cerebral lateralization could provide more information on the cognitive status of children with unilateral brain damage.
3. Epilepsy in children with congenital hemiparesis means a high additional risk for developing cognitive decline. The children with seizure disorders have a diffuse or multiple patterns of cognitive disorders rather than specific cognitive impairment. In addition, the pattern of typical cerebral lateralization and functional reorganization is affected by seizure disorders, and epileptic hemisphere may lose thereby some of its special cognitive functions.
4. Boys and girls have different pattern of neurocognitive development: in boys handedness is more coherent with language, verbal memory and attention functions, while in girls it is coherent with visuomotor and spatial functions.

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Table 1. Study Group

	No. of children		
	Total	Boys	Girls
Left hemisphere lesion	32	16	16
left-handers	23	13	10
right-handers	9	3	6
Right hemisphere lesion	24	15	9
ambidextrous	3	2	1
right-handers	21	13	8
Controls	14	7	7
right-handers		7	7

Table 2. Main characteristics of study groups

	Left HL group		Right HL group	
	Left-handed n=23	Right-handed n=9	Ambidextrous n=3	Right-handed n=21
Birth weight (M±SD)	3281.6± 717	2747.8± 856	3373.3± 300	3332.2± 714
Age during study (M±SD)	6 yrs. 0 month	7 yrs. 3 month	7 yrs. 1 month	7 yrs. 5 month
Degree of hemiparesis				
Mild	11	9	2	13
Moderate	12	0	1	8
Seizures				
Yes	7	7	1	10
No	16	2	2	11
CT/MRI findings				
Normal findings	4	2	2	4
Symmetrical ventricular dilatation	5	2		5
Focal lesion in left HP	14	5		
Focal lesion in right HP			1	12

Table 3. Subtest Scores of Subgroups on Neuropsychological Assessment

	LHL left-handers G I n=23		RHL right-handers G II n=21		G I				G II				Differ. by groups: P
					Boys n=13		Girls n=10		Boys n=13		Girls n=8		
	M	SD	M	SD	M	SD	M	SD	M	SD	M	SD	
General Orientation	0.52	0.59	0.11	0.69	0.4	0.7	0.7	0.5	0	0.7	0.4	0.5	I/II* I B/G**
Inhibition and Control	-1.13	1.37	-1.6	1.21	-1.7	1.3	-1.4	0.9	-1.9	1.2	-1.1	1.1	
Sustained Concentration	-1.5	1.37	-2.0	1.32	-2.0	1.3	-0.8	1.1	-2.1	1.3	-1.8	1.5	
Auditory Anal. of Speech	-1.52	1.37	-1.4	1.38	-1.5	1.5	-1.5	1.4	-1.5	1.3	-1.3	1.6	
Verbal Fluency	-0.05	0.48	-0.2	0.46	-0.1	0.7	0.0	0.0	-0.4	0.5	0.0	0	
The Token Test	-1.0	1.29	-1.8	1.1	-1.5	1.3	-0.5	1.0	-2.1	1.1	-1.3	1.0	
Relative Concepts A	-1.7	1.42	-2.0	1.22	-1.7	1.5	-1.6	1.3	-1.8	1.3	-1.8	0.9	
Reading Readiness	-0.7	1.42	-1.3	1.3	-0.9	1.7	-0.4	1.0	-1.3	1.4	-1.3	1.4	
Repeating Words & Non-Words	-0.3	0.8	-0.8	1.22	-0.4	0.9	-0.1	0.6	-0.9	1.3	-0.5	1.2	
Naming Tokens, errors	-0.4	0.95	-0.7	1.0	-0.6	0.0	-0.1	0.6	-1.0	1.2	-0.4	0.5	
Naming Token, time	-1.3	1.5	-1.3	1.5	-0.9	1.7	-1.8	1.2	-1.8	1.5	-0.7	1.4	
Visuo-Motor Precision	-1.5	1.2	-1.3	1.3	-1.4	1.5	-1.8	1.0	-1.2	1.3	-1.5	1.4	
Dynamic Praxis	0.05	0.89	-0.3	1.07	0.0	1.1	0.1	0.6	-0.5	1.2	0.2	0.4	
Kinesthetic Praxis	-0.35	0.74	-0.33	0.84	-0.4	0.9	-0.3	0.5	-1.1	1.3	-1.1	0.9	
Venger's Test	-1.05	0.89	-1.6	1.1	-0.7	0.8	-1.4	0.8	-1.5	1.1	-1.7	1.1	I/II* I B/G*
Word Span	-0.1	-0.5	0.3	1.2	-0.1	0.5	-0.1	1.1	-0.6	1.1	-0.1	1.3	I/II* I B/G**
Name Learning	-0.6	0.98	-1.3	1.25	-1.0	1.0	0.3	0.9	-1.2	1.2	-1.4	1.4	
Logic Learning	-0.6	1.2	-1.3	1.03	-1.0	1.4	-0.2	0.8	-1.3	1.3	-1.4	1.1	

Note. * p<0.05; ** p<0.01

Table 4. Subtest Scores of Right- and Left-handers in Left HP Lesion on Neuropsychological Assessment

	Groups						Differences by groups: p					
	Right-Handers n=23 (1)		Left-Handers n=9 (2)		Control n=14 (3)		1-2	1-3	2-3			
	M	SD	M	SD	M	SD						
General Orientation	0.42	0.53	0.52	0.59	0.86	0.36	0.6	0.03	0.002			
Inhibition and Control	-1.0	1.5	-1.1	1.32	-0.14	0.86						
Sustained Concentration	-1.0	1.2	-1.5	1.37	0.0	0.0						
Auditory Anal. of Speech	-2.2	1.3	-1.5	1.4	0.62	0.63	0.03	0.0	0.001			
Verbal Fluency	-0.3	0.9	-0.05	0.5	0.21	0.42						
The Token Test	-2.1	1.2	-1.0	1.3	-0.07	0.9						
Relative Concepts B	-1.3	1.6	-0.8	1.3	0.46	0.51						
Reading Readiness	-1.37	1.4	-0.6	1.4	0.21	0.42						
Repeating Words & Non-Words	-1.0	1.3	-0.3	0.8	0.0	0.32						
Naming Tokens, errors	-1.1	1.3	-0.4	0.9	0.07	0.27						
Comprehension of Syntactic Structures	-0.4	0.5	-0.2	0.9	-0.07	0.27						
Visuo-Motor Precision	-1.9	1.3	-1.5	1.3	-0.28	0.82				0.4	0.001	0.0004
Dynamic Praxis	-0.4	1.1	0.1	0.9	0.0	0.0						
Kinesthetic Praxis	-0.8	1.2	-0.6	0.9	0.85	0.36						
Venger's Test	-0.7	1.3	-1.1	0.9	0.21	0.69		0.001	0			
Digit Span	-0.8	1.4	-0.9	1.4	0.61	0.65	0.5	0.001	0.0001			
Word span	-0.8	0.9	-0.1	0.8	0.21	0.42						
Logic. Learning	-0.7	1.2	-0.8	0.7	-0.15	0.55						
Name Learning	-0.8	1.2	-0.7	0.9	0.43	0.51						
Memory Faces	-0.7	1.0	-0.8	1.2	0.07	0.47						
Storytelling	-1.3	1.3	-0.6	1.2	-0.15	0.55						
Delayed Recall Names	-0.5	1.2	0.0	0.9	-0.23	0.59	0.5	0.04	0.5			
Delayed Recall Faces	-0.4	0.5	0.0	0.7	0.14	0.53						

Table 5. Subtest Scores of Right-handers and Ambidextrous in Right HP Lesion on Neuropsychological Assessment

	Groups						Differences from controls: p			
	Right-handers n=21 (1)		Ambi- dextrous n=3 (2)		Control n=14 (3)		1-3	2-3		
	M	SD	M	SD	M	SD				
General Orientation	0.12	0.69	0.0	0.0	0.86	0.36	0.03	0.001		
Inhibition and Control	-1.63	1.2	-1.3	1.5	-0.14	0.86				
Sustained Concentration	-1.95	1.32	-0.7	1.37	0.0	0.0				
Auditory Anal. of Speech	-1.47	1.3	-2.0	1.7	0.62	0.63	0.0	0.001		
Verbal Fluency	-0.28	0.5	0.0	0.0	0.21	0.42				
The Token Test	-1.8	1.2	-0.3	0.6	-0.07	0.9				
Relative Concepts A	-2.1	1.2	-1.3	1.5	0.46	0.51				
Reading Readiness	-1.3	1.4	0.0	0.0	0.21	0.42				
Repeating Words & Non-Words	-0.8	1.2	0.0	0.0	0.0	0.32				
Naming Tokens, errors	-0.8	1.0	-1.3	1.5	0.07	0.27				
Comprehension of Syntactic Structures	-0.4	0.9	0.0	0.0	0.14	0.5				
Visuo-Motor Precision	-1.27	1.3	-1.3	1.5	-0.01	0.3			0.001	0.0004
Dynamic Praxis	-0.3	1.1	1.0	0.0	0.0	0.0				
Kinesthetic Praxis	-0.3	0.8	0.0	0.0	0.85	0.36				
Venger's Test	-1.6	1.3	-0.7	0.6	0.21	0.69	0.001	0		
Digit Span	-0.7	1.4	0.0	0.0	0.61	0.65	0.001	0.0001		
Word span	-0.5	1.2	0.0	0.8	0.21	0.42				
Logic. Learning	-1.3	1.3	-0.3	0.6	0.4	0.5				
Name Learning	-1.3	1.3	0.0	0.0	0.3	0.6				
Memory Faces	-0.7	1.1	0.0	0.0	0.14	0.4				
Storytelling	-1.3	1.2	0.0	0.0	-0.15	0.6				
Delayed Recall Names	-0.5	1.2	-0.7	1.2	-0.2	0.6	0.04	0.5		
Delayed Recall Faces	-0.4	0.5	0.0	0.7	0.14	0.53				

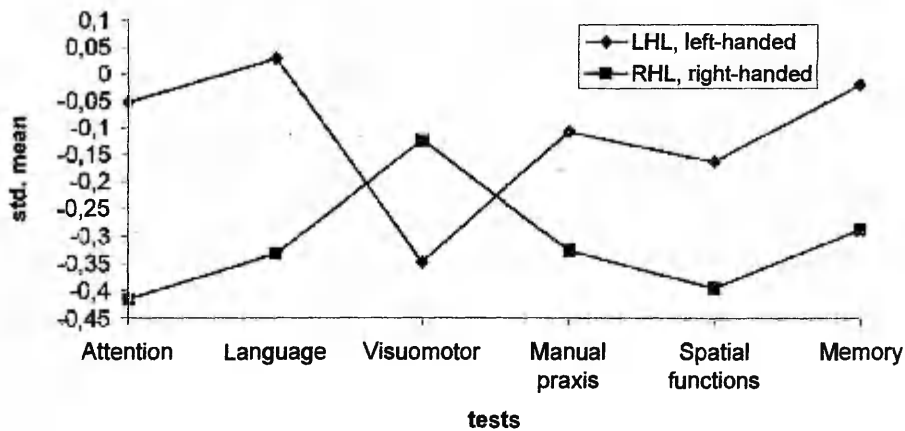


Figure 1. indicates significant impairment in composite scores for attention, visuospatial and short-term memory tasks ($P= 0.03, 0.03$ and 0.04 respectively) performed by right-handed children with right hemisphere lesion (had lower scores) compared to left-handed children with left hemisphere lesion, who were more affected in the visuomotor task.

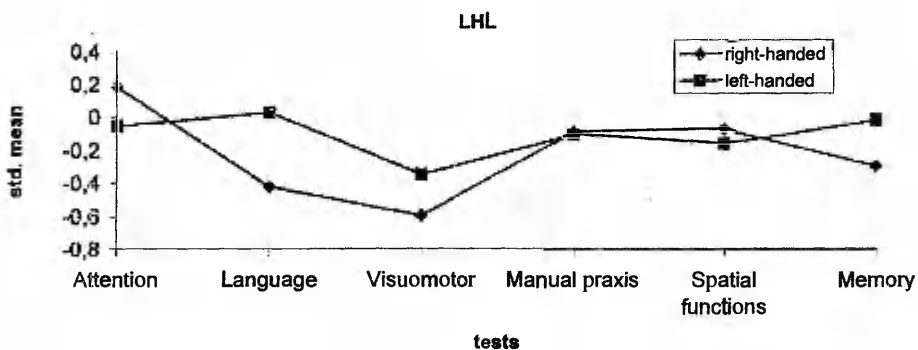


Figure 2. indicates significant impairment in composite scores for language domain ($P= 0.03$) and visuo-spatial precision ($P= 0.04$) performed by right-handed compared to left-handed children with left hemisphere lesion (LHL); here the language function was more impaired in right-handed children and visuo-spatial precision in left-handed children.

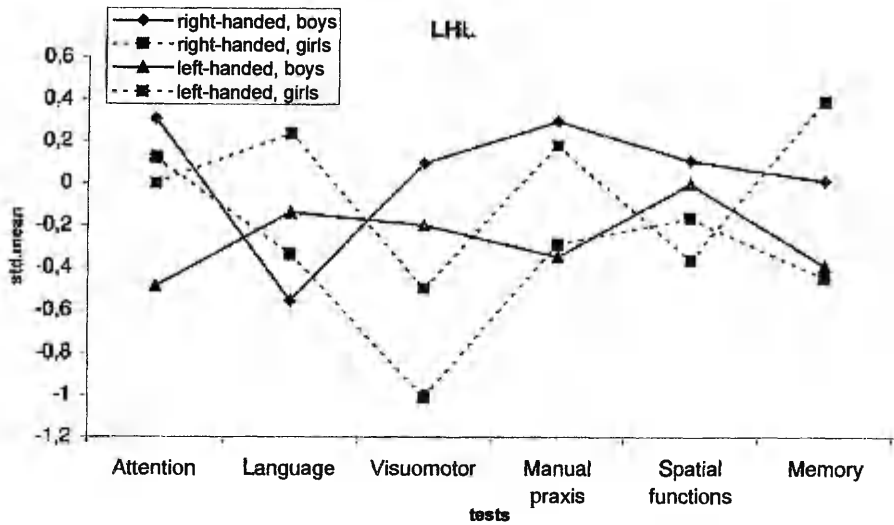


Figure 3. indicates significant impairment in composite scores for attention ($P = 0.04$) and short-term memory tasks ($P = 0.01$) performed by left-handed boys compared to left-handed girls with left-hemisphere lesion (LHL); here boys had lower scores, and girls performed less well in spatial function ($P = 0.03$). The figure also indicates the composite test score of right-handed boys and girls with LHL, note the low score in the visuomotor task in girls, but the differences were not significant.

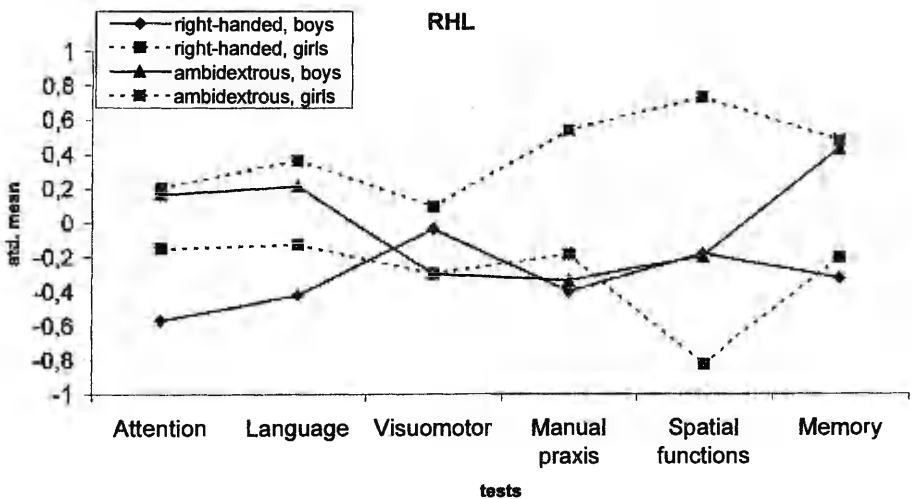


Figure 4. indicates impairment in composite scores of cognitive domains of right-handed compared to ambidextrous boys and girls with right hemisphere lesion (RHL). Note that right-handed children were more affected in attention, language and spatial skills, but the differences were not significant.

Appendix

The following 24 subtests were administered within the present study:

1. General Orientation – a test of knowledge of personal and environmental data.
2. Inhibition and Control – a test evaluating control impulses.
3. Sustained Concentration – the time the subject is able to keep working during the test sessions.
4. Verbal Fluency — naming as many animals as possible in 1 min and, similarly, things to eat or drink.
5. Auditory Analysis of Speech — a test that demands recognition of words that are pronounced by the examiner as separate parts (“g-irl”).
6. Comprehension of Instructions — measures the ability to follow complex instructions in paper-and-pencil tasks.
7. Relative Concepts — comprehension of concepts such as “between”, “forward”, etc.
8. The Token Test, the subject points out or manipulates tokens according to spoken instructions.
9. Naming Tokens, the child is to name size, color and shape of the tokens from the Token Test as quickly as possible; the score used in the context consists of the number of correct answers rather than a time score.
10. Naming Token, time.
11. Repeating Words and Non-Words, for example “screwdriver” and “pylobitry”.
12. Reading Readiness — a test that demands recognition of the letters in a child’s name or written on paper (A, E, U, I, P, M), and also reading words such as CAR...
13. Storytelling — a story is read out to the child, who is then asked to retell it.
14. Kinesthetic Praxis — the subject imitates complex positions of fingers.
15. Dynamic Praxis — the subject has to produce motor series with both hands simultaneously.
16. Visual-Motor Precision — is assessed by having the subject draw lines along given intricate shapes.
17. Venger’s Test of Strategy — the task is to find the right path using maps (picture book, six tasks).
18. Digit Span — the child has to continue series of digits.
19. Word span — the child has to continue series of words.
20. Memory for Faces — the task is to find eight pictures of faces previously presented among other pictures.
21. Logical Learning — the subject first listens to a story and then answers questions concerning the content.
22. Name Learning — learning the names of seven children on photographs.
23. Delayed Recall for Faces — the task is to find eight pictures with faces half an hour after their first presentation (test 30).
24. Delayed Recall of Name Learning, the same photos and names as in test 22 to be remembered after 30 min.

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