Neuropsychological assessment of cognitive and emotional functioning in patients with epilepsy.

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Contents

1. ACKNOWLEDGEMENTS

2. LIST OF ARTICLES

REPORT I:

Gramstad, A., Iversen, E., & Engelsen, B.A. (2001). The impact of affectivity dispositions, self-efficacy and locus of control on psychosocial adjustment in patients with epilepsy. *Epilepsy Research, 46,* 53-61.

REPORT II:

Gramstad, A., Engelsen, B.A., & Hugdahl, K. (2003). Left hemisphere dysfunction affects dichotic listening in patients with temporal lobe epilepsy. *International Journal of Neuroscience, 113,*1177-1196.

REPORT III:

Gramstad, A., Engelsen, B.A., & Hugdahl, K. (accepted for publication). Dichotic listening with forced attention in patients with temporal lobe epilepsy: Significance of left hemisphere dysfunction. *Scandinavian Journal of Psychology.*

3. SUMMARY

The general aim of the thesis has been to contribute to a deeper understanding of central psychosocial and cognitive problems experienced by patients with epilepsy. In the first paper, the aim was to evaluate the impact of dimensions derived from contemporary personality and social learning theory on psychosocial functioning in patients with epilepsy. The procedure was to correlate scores on scales measuring positive and negative affectivity, self-efficacy and health related locus of control with scores on a multidimensional inventory with established clinical validity in patients with epilepsy. As expected, high correlations were found between negative affectivity and general emotional adjustment, general psychosocial functioning and quality of life. Also, both positive affectivity and self-efficacy explained unique variances of these dimensions in a multiple regression analysis. In the second paper, the aim was to assess whether left side of seizure onset or left hemisphere cognitive functioning best predicted dichotic listening performance in patients with temporal lobe epilepsy and left hemisphere speech dominance. Left hemisphere general functioning predicted dichotic listening results significantly, and to a stronger degree than left-sided seizure onset. In the third paper, the aim was to validate the findings of the second paper in a larger group of patients, and to investigate whether the same effects would be present also under conditions of forced attention in dichotic listening. The effect of left hemisphere dysfunction remained present also in the forced attention conditions, with the strongest effect being an increased tendency to report left ear stimuli. Multiple regression analyses showed that general cognitive factors influenced dichotic listening stronger in the forced-attention conditions than in the nonforced condition. This effect was strongest in the forced-left attention condition.

4. EPILEPSY

4.1. Definitions

In a recent paper (Fisher et al, 2005), epilepsy was defined as "a disorder of the brain characterized by an enduring predisposition to generate epileptic seizures and by the neurobiologic, cognitive, psychosocial and social consequences of this condition. The definition of epilepsy requires the occurence of at least one epileptic seizure." An epileptic seizure was defined as "a transient occurence of signs and/or symptoms due to abnormal excessive or synchronous neuronal activity in the brain". One may note that this definition includes cognitive, psychological and social consequences, being at the very core of the disorder. Engel and Pedley (1997) defined epilepsy as "...a broad category of symptom complexes arising from any number of disordered brain functions that themselves may be secondary to a variety of pathologic processes...(with)...recurrent paroxysmal episodes of brain dysfunction manifested by stereotyped alterations of behavior". Thus, current definitions of epilepsy go beyond the mere existence of epileptic seizures, and highlight the complexity of impaired functions associated with the disorder, including psychological and social deficits.

4.1.1. Seizure classification

The classification of epileptic seizures has been and is the subject of much discussion, and effort has been put into making a generally accepted classification and terminology. The most widely used classification, proposed by the International League Against Epilepsy (ILAE) (Commision on classification and terminology of the ILAE, 1981, 1989, Commission on epidemiology and prognosis of the ILAE, 1993) regards epileptic seizures as either generalized, partial or unclassified. In generalized seizures, no focal starting point in the brain for the seizure is known, and both brain hemispheres are involved in the seizure. In partial seizures, the seizure starts in a part of the brain, the epileptic focus. Partial seizures may develop into generalized seizures, and in this case they are called secondary generalized seizures. Generalized seizures are further subdivided into absences, atypical absences, tonic seizures, clonic seizures, tonic-clonic seizures, myoclonic seizures and atonic seizures. Partial seizures are subdivided into simple and complex partial seizures. In simple partial seizures, consciousness is not affected. In complex partial seizures, consciousness is in some way affected. Symptomatology in partial seizures depends on where in the brain the focus is, and a

very wide range of symptoms may occur. A detailed glossary of ictal seizure semiology is given by Blume et al (2001).

4.2. Epidemiology of epilepsy

Naturally, epidemiological estimates depend upon how epilepsy is defined. Most often, a definition involving two or more unprovoked epileptic seizures has been used. Population studies in Western, industrialized countries have given estimates of the incidence of epilepsy between 26-70/100 000 person-years (Hauser, 1997). The incidence may be higher in developing than in industrialized countries (Lavados, Germain, Morales, Campero & Lavados, 1992; Rwiza et al, 1992). Incidence is higher in early childhood and late adulthood, and is particularly high in the first year of life, at least in industrialized countries (Hauser, 1997). Age-adjusted prevalence in whole populations are in the range 4-8/1000 in most studies (Hauser & Hesdorffer, 1990). A recent study in Hordaland county in Western Norway showed a prevalence of 5.1/1000 in 6 to 12-year old children (Waaler, Blom, Skeidsvoll & Mykletun, 2000). Certain populations are at higher risk of developing epilepsy. Brain damage, mental retardation, cerebral palsy, febrile seizures, overconsumption of drugs or alcohol, depression and a family history of epilepsy are regarded as general risk factors (Hesdorffer & Verity, 1997). However, in more than half the cases the etiology is unknown. Evidence exists that a number of psychiatric and somatic health problems are overrepresented in people with epilepsy (Gaitatzis, Carroll, Majeed & Sander, 2004). People with epilepsy are also at a higher than normal risk of personal injury due to accidents, and patients with chronic, therapy-resistant epilepsy have a higher mortality than the ordinary population, to some extent due to sudden unexpected death (SUDEP) (van den Broek & Beghi, 2004; Tomson, Beghi, Sundqvist & Johannessen, 2004).

4.3. Emotional and psychosocial problems in epilepsy

4.3.1. Stigma
During history, epilepsy has been associated with many myths and prejudices (Temkin, 1971). Still, substantial social stigma (Goffman, 1963) is associated with the condition, particulary in the developing countries (Baskind & Birbeck, 2005), but in industrialized countries as well (Jacoby, Snape & Baker, 2005). This may lead to adjustment difficulties for people with

epilepsy at important social arenas such as the workplace (Thorbecke & Fraser, 1997; Harden, Kossoy, Vera & Nikolov, 2004), at school (Prpic et al, 2003) and among peers of adolescents (MacLeod & Austin, 2003), and this in turn may lead to a predisposition to develop psychosocial problems.

4.3.2. Theoretical formulations of psychosocial problems

A comprehensive attempt to define the complex of psychopathology in patients with epilepsy was formulated by Hermann and Whitman (1986). Determinants of psychopathology were grouped in three main "hypotheses": The neuroepilepsy hypothesis, the psychosocial hypothesis and the medication hypothesis. Each hypothesis had its more specified determinants, which can be studied scientifically. One strenght of this model is that it is possible to test the relative influences of each variable in the model against a criterion variable. Unfortunately, little effort has been directed towards testing this model since its publication. However, it serves as a reminder of the complexity of psychosocial problems in epilepsy. Another attempt to define the range of psychosocial problems in epilepsy was made by Dodrill, Batzel, Queisser and Temkin (1980), implicit in their construction of the Washington Psychosocial Seizure Inventory (WPSI) (see also Levin, Banks & Berg, 1988). In this scale, adjustment in different areas of psychosocial functioning is assessed. Items measuring these different areas were chosen on an empirical basis. A severity judgment in each area was defined based on a consensus between the authors as to what degree a certain score reflects problems in real life. Psychosocial areas of interest are: family background, emotional adjustment, interpersonal adjustment, vocational adjustment, financial status, adjustment to seizures and medicine and medical management. A summary scale, named Overall psychosocial functioning, was also constructed. The fact that the concepts are formulated as scales makes the model directly testable, and this inventory has been used in a large number of studies of psychosocial problems in epilepsy.

4.3.3. Quality of life

In addition, quality of life (QoL) assessment has become increasingly popular (Leone, Beghi, Righini, Apolone & Mosconi, 2005). Questionnaires measuring QoL are rarely firmly based in any particular theory, but they normally are expected to fulfill certain methodological and conceptual criteria, such as assessing both physical, psychological and social aspects of illness and treatment (Spilker, 1996).

4.3.4. Psychological concepts

There are few studies explicitly based on contemporary psychological theory applied to the field of psychosocial problems in epilepsy. The concept of neuroticism has been applied in some studies, showing a close correlation between this concept and measures of general psychosocial functioning (Rose, Derry & McLachlan, 1996; Zhu, Jin, Xie & Xiao, 1998). A number of studies have investigated impact of self-efficacy (Bandura, 1977) on psychosocial and behavioral problems in epilepsy (DiIorio, Faherty & Manteuffel, 1992; Amir, Roziner, Knoll & Neufeld, 1999; Kobau & DiIorio, 2003; DiIorio et al, 2004; van Empelen, Jennekens-Schinkel, van Rijen, Helders & van Nieuwenhuisen, 2005). The concept of coping strategies (Lazarus & Folkman, 1984) has been studied extensively in patients with epilepsy. However, the predictive value of this concept to criterion variables seems to be only moderate (e.g. Upton & Thompson, 1992; Livneh, Wilson, Duchesneau & Antonak, 2001; Goldstein, Holland, Soteriou & Mellers, 2005). In general, measures of depressed mood have been closely correlated to QoL in epilepsy (e.g. Boylan et al, 2004). More disease-specific measures such as Seizure worry may also influence QoL, but normally to a lesser degree than depressed mood (Loring, Meador & Lee, 2004).

4.4. Cognitive impairment in epilepsy

4.4.1. Intelligence and general cognitive functioning

The relationship between epilepsy and cognitive impairment is complex. In the early days of intelligence testing, several investigations suggested that patients with epilepsy had lowered IQ compared to the normal population (e.g. Fox, 1924; Hilkevitch, 1946; Davies-Eysenck, 1952). However, study subjects often were inhabitants of special institutions for patients with severe epilepsy, and effects of antiepileptic medication were often not considered adequately (Hermann, 1991). In contrast, above average IQs were found in an early outpatient study (Collins & Lennox, 1942). Obviously, great variations in cognitive function existed in this patient group. Later, more well-controlled studies showed an association between cognitive deficit and etiology and seizure type. Cognitive deficit was associated with the coexistense of brain damage and to some degree also with the existence of major motor seizures. Patients with only psychomotor (partial) seizures of unknown etiology were essentially unimpaired (Kløve & Matthews, 1966; Matthews & Kløve, 1967). Later, a detrimental effect of a high

(>100) lifetime frequency of generalized tonic-clonic seizures and of status epilepticus for generalized cognitive function has been suggested (Dodrill, 1986). However, the detrimental effect of status epilepticus has been questioned (Ellenberg, Hirtz & Nelson, 1986; Adachi et al, 2005), and may be an artifact of associated neurological disease. Early age at seizure onset and long duration of epilepsy have been considered risk factors. Severe, recurrent seizures of childhood onset may lead to a gradually reduction of IQ during the childhood period (Bjørnæs, Stabell, Henriksen & Løyning, 2001). Duration of epilepsy may be the strongest factor affecting cognitive functioning in adults with chronic intractable epilepsy, and refractory temporal lobe epilepsy may lead to a very slow but ongoing cognitive deterioration in adults (Jokeit & Ebner, 2002).

4.4.2. Memory

Deficits in particular areas of cognitive functioning have also been studied in patients with epilepsy. The most prominent area of research have been that of memory function. Since the first reports of amnesia after bilateral removal of the hippocampal structure (Scoville & Milner, 1957, Penfield & Milner, 1958), and the finding of sclerotic changes in the nonoperated hippocampus of patients with amnesia after unilateral operations (Penfield & Mathieson, 1974), the important role of medial temporal structures (hippocampus and surrounding structures) in memory consolidation has been recognized. This region also is a frequent starting point of epileptic seizures, and therefore a frequent target of epilepsy surgery. Thus, memory studies have been of clinical interest, particulary in the context of surgical treatment of epilepsy (e.g. Cascino, 2004). A material specific memory decline is found in patients with hippocampal sclerosis visible on MR scan, with a decline in verbal memory in patients with left-sided sclerosis and a decline in nonverbal memory in patients with right-sided sclerosis. This effect is stronger for verbal memory in left sided sclerosis than for nonverbal memory in right sided sclerosis (Hermann, Seidenberg, Schoenfeld & Davies, 1997). Many other aspects of the relation between hippocampal integrity and memory function in patients with epilepsy have been studied, such as amount of hippocampal cell loss (Sass et al, 1992; Baxendale et al, 1998) hippocampal and extrahippocampal volumes (Trenerry et al, 1993; Sawrie at al, 2001; Reminger et al, 2004) and cognitive potentials from the medial temporal lobe (Elger et al, 1997). Also, the functional reserve represented by function of the hippocampus contralateral to the damaged one has been subject of interest because of its role in the maintenance of postoperative memory function (Chelune, 1995).

4.4.3. Other specific cognitive impairments

Temporal lobe epilepsy has been the most frequent epilepsy type studied, probably because the availability of data from surgical centra, in which the temporal lobes are the most frequent target of operation. Even within the group with temporal lobe epilepsy, function varies according to location of focus within the temporal lobe (e.g. Helmstaedter, Grunwald, Lehnerz, Gleissner & Elger, 1997; Helmstaedter, Sonntag-Dillender, Hoppe & Elger, 2004). Patients with extratemporal focal epilepsies show even more diversities depending upon the exact localization of the focus, the amount of brain tissue involved etc. However, as a broad generalization, patients with frontal lobe foci show deficits in executive functioning and in selection, initiation and inhibition of responses, in contrast to the memory deficit most prominently shown by patients with temporal lobe foci. The groups also differ according to emotional profiles, with depression, anxiety and neuroticism being frequent with temporal lobe epilepsy, and hyperactivity, conscientiousness, obsession and addictive behaviors being more prominent with frontal lobe epilepsies (Helmstaedter, 2001). Cognitive function associated with epilepsies of parietal or occipital origin has been much less studied. After surgery in this area, a slight decline in nonverbal IQ may be seen (Luerding, Boesebeck & Ebner, 2004). Presence or absence of mithocondrial disease seems to be important. Interictal symptoms may include visual field defects, altered spatial orientation, inattention and visual color agnosia. Specific behavioral alterations related to parieto-occipital focus localization are not described (Engelsen & Aarli, 1999).

4.5. The patient perspective: coexistence of cognitive and psychosocial problems

Traditionally, the psychological study of patients with disorders of brain functions has concentrated on the cognitive impairments and deficits faced by these patients. The reasons for this are diverse. One important reason is that it has been possible to show clear correlations between brain disorder and certain tests of cognitive function. Measures of emotional dysfunction, such as commonly used questionnaires, have been much less clear-cut in their relation to brain dysfunction. Moreover, a majority of people with primary emotional problems score in the normal range of cognitive neuropsychological tests (Reitan & Wolfson, 1997). However, modern clinical neuroscience gives increasingly more insights about the role of brain functions in emotional responding (e.g. Le Doux, 1996; Rolls, 1999). From the patient perspective, both cognitive and emotional aspects of their situation are important, and

need to be taken into consideration in the plan of treatment for their condition. Increasingly, both cognitive and emotional characterista of particular diseases are simultaneously adressed by clinical neuropsychologists, such as the differences between temporal and frontal lobe epilepsy as described by Helmstaedter (2001) and the relation between cognitive and emotional aspects of differential focus localization within the left temporal lobe, described by Helmstaedter et al (2004). Therefore, further neuropsychological study of patients with epilepsy, as well as other diseases affecting the brain, should include both emotional and cognitive aspects.

6.   BRAIN LATERALITY OR HEMISPHERIC ASYMMETRY

The research field of brain laterality or hemispheric asymmetry (the terms are treated synonymously) is historically an old field of interest among brain researchers. One of the most solid findings of hemispheric differences is the left hemisphere dominance for language, dating back to the findings of Broca, Wernicke, Lichtheim and other neuroscientists of the 19th century (see Goodglass (1993), pp. 13-38, for a historical overview). The obvious asymmetrical property of handedness has also been studied for a long time, although the understanding of the relation to brain laterality is younger than for language (Beaton, 2003). However, recent research has provided more elaborate models of lateral asymmetries, and a deeper understanding of the significance of this aspect of brain function (Hugdahl, 2000). In human subjects, this research has partly been driven by the emergence of methods such as the electroenchephalogram (EEG; Berger, 1929), the Sodium Amobarbital test (Wada & Rasmussen, 1960) and more recently by modern imaging techniques such as computerized tomography (CT), structural and functional magnetic resonance imaging (MRI), positron emission tomography (PET) etc (see Toga and Thompson (2003) for a review). Often, such methods have in different ways been correlated with behavioral procedures such as visual half-field, dichotic listening, tactile tests, motor tests, eye movements etc. Bouma (1990, p.45) has proposed a subdivision of theoretical models of lateral asymmetries. She defines the dynamic structural model as a synthesis of structural models and attentional models of laterality. She further subdivides the structural models into models of absolute specialization and models of relative specialization. Attentional models are subdivided into models focusing on priming mechanisms and models focusing on hemispheric capacity limitations. An overview of this subdivision is seen in figure 1.
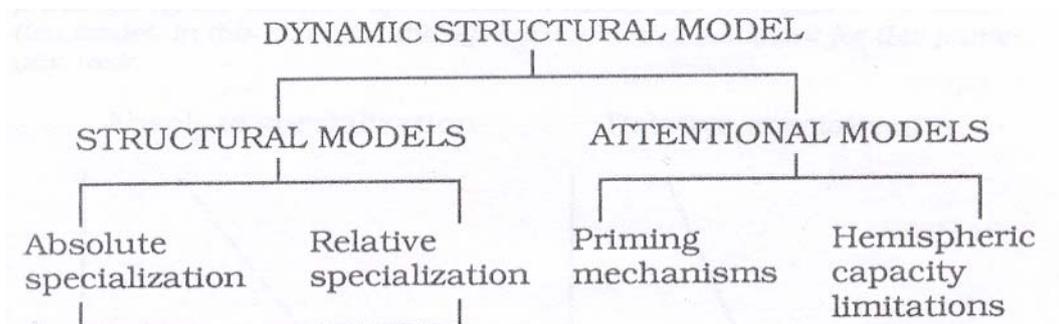
Figure 1. Theoretical models of hemispheric specialization (from Bouma, 1990, p. 45).

5.1. Structural models

Among structural models, the model originally developed by Kimura (1966, 1967) is a prominent example. In this model, each hemisphere show preponderance to the processing of certain stimuli. Thus, direct access of the stimuli to that hemisphere by means of contralateral projections leads to more efficient processing. Input from the ipsilateral side is inhibited, and mainly follows contralateral projections to the opposite hemisphere. Then, this input is transferred over the corpus callosum to the dominant hemisphere for processing. Evidence for this may be the increased right ear advantage found in patients with lesions of the corpus callosum (Sparks & Gescwind, 1968; Pollmann, Maertens, von Cramon, Lepsien & Hugdahl, 2002), or the correlation between auditory laterality and anatomical asymmetry of the planum temporale (Jäncke & Steinmetz, 1993; Sequeira et al, 2006). The specialization of the hemisphere to the specific tasks may be absolute or relative. In absolute specialization, an all-or-none capacity difference between the hemispheres is postulated. In relative specialization, the two hemispheres may be regarded as having different degrees of competence in processing certain stimuli, and asymmetrical performance reflects this difference. Most

studies support the relative specialization model, with representation in the (non-dominant) right hemisphere for aspects of language (Lavidor, Brinksman & Gödel, 2004; Coulson & Williams, 2005; Jung-Beeman, 2005; Mashal, Faust & Hendler, 2005) and representation in the (non-dominant) left hemisphere for spatial processing (Jansen, Flöel, Menke, Kanowski & Knecht, 2005). Moreover, aspects of dominance, such as language and even handedness, can change as a result of brain plasticity in focal brain damage. After early left hemisphere damage, language and motor dominance can be shifted to the right hemisphere, at the cost of reduced capacity to perform tasks ordinarily subserved by this hemisphere, such as spatial representations (the "crowding" hypothesis, see for example Orsini & Satz, 1986; Strauss, Satz & Wada, 1990). Atypical language representation, probably due to early brain damage, has been demonstrated in patients with epilepsy (Rasmussen & Milner, 1977; Goldmann & Golby, 2005) as well as in other brain disorders (Carlsson, Hugdahl, Uvebrant, Wiklund & von Wendt, 1992; DeVos, Wyllie, Geckler, Kotagal & Comair, 1995; Brizzolara et al, 2002; Ewing-Cobbs, Barnes & Fletcher, 2003). Moskovitch (1979) regarded processing of purely sensory material as non-lateralized, but that any higher order involvement in the perceptual process may introduce laterality differences. The relative difficulty of processing within a particular task may also be of importance (Hellige & Sergent, 1986). Goldberg and Costa (1981) suggested that the right hemisphere is superior in the initial stages of learning new skills, and the left hemisphere is superior in utilizing well-routinized codes. Thus, a shift in superiority from the right to the left hemisphere may occur with increased experience.

5.2. Attentional models

Kinsbourne (1970, 1975) argued that asymmetric hemispheric function is a function of the relative activation of the hemispheres. The hemispheres are acting in a reciprocally inhibitory fashion towards one another, so that activation of one hemisphere will inhibit the other. Then attention deviates in a direction contralateral to the activated hemisphere, to facilitate the general information processing. A specific expectancy, or set, leads to a priming of one of the hemispheres to attend to the contralateral hemispace. Thus, an expectancy for verbal material activates the left hemisphere and leads to a stronger attention focus to the right hemispace. Moreover, each hemisphere may have limited attentional capacity, so that processing of a certain task may interfere stronger with another task if they share the processing capacity of the same hemisphere. This has led to a number of studies of intrahemispheric interference, for example by simultaneous processing of parallel tasks (Kinsbourne & Hiscock, 1983; Dalen,

1992). Such interference effects are most often observed with increased task difficulty (Bouma, 1990).

In summary, experimental evidence has supported both structural and attentional models of brain laterality. A dynamic structural model, with a relative view of hemispheric specialization and incorporating attentional mechanisms at all stages of processing, may be regarded as a synthesis of the structural and attentional models (Bouma, 1990; O`Leary, 2003).

6. NEUROPSYCHOLOGICAL TESTING

Due to the varieties of tests used in neuropsychological practice, no attempt to cover the full range of neuropsychological tests or test batteries is made. For this purpose, there are several textbooks (e.g. Spreen & Strauss, 1998; Lezak, Howieson & Loring, 2004). For an even more comprehensive overview, the Handbook of Neuropsychology, edited by Boller and Grafman and published in 11 volumes in the period 1988-1997 by Elseviere Science, is recommended.

6.1. Assessment of emotional and psychosocial problems

Within the field of clinical neuropsychology, many different methods of assessing emotional and psychosocial problems have been used. Most of these have been developed for use among people with primary emotional problems, and some have been developed for use within specified groups such as patients with epilepsy. The overwhelming number of assessment methods used in patients with epilepsy are questionnaires. A search in the database PubMed for publications about epilepsy and Rorschach or epilepsy and projective tests gave no hits from english-language journals from later than 1983, with the exception of three articles on nonepileptic seizures and one article from a forensic population. However, a very wide range of questionnaires have been used, especially within the field of quality of life studies (see Leone et al (2005) for an overview). In the following, a short presentation of two of the most frequently used methods will be given.

6.1.1. Minnesota Multiphasic Personality Inventory (MMPI/MMPI-2)

The MMPI, and its contemporary version, the MMPI-2 (Butcher, Dahlstrom, Graham, Tellegen & Kaemmer, 1989), is a frequently used questionnaire to screen for emotional problems within the field of clinical neuropsychology and epileptology. Early studies showed that the MMPI was not particularly sensitive to seizure variables (Matthews & Kløve, 1968), although it was shown to be sensitive to the presence of psychiatric problems among patients with epilepsy (Dikmen, Hermann, Wilensky & Rainwater, 1983). Epileptic seizures may by themselves influence scores of some of the subscales, and there is a need for caution when using standardized interpretation based on results from psychiatric patients (Bornstein, Rosenberger, Harkness-Kling & Suga, 1989; Nelson, Elder, Groot, Tehrani & Grant, 2004). However, the method is continually in use in many centra and hospitals treating neurological patients and patients with epilepsy. Among areas of application, it has been used in screening patients with epilepsy in surgical centra for general psychopathology (e.g. Trenerry, 1996; Trenerry et al, 1996; Derry et al, 2002; King et al, 2002), and as an aid in differentiating epileptic from non-epileptic seizure disorders (Wilkus & Dodrill, 1989; Cuthill & Espie, 2005).

6.1.2. Washington Psychosocial Seizure Inventory (WPSI)

Among questionnaires specifically constructed for patients with epilepsy, the WPSI (Dodrill et al, 1980) remains among the most widely used instruments. In a recent review (Leone et al, 2005) WPSI was selected as one of six questionnaires fulfilling the methodological demands put to a comprehensive instrument measuring quality of life in epilepsy. Studies comparing the WPSI to other measures of quality of life in epilepsy generally reveal both strengths and weaknesses. One study (Wiebe, Rose, Derry & McLachlan, 1997) found a relatively low responsiveness to small changes in seizure status of WPSI compared to two other scales. Another study (Langfitt, 1995) concluded that WPSI assessed a more specific range of functions than two other methods. However, none of these studies disputed the validity of the WPSI as a measure of quality of life and psychosocial functioning in patients with epilepsy. Analyses generally show satisfactory psychometric properties of the WPSI, but potentials for shortening the questionnaire have been suggested (Chang & Gehlert, 2003; Swinkels, Kuyk, van Dyck & Spinhoven, 2004).

6.2. Assessment of cognitive functioning

Historically, within the field of clinical neuropsychology, assessment of cognitive function has been the core issue (Reitan & Davison, 1974). Valid contributions to the detection and closer description of the effects of brain damage have been possible using tests of cognitive functioning. The most successful results have been obtained using test-batteries, that is, a series of tests administered together. By using this method, clinicians or researchers are able to make use of intratest variability in the single person being tested, as well as level of performance and pathognomonic signs of brain damage, as sources of interpretation (Reitan, 1974). The relationship of many single cognitive tests to brain damage have been established (see Lezak, Howieson & Loring, 2004, for an overview). However, only a few test-batteries have been thoroughly validated. Many neuropsychologists use flexible test-batteries, that is, test-batteries constructed for the clinical purpose at hand (Kane, 1991; Bauer, 2000). However, this approach leads to certain methodological problems. These test-batteries are, by their nature, not validated as a whole, and interpretations made from intratest variability therefore lack a clear scientific basis (Russell, Russell & Hill, 2005). Under the "Daubert standard" in USA law flexible test-batteries are not considered scientific evidence, unlike a fixed test-battery (Reed, 1996). In the following, a short presentation of one neuropsychological test-battery and one test of a more specific brain related function, used in this thesis, is given.

6.2.1. The Halstead-Reitan Battery (HRB)

This specific battery of tests is originally developed by Halstead (1947), and modified and refined by Reitan and coworkers (Reitan & Davison, 1974; Reitan & Wolfson, 1993). A slightly modified version of the HRB was adopted by Kløve and coworkers at the University of Wisconsin at Madison (Kløve, 1963), and this version has been translated into Norwegian and is used in this thesis. The HRB has been cross-validated, and it has been proven to have the same properties when used in Norway compared to North America (Kløve, 1974). Also, a large number of validation studies have proved its sensitivity to brain damage as well as its utility in making diagnostic inferences (see Kløve (1974) and Reitan & Wolfson (1993) for reviews). Included in the test-battery are tests of lateral dominance, tests of motor and sensory-perceptual function, tests of general adaptive abilities and a screening test for aphasia. Wechslers Adult Intelligence Scale (Wechsler, 1955) is also included. There are separate

versions of the test-battery for children aged 9-14 years (Reitan & Wolfson, 1992a) and for children aged 5 to 8 years (Reitan & Wolfson, 1992b). A modification of the HRB has been specifically validated for use in patients with epilepsy (Dodrill, 1978).

Several attempts have been made at making summary scores of the tests of the HRB. Halstead (1947) introduced the Impairment Index as the fraction of ten test results of an individual person that fell below a given cut-off value. In later revisions, three of these test results were excluded, and Reitan & Wolfson (1993) use the remaining seven test results as a basis of calculating the Impairment index. One modification of the impairment index includes three other measures instead of the excluded ones (Matthews, Shaw & Kløve, 1966). Dodrill (1978), in his test battery for epilepsy, introduced a similar measure, which was named "number of tests outside normal limits". A statistically more refined measure, the Average Impairment Rating (Russell, Neuringer & Goldstein, 1970) has been proposed, but the difference between this measure and the original index is in most cases small (e.g. Heaton, Miller, Taylor & Grant, 2004). The most elaborate effort in this direction, however, has been the construction of the neuropsychological deficit scales by Reitan & Wolfson (1993). In this formulation, a specific measure of left hemisphere deficit (Left Neuropsychological Deficit Scale; LNDS) and a specific measure of right hemisphere deficit (Right Neuropsychological Deficit Scale; RNDS) is calculated, in addition to a general measure of brain deficit (General Neuropsychological Deficit Scale; GNDS). In a cross-validation study, (Sherer & Adams, 1993) it was found support for the sensitivity of the GNDS, but the measure correlated highly both with the Impairment index and the Average Impairment Rating. The sensitivity of LNDS and RNDS was weaker, but they were found to be sensitive to group differences. These authors concluded that the measures may be useful in research and clinical work if interpreted with caution and augmented with other data. Later studies (Wolfson & Reitan, 1995; Oestreicher & O`Donnell, 1995) have confirmed the validity of the GNDS. One problem is that the scales are developed using the 1955 version of Wechslers Adult Intelligence Scale (Wechsler, 1955). Most psychologists now use updated versions of this scale. However, Horton (2000) has shown that the GNDS is about equally sensitive if items drawn from the Wechsler scale are omitted. Further studies of these scales, particularly the LNDS and RNDS, are needed. It would seem, however, that sufficient validation data exists to support the use of the scales in group studies.

The modification of the test battery made by Hallgrim Kløve and coworkers mainly affected the aphasia screening test and the calculation of the Impairment index (Matthews, Shaw & Kløve, 1966). In the translation process, the Speech Perception Test, which was one of

Halsteads original tests, was omitted because the test consists of perception of spoken North American language, making it unreasonably difficult for speakers of other languages. To make calculation of the NDS-scales more comparable to the manual, Reitan and Wolfson (1993)`s method of calculating the Impairment index was adopted in this thesis, calculating the fraction of six tests that fell below the cut-off. However, the aphasia screening test used is different from the Reitan-Indiana test in several aspects. The main differences are the following:

1. The copy of the key is omitted in the Norwegian version, diminishing the probability of detecting constructional apraxia.

2. The items measuring central dysarthria are easier in the Norwegian version, diminishing the probability of detecting central dysarthria.

3. The Norwegian version contains more spelling and writing of words, increasing the probability of detecting spelling dyspraxia and dysgraphia.

4. The Norwegian version contains a more elaborate test of right-left discrimination, increasing the probability of detecting right-left confusion.

5. The Norwegian version contains more items on verbal understanding, increasing the probability of detecting auditory verbal dysgnosia.

However, in appreciating these differences it is important to bear in mind the principle behind interpretation of results from the aphasia screening test. All the items are not scored on a pass-fail basis, as suggested by Russell, Neuringer and Goldstein (1970). Instead, a qualitative decision is made whether a particular performance reflects a specific symptom of aphasia or constructional dyspraxia. Then, the performance is given a weighted score on the NDS scales, depending upon which symptom it is interpreted to reflect. Many patients with brain damage pass all the items. Thus, the test is not particularly sensitive to brain damage. However, it is meant to be highly specific for the presence of brain damage. This is probably also the case with the Norwegian version, and one would not expect large differences between the two tests on a group basis. If a person has symptoms of aphasia, it should be detected by both versions of the test.

6.2.2. Dichotic listening

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Fig. 2. Overview of the dichotic listening situation used in this thesis. CV-syllables (/ba/, /ta/) are given simultaneously to each ear by earphones. Due to the preponderance of the contralateral neuronal pathways and the blocking of the ipsilateral pathways, the right ear signal is directly fed to the left hemisphere, where signal processing is done.

Dichotic listening consists of simultanous presentation of different auditory stimuli to the left and right ears. Often, some kind of selection is made by the subject taking the test, and the percentage of correct reports from each ear is noted. A very wide range of stimuli and scoring procedures has been used. Normally, a right ear advantage (REA) for verbal stimuli and a left ear advantage (LEA) for most nonverbal stimuli is found (Bryden, 1988). The findings of asymmetry, among other properties, make the test suitable for studies on brain laterality, and it has gained a prominent role in experimental brain research. There is a wide variety in methodology, and comparisons between studies can be difficult. Also within the verbal domain, stimulus properties may affect results. For example, Asbjørnsen and Bryden (1996) showed that performance with consonant-vowel (CV) syllables was easier affected in the

forced-attention condition than performance with fused words, although both procedures gave an REA in the standard, non-forced attention condition. When comparing different studies, it is important to have information of the exact nature of stimuli used. A large number of studies have used the consonant-vowel stimuli with the six stop consonants b, p, d, g, t and p, paired with the vocal a (see Hugdahl, 1995; 2003 for overviews). However, in the published literature on epilepsy patients where speech lateralization is determined with the sodium amobarbital test (Wada & Rasmussen, 1960), most studies (Kimura, 1961,1967; Strauss, Gaddes & Wada, 1987; Zatorre, 1989; Lee et al, 1994; Grote, Pierre-Louis, Smith, Roberts & Varney, 1995) use other stimuli, such as digits or fused words. However, the studies using CV-syllables (Berlin, Lowe-Bell, Jannetta & Kline, 1972; Hugdahl, Carlsson, Uvebrant & Lundervold, 1997) generally agree with the other studies that an effect of speech lateralization is seen. Most patients with left hemisphere speech dominance showed an REA. Also, most patients with right sided speech dominance showed an LEA. In the studies by Zatorre (1989: 4 patients with LEA, fused words) and Hugdahl et al (1997: 3 patients with LEA, CV-syllables), this was the case in all patients. In the study by Kimura (1967), one of thirteen patients with right hemisphere speech showed a REA, using digits as stimuli. In the study by Strauss, Gaddes & Wada (1987), five of fifteen patients with right hemisphere speech showed an REA, with three pairs of monosyllabic words as stimuli in each trial.

In our own material from Haukeland University Hospital, three patients have shown right hemisphere speech lateralization on the sodium amobarbital test. Their results on dichotic listening with CV-syllables are given in Table 1.

Table 1. Number correct reports in dichotic listening by patients with right hemisphere speech dominance.

Age	Gender	Handedness	RENF	LENF	REFR	LEFR	REFL	LEFL
54	Female	Right	8	19	11	18	18	7
22	Female	Left	12	12	10	13	11	11
40	Male	Left	10	10	9	8	10	11

Abbreviations: RE = right ear, LE = left ear, NF = Nonforced attention condition, FR = forced right attention condition, FL = forced left attention condition.

As can be seen from Table 1, no patient with right hemisphere speech dominance showed an REA in the standard NF attention condition. However, 2 of 3 patients showed a no-ear advantage (NEA). In the forced left condition, one of the patients managed to achieve an LEA with the smallest possible margin, whereas one patient showed a paradoxical performance with a definite REA in this condition. In summary, patients with right hemisphere speech seem to show an LEA or NEA. The procedure used in the study showing the largest percentage of REA in individuals with right hemisphere speech dominance (Strauss, Gaddes & Wada, 1987) was quite different, relying heavily on a memory recall procedure and not on a perceptual procedure as in the other studies. The correspondence between right hemisphere speech dominance and lack of REA seems to be strong, but it may not be perfect, and there is a need for further studies. Most authors would probably agree that dichotic listening cannot be trusted as the only measure in determining speech dominance before epilepsy surgery. However, some studies indicate that dichotic listening may be useful in combination with other noninvasive test procedures (Hund-Georgiadis, Lex, Friederici & von Cramon, 2002; Fernandes, Smith, Logan, Crawley & McAndrews, 2006), thereby making it possible to avoid the invasive procedure of sodium amobarbital testing before epilepsy surgery (for recent reviews on this subject, see Helmstaedter & Kurthen, 2002; Klöppel & Büchel, 2005). Several studies have evaluated the sensitivity of dichotic listening to lesions in the contralateral hemisphere. In patients with epilepsy, a relative deficit of reporting stimuli to the ear contralateral to lesions is shown in many studies (see Lee et al (1994) for a review). This effect has not been consistently shown in focal epilepsy without visible structural lesions (Mazzucchi & Parma, 1978; Mazzucchi, Visintini, Magnani, Cattelani & Parma, 1985, Lee et al, 1994).

Another procedural variant of dichotic listening is the "top-down" aspect introduced by instructing subjects to attend only to stimuli given to one ear at the time. This was originally labelled the "forced-attention" paradigm by Hugdahl & Andersson (1986). To date, this paradigm has been neglected in the study of patients with epilepsy. Further study using this paradigm may well give important insight in attentional problems associated with the epilepsy condition, as it has in other experimental and clinical studies (see O`Leary (2003) for an overview).

7. RESEARCH OBJECTIVES

The main research objectives investigated in this thesis are:

- To what extent are scores on a clinical scale measuring psychosocial problems in epilepsy affected by scores from clinical scales based on contemporary personality theory and social learning theory?

- Is lateralized neuropsychological deficit more important than side of epileptic focus for performance in the standard non-forced attention condition of dichotic listening in patients with epilepsy?

- Is lateralized neuropsychological deficit more important than side of epileptic focus for performance in the forced-attention paradigm of dichotic listening?

- Is general neuropsychological deficit more important than lateralized neuropsychological deficit in the forced-attention relative to the non-forced attention paradigm of dichotic listening?

8. SUMMARY OF REPORTS

Report I

One hundred and one patients answered a questionnaire, consisting of Washington Psychosocial Seizure Inventory (WPSI; Dodrill et al, 1980), Positive and Negative Affect Schedule (PANAS-X; Watson & Clark, 1991), Multidimensional Health Locus of Control sclae (MHLC; Wallston, Wallston & DeVellis, 1978), the General Self-efficacy Scale (Schwarzer, 1993) and a self-constructed scale of self-efficacy in epilepsy. High correlations were found between Negative Affectivity from the PANAS-X and several clinical scales from the WPSI. In particular, the highest correlations were found between Negative Affectivity and scales measuring general psychosocial and emotional functioning (the scales Emotional

adjustment, Overall psychosocial functioning and Quality of Life). Positive Affectivity correlated with the same WPSI scales, but in the opposite direction. Both scales measuring self-efficacy also correlated with the same WPSI scales. The scales of the MHLC in general showed low correlations with WPSI scales. Regression analyses showed independent effects of Positive Affectivity and one scale measuring self-efficacy on these WPSI scales. The combined regression model explained 55% of the variance on the Quality of Life scale, and 60% of the variance on the two other scales, suggesting a strong predictive power of the constructs. It was concluded that, among patients with epilepsy, perceived psychosocial and emotional functioning and quality of life to a large degree are affected by personality trait-based properties such as negative and positive affectivity, but that self-efficacy also is an important factor. These findings are of importance for the future assessment of quality of life in patients with epilepsy.

Report II

Seventeen patients with focal temporal lobe epilepsy and a left hemisphere dominance for speech were tested with dichotic listening and the Halstead-Reitan battery (HRB). A summary measure of left hemisphere functioning (LNDS) derived from scores on the HRB was calculated. A cut-off point between 5 and 6 on this scale divided the patients in two groups comparable in most respects, but the group with the highest score also had a significantly higher score on a scale measuring general neuropsychological deficit (GNDS). Then, the patients were divided in groups in two ways: First, they were divided according to seizure focus lateralization, yielding one group with right seizure focus and one group with left seizure focus. When these groups were compared according to dichotic listening results, no significant differences appeared. However, when dividing the patients according to scores on the LNDS, yielding one group with normal scores and one group with pathological scores, there were significant differences in dichotic listening. The group with pathological scores on the LNDS showed a higher percentage correct responses to left ear stimuli, a lower laterality index and a trend towards lower percentage correct responses to right ear stimuli. This was found to be true regardless of seizure focus lateralization. Moreover, a multiple regression analysis showed that the difference between the groups in general neuropsychological deficit had little impact on dichotic listening compared to the LNDS. The study demonstrated that left hemisphere cognitive dysfunction is a strong determinant for dichotic listening results in this patient group, whereas seizure focus lateralization in itself does not seem to influence the

results significantly. In addition, the strongest effect of left hemisphere dysfunction was in releasing inhibition of left ear signals rather than facilitating perception of right ear signals. The findings explain some discrepancies in the earlier literature, and point towards perceptual effects of left hemisphere dysfunction which may be of clinical interest.

Report III

Fifty right-handed patients with focal temporal lobe epilepsy were tested in a similar way to the patients in paper I, but this time results of the forced-attention paradigm in dichotic listening (DL) were also analyzed. The findings of the prior study (paper I) were largely confirmed also in this larger group of patients. Also, the effect of left hemisphere dysfunction in the non-forced attention condition of DL remained as an influence in the forced-attention conditions. However, regression analyses showed that this effect was weaker in the forced-attention conditions, and that the relative influence of general neuropsychological deficit, measured by the GNDS, was larger in these conditions. Moreover, the relative influence of general deficit was stronger in the forced-left than in the forced-right condition. The results were explained by stronger influence of "top-down" or instruction-driven cognitive processes in the forced-attention conditions. In addition, the forced-left condition, demanding reversal of the perceptual asymmetry, may be regarded as a condition with a heavier cognitive load on the brain`s total capacity than the forced right condition, which acts synergistically with the non-forced condition.

7. DISCUSSION

9.1   Determinants of psychosocial functioning

In Report I, a significant impact of personality factors and self-efficacy on general measures of psychosocial functioning and quality of life was found. In fact, 55-60% of the variance could be explained by a combined model consisting of Negative affectivity, Positive affectivity and one measure of self-efficacy. This is an impressive amount of explained variance, suggesting that these factors are central in the understanding of a concept such as Quality of Life. Interestingly, in still unpublished data from a long-term follow-up study of patients with head injury, personality traits measured by Eysenck`s questionnaire and self-efficacy measured with Schwarzer`s scale significantly predicted psychosocial outcome

whereas several other scales measuring aspects of psychological and social functioning did not reach a significant degree of prediction (Wood, 2005). This finding strengthens the impression that these constructs are indeed important for psychosocial functioning in patients with chronic brain dysfunction, probably overriding the importance of such concepts as Health Locus of Control and Coping style. However, the number of studies showing this are limited, and further studies are needed. In further studies, patients may be divided into subgroups according to background and seizure variables to investigate if there are differences between subgroups. Age, duration and severity of epilepsy, seizure types, medication variables, degree of cognitive dysfunction, focal versus generalized epilepsy and focus localization are all of interest for further studies. The comorbidity of depression or other psychiatric disorders also should be further investigated. Further studies are probably also needed into the meaning of concepts such as negative and positive affectivity and self-efficacy in a chronic patient group. Do childhood seizures influence development of personality traits or outcome expectations? In addition, given the importance of these factors in psychosocial functioning, one may imagine clinical use of scales such as PANAS-X and the self-efficacy scales in therapy planning for individual patients. Positive increase in self-efficacy may also serve as an indicator of successful therapy. However, to achieve this end, further validation studies of the scales in various populations are needed.

9.2. Determinants of non-forced attention dichotic listening performance

Reports II and III clearly supported the view that left hemisphere dysfunction, measured by neuropsychological testing, is important for dichotic listening in patients with temporal lobe epilepsy. Lateralization of the epileptic focus was not found to be that important, and only one significant correlation between dichotic listening (DL) and focus lateralization was found. The neuropsychological deficit in this study is probably best understood as an indicator of structural tissue damage in the left hemisphere, because validation studies of the measure used have been done in patients with structural brain damage. Focus lateralization, on the other hand, may represent a lateralized neurophysiological variable of another character. Thus, the finding of a stronger effect of neuropsychological than of neurophysiological left hemisphere dysfunction in this case may support a structural model of laterality. A measure (although indirect) of structural pathology was more effective than neurophysiological dysfunction in the form of an epileptic focus, in predicting DL results.

Interestingly, in an unpublished study of MMPI-2 results in the same patient population, left-sided epileptic focus predicted elevated scores on several clinical scales, whereas no effect of

left-sided neuropsychological dysfunction was found (Gramstad, Helgeland, Ellertsen & Engelsen, 2005). This may implicate that lateralized neurophysiological properties are more important than structural pathology in emotional processing, whereas structural pathology is more important for perceptual processing as in DL. However, although this could be in keeping with current theories of emotional laterality (for example Davidson, 1995; 2004), clearly further studies are needed to support this notion.

The more precise localization within the temporal lobe may also be of importance. Preliminary results suggest that DL results may be more affected by lateral temporal than mesial temporal foci (Haettig, Burckhardt, Bengner & Meencke, 2003). This preliminary finding needs further validation, however. Factors like lesion type and size, seizure severity and degree of cognitive dysfunction need to be considered in comparison of the different intratemporal localizations. Following a structural model of DL, lesions close to the primary auditory cortex in the temporal lobe or to the subcortical auditory projections would be expected to have a larger impact on DL performance than more remote lesions in the temporal lobe.

Another interesting aspect of the present studies is that neuropsychological test results using a general, battery-based approach can be used as a valid estimate of hemisphere-specific dysfunction that may predict the results of a more specific measure of auditory perception like DL. The other way around, DL performance may give insight into particular aspects of brain functioning of definite clinical interest. The findings of papers II and III may have taken the understanding of the nature of attentional difficulties in patients with temporal lobe epilepsy and dysfunction of the left hemisphere one step further. Even a relative discrete left hemisphere dysfunction may lead to difficulties in normal perception of verbal auditory signals.

Practical usage of DL in patients with epilepsy may be as part of a noninvasive test battery aiming to replace the sodium amytal test as a measure of language lateralization. DL is probably affected by too many variables to be suitable as a stand-alone measure of language lateralization, but it represents a perceptual language task that could supplement tasks of expressive language traditionally used in the mapping of lateralized language representation by methods such as fMRI. Results of papers II and III of this thesis suggest that standard neuropsychological testing also may be valuable in understanding the meaning of DL results related to lateralized language representation.

9.3 Determinants of forced-attention dichotic listening performance

With forced attention, the demand of the test changes from perception to wilful attention. However, the determinants of results in the nonforced condition of DL also affected performance in the forced attention condition. In paper III, this was most clearly shown as a "leakage" of left ear stimuli, in that those stimuli were more often reported by patients with left hemisphere dysfunction. This effect was strongest in the non-forced attention condition, but group differences in perception of left ear stimuli were significant in all three conditions. This was interpreted as a result of deficient inhibition of left ear stimuli by the left hemisphere. Based on an attentional model of laterality, these findings could have been explained by a relative increase in activation of the right hemisphere due to left hemisphere dysfunction. If this had been the case, however, one would expect a similar effect, in the opposite direction, of right hemisphere dysfunction as of left hemisphere dysfunction on DL results. This was not the case in the present studies. Most correlations between a measure of right hemisphere dysfunction and DL results were low and insignificant. Thus, the results of study III also support a structural model of DL. The exact mechanism and anatomical locus of reduced inhibition, however, are not clear. One may hypothesize reduced inhibition of the ipsilateral signals, reduced inhibition of signals entering via the corpus callosum, or a combination. Also, indicating an exact localization of the source of reduced inhibition within the left hemisphere is not possible from our data. The neuropsychological scale used to detect dysfunction has no further localizing value than the left hemisphere. However, the fact that defect inhibition was stronger in the non-forced attention condition than in the forced-attention conditions may suggest that the temporal lobes are involved to a larger degree than other structures, given a stronger association between temporal lobe and DL in stimulus-driven (Binder, Frost, Hammeke, Rao & Cox, 1996) than in instruction-driven conditions, where the frontal lobes may be involved to a larger degree (Thomsen, Rimol, Ersland & Hugdahl, 2004). However, both the temporal and the frontal lobes are heterogenous structures, and different substructures must be expected to play differential roles both in perception and attention. The finding of a stronger explanatory value of generalized cognitive dysfunction in the forced-attention conditions than in the non-forced attention condition is compatible with a view that widely distributed, integrated bilateral networks affect performance stronger in a "top-down" situation. However, the finding that this effect is more pronounced in the forced-left than in the forced-right attention condition may be best explained by an attentional model, where the right hemisphere has allocated limited

attentional resources. Thus, the need for bilateral, integrated networks to perform successfully may be stronger when a demand is made to overcome a perceptual asymmetry than to increase an asymmetry that already exists.

To further illustrate this point, a recalculation of data from the same patients that participated in study III of this thesis was done. Results of patients with a right ear advantage (REA) in the non-forced attention condition (N=25) were compared to results of patients without an REA (N=25). In the subgroup with REA, a comprehensive model including five cognitive summary variables (IQ, Memory Quotient, GNDS, LNDS and RNDS) explained 63% of the variance in reports of left ear signals, and 49% of the variance in reports of right ear signals, in the forced-left attention condition. In the subgroup without REA, the model explained a much lower and insignificant amount of variance. In neither subgroup did the model explain a significant amount of variance in the forced-right attention condition (Gramstad, Engelsen & Hugdahl, 2004).

These results suggest that the impact of generalized cognitive functioning in the forced-left attention condition is strongest in patients with an REA in the non-forced attention condition, and that this impact largely disappears in patients without an REA. In these right-handed patients, REA may be regarded as an indication of normal auditory perception, whereas no REA most likely indicates abnormal auditory perception. Such perceptual abnormalities probably affected DL performance strongly also in the forced-attention conditions, and the relative influence of higher order cognitive variables was diminished. With normal auditory perception, however, the ability to overcome the existing asymmetry in favor of the right ear seems to be largely dependent upon general cognitive functioning. This is in agreement with the idea that more general attentional resources are needed to overcome this perceptual asymmetry than the right hemisphere can contribute on its own, and thus that large and integrated, bilateral cerebral networks are highly involved in this situation.

Future studies of DL in patients with epilepsy should probably make use of modern imaging techniques to further characterize structural lesions in the brain, and compare subgroups with more discrete lesion location, such as mesial versus lateral aspects of the temporal lobe. Differential lesion location may also influence DL results on nonforced and forced attention differentially. One hypothesis is that focal frontal lobe epilepsy may interfere with forced attention to a larger degree than focal temporal lobe epilepsy. Again, one can imagine that factors such as differential lesion localization within the frontal lobe and size of cortical seizure-giving area may also have different implications for DL results.

9.4. Summary and conclusions

To conclude, the present thesis gives some tentative answers to the research questions posed: It was found that results from scales based on contemporary personality and social learning theory to a large and significant extent influenced results on well-validated clinical scales measuring general psychosocial problems. This finding may have implications for future research in the field of psychosocial functioning and quality of life among patients with epilepsy. Negative and positive affectivity, and self-efficacy, each seem to represent solid constructs with high validity in explaining individual behavior in patients with epilepsy.

It was also found that results of dichotic listening with CV-syllables in a standard nonforced condition were better explained by lateralized cognitive dysfunction than by lateralized neurophysiological dysfunction represented by seizure focus in the temporal lobe, in patients with left hemisphere speech dominance. This was taken as support for a structural model of dichotic listening, where structural changes represented by lateralized cognitive dysfunction explained results better than functional changes represented by seizure focus laterality. Also, the study helped to resolve some disparities in the literature regarding the impact of lateralized temporal epileptic foci without any corresponding structural lesion on dichotic listening results.

Finally, it was found that the impact of lateralized versus generalized neuropsychological function varied across three different attenion conditions of dichotic listening. In the non-forced attention condition, lateralized cognitive dysfunction of the left hemisphere clearly was more important for performance than generalized cognitive dysfunction. In the forced-right attention condition, generalized and lateralized dysfunction was of about equal importance, but the amount of unexplained variance was larger in this condition. In the forced-left attention condition, the relative influence of general dysfunction, and also of factors such as intelligence and general memory performance, were stronger. However, the lateralized left-hemisphere dysfunction influenced performance also in this attention condition. These results were discussed in terms of differential cognitive mechanisms in "top-down" and "bottom-up", or instruction- versus stimulus-driven, processing. Left-hemispheric cerebral structures, perhaps located within the temporal lobe, are probably particularly involved in the stimulus-driven processing in dichotic listening with CV-syllables when the left hemisphere is speech-dominant. More widespread, bilateral cerebral networks, perhaps involving the frontal lobes to a larger degree, are probably involved in the instruction-driven conditions. With more

demanding tasks, such as overcoming an existing perceptual asymmetry, increased

dependence upon these networks for effective performance is suggested.

REFERENCES

Adachi, N., Kanemoto, K., Muramatsu, R., Kato, M., Akanuma, N., Ito, M., Kawasaki, J., & Onuma, T. (2005). Intellectual prognosis of status epilepticus in adult epilepsy patients: Analysis with Wechsler Adult Intelligence Scale-Revised. *Epilepsia, 46,* 1502-1509.

Amir, M., Roziner, I., Knoll, A., & Neufeld, M.Y. (1999). Self-efficacy and social support as mediators in the relation between disease severity and quality of life in patients with epilepsy. *Epilepsia, 40,* 216-224.

Asbjørnsen, A.E., & Bryden, M.P. (1996). Biased attention and the fused dichotic words test. *Neuropsychologia, 34,* 407-411.

Bandura, A. (1977). Self-efficacy: toward a unifying theory of behavioral change. *Psychological Review, 84,* 191-215.

Baskind, R., & Birbeck, G.L. (2005). Epilepsy-associated stigma in sub-Saharan Africa: The social landscape of a disease. *Epilepsy & Behavior, 7,* 68-73.

Bauer, R.M. (2000). The flexible battery approach to neuropsychological assessment. In R.D. Vanderploeg (Ed.), *Clinicians Guide to Neuropsychological Assessment* (2nd Ed., pp. 419-448). Hillsdale, NJ: Lawrence Erlbaum Associates.

Baxendale, S.A., Van Paesschen, W., Thompson, P.J., Duncan, J.S., Harkness, W.F., & Shorvon, S.D. (1998). Hippocampal cell loss and gliosis: relationship to preoperative and postoperative memory function. *Neuropsychiatry, Neuropsychology & Behavioral Neurology, 11,* 12-21.

Beaton, A.A. (2003). The nature and determinants of handedness. In K. Hugdahl & R.J. Davidson (Eds.). *The Asymmetrical Brain* (pp. 105-158). Cambridge: The MIT Press.

Berger, H. (1929). Über das Elektrenkephalogram des Menschen. 1. Mitteilung. *Archieve für Psychiatrie und Nervenkrankheit, 87,* 527.

Berlin, C.I., Lowe-Bell, S.S., Jannetta, P.J., & Kline, D.G. (1972). Central auditory deficits after temporal lobectomy. *Archives of Otolaryngology, 96,* 4-10.

Binder, J.R., Frost, J.A., Hammeke, T.A., Rao, S.M., & Cox, R.W. (1996). Function of the left planum temporale in auditory and linguistic processing. *Brain, 119,* 1239-1247.

Bjørnæs, H., Stabell, K., Henriksen, O., & Løyning, Y. (2001). The effects of refractory epilepsy on intellectual functioning in children and adults. A longitudinal study. *Seizure, 10,* 250-259.

Blume, W.T., Lüders, H.O., Mizrahi, E., Tassinari, C., Van Emde Boas, W., & Engel, J.Jr. (2001). Glossary of descriptive terminology for ictal semiology: report of the ILAE task force on classification and terminology. *Epilepsia, 42,* 1212-1218.

Bornstein, R.A., Rosenberger, P., Harkness-Kling, K., & Suga, L. (1989). Content bias of the MacAndrew`s Alcoholism Scale in seizure disorder patients. *Journal of Clinical Psychology, 45,* 339-341.

Bouma, A. (1990). *Lateral Asymmetries and Hemispheric Specialization. Theoretical Models and Research.* Amsterdam/Lisse: Swets & Zeitlinger B.V.

Boylan, L.S., Flint, L.A., Labovitz, D.L., Jackson, S.C., Starner, K., & Devinsky, O. (2004). Depression but not seizure frequency predicts quality of life in treatment-resistant epilepsy. *Neurology, 62,* 258-261.

Brizzolara, D., Pecini, C., Brovedani, P., Ferretti, G., Cipriani, P., & Cioni, G. (2002). Timing and type of congenital brain lesion determine different patterns of language lateralization in hemiplegic children. *Neuropsychologia, 40,* 620-632.

Bryden, M.P. (1988). An introduction to the dichotic listening procedure and its relation to cerebral organization. In K. Hugdahl (Ed.), *Handbook of Dichotic Listening: Theory, Methods and Research* (pp. 1-43). Chichester: John Wiley & Sons.

Butcher, J.N., Dahlstrom, W.G., Graham, J.R., Tellegen, A., & Kaemmer, B. (1989). *MMPI-2. Manual for Administration and Scoring*. Minneapolis: University of Minnesota Press.

Carlsson, G., Hugdahl, K., Uvebrant, P., Wiklund, L.M., & von Wendt, L. (1992). Pathological left-handedness revisited: dichotic listening in children with left vs right congenital hemiplegia. *Neuropsychologia, 30,* 471-481.

Cascino, G.D. (2004). Surgical treatment for epilepsy. *Epilepsy Research, 60,* 179-186.

Chang, C-H., & Gehlert, S. (2003). The Washington Psychosocial Seizure Inventory (WPSI): psychometric evaluation and future applications. *Seizure, 12,* 261-267.

Chelune, G.J. (1995). Hippocampal adequacy versus functional reserve: predicting memory functions following temporal lobectomy. *Archives of Clinical Neuropsychology, 10,* 413-432.

Collins, A.L., & Lennox, W.G. (1947). The intelligence of 300 private epileptic patients. *Association for Research in Nervous and Mental Disease, 26,* 586-603.

Commission on Classification and Terminology, International League Against Epilepsy (1981). Proposal for revised clinical and electroencephalographic classification of epileptic seizures. *Epilepsia, 22,* 489-501.

Commission on Classification and Terminology, International League Against Epilepsy (1989). Proposal for revised classification of epilepsies and epileptic syndromes. *Epilepsia, 30,* 389-399.

Coulson, S., & Williams, R.F. (2005). Hemispheric asymmetries and joke comprehension. *Neuropsychologia, 43,* 128-141.

Cuthill, F.M., & Espie, C.A. (2005). Sensitivity and specificity of procedures for the differential diagnosis of epileptic and non-epileptic seizures: A systematic review. *Seizure, 14,* 293-303.

Dalen, K. (1992). *Hemispheric Asymmetry and the Dual-Task Paradigm: An Experimental Approach.* Doctoral dissertation, University of Bergen, Norway.

Davidson, R.J. (1995). Cerebral asymmetry, emotion and affective style. In R.J. Davidson & K. Hugdahl (Eds.). *Brain Asymmetry* (pp. 361-387). Cambridge: The MIT Press.

Davidson, R.J. (2004). Well-being and affective states: neural substrates and biobehavioural correlates. *Philosophical Transactions of the Royal Society of London, 359,* 1395-1411.

Davies-Eysenck, M. (1952). Cognitive factors in epilepsy. *Journal of Neurology, Neurosurgery and Psychiatry, 15,* 39-44.

Derry, P.A., Harnadek, M.C.S., McLachlan, R.S., Sontrop, J., Blume, W.T., & Girvin, J.P. (2002). A longitudinal study of the effects of seizure symptoms of the Minnesota Multiphasic Personality Inventory - 2 (MMPI-2) clinical interpretation. *Journal of Clinical Psychology, 58,* 817-826.

DeVos, K., Wyllie, E., Geckler, C., Kotagal, P., & Comair, Y. (1995). Language dominance in patients with early childhood tumors near left hemisphere language areas. *Neurology, 45,* 349-356.

DiIorio, C., Faherty, B., & Manteuffel, B. (1992). Self-efficacy and social support in self management of epilepsy. *Western Journal of Nursing Research, 14,* 292-307.

DiIorio, C., Shafer, P.O., Letz, R., Henry, T.R., Schomer, D.L., & Yeager, K. (2004). Project EASE: a study to test a psychosocial model of epilepsy medication management. *Epilepsy & Behavior, 5,* 926-36.

Dikmen, S., Hermann, B.P., Wilensky, A.J., & Rainwater, G. (1983). Validity of the Minnesota Multiphasic Personality Inventory (MMPI) to psychopathology in patients with epilepsy. *Journal of Nervous and Mental Disease, 171,* 114-122.

Dodrill, C.B. (1978). A neuropsychological battery for epilepsy. *Epilepsia, 19,* 611-623.

Dodrill, C.B. (1986). Correlates of generalized tonic-clonic seizures with intellectual, neuropsychological, emotional and social function in patients with epilepsy. *Epilepsia, 27,* 399-411.

Dodrill, C.B., Batzel, L.W. Queisser, H.R., & Temkin, N.R. (1980). An objective method for the assessment of psychological and social problems among epileptics. *Epilepsia, 21,*123-135.

Elger, C.E., Grunwald, T., Lehnertz, K., Kutas, M., Helmstaedter, C., Brockhaus, A., van Roost, D., & Heinze, H.J. (1997). Human temporal lobe potentials in verbal learning and memory processes. *Neuropsychologia, 35,* 657-667.

Ellenberg, J.H., Hirtz, D.G., & Nelson, K.B. (1986). Do seizures in children cause intellectual deterioration? *New England Journal of Medicine, 314,* 1085-1088.

Engel, J. Jr., & Pedley, T.A. (1997). Introduction: What is epilepsy? In J. Engel Jr., & T.A. Pedley (Eds.) *Epilepsy. A Comprehensive Textbook* (pp. 1-7). Philadelphia: Lippincott-Raven.

Engelsen, B.E., & Aarli, J.A. (1999). Occipital lobe epilepsy: special reference to mitochondrial encephalomyopathy and therapy resistant epilepsy. *Advances in Clinical Neurosciences, 9,* 275-289.

Ewing-Cobbs, L., Barnes, M.A., & Fletcher, J.M. (2003). Early brain injury in children: development and reorganization of cognitive function. *Developmental Neuropsychology, 24,* 669-704.

Fernandes, M.A., Smith, M.L., Logan, W., Crawley, A., & McAndrews, M.P. (2006). Comparing language lateralization determined by dichotic listening and fMRI activation in frontal and temporal lobes in children with epilepsy. *Brain and Language, 96,* 106-114.

Fisher, R.S., van Emde Boas, W., Blume, W., Elger, C., Genton, P., Lee, P., & Engel, J. Jr. (2005). Epileptic seizures and epilepsy: definitions proposed by the International League Against Epilepsy (ILAE) and the International Bureau for Epilepsy (IBE). *Epilepsia, 46,* 470-472.

Fox, J.T. (1924). The response of epileptic children to mental and educational tests. *British Journal of Medical Psychology, 4,* 235-248.

Gaitatzis, A., Carroll, K., Majeed, A., & Sander, J.W. (2004). The epidemiology of the comorbidity of epilepsy in the general population. *Epilepsia, 45,* 1613-1622.

Goffman, E. (1963). *Stigma. Notes on the Management of Spoiled Identity.* New Jersey: Prentice Hall.

Goldberg, E., & Costa, L. (1981). Hemisphere differences in the acquisition of descriptive systems. *Brain and Language, 14,* 144-173.

Goldmann, R.E., & Golby, A.J. (2005). Atypical language representation in epilepsy: implications for injury-induced reorganization of brain function. *Epilepsy & Behavior, 6,* 473-487.

Goldstein, L.H., Holland, L., Soteriou, H., & Mellers, J.D.C. (2005). Illness representations, coping styles and mood in adults with epilepsy. *Epilepsy Research, 67,* 1-11.

Goodglass, H. (1993). *Understanding Aphasia.* San Diego: Academic Press.

Gramstad, A., Engelsen, B.A., & Hugdahl, K. (2004). Differential performance in forced left and forced right attention conditions of dichotic listening by patients with temporal lobe epilepsy. (Abstract). *Epilepsia, 45,* Suppl. 3, 182.

Gramstad, A., Helgeland, A., Ellertsen, B., & Engelsen, B.A. (2005). Higher scores on clinical MMPI-2 scales in patients with left than in patients with right temporal epileptic foci. (Abstract). *Epilepsia, 46,* Suppl. 6, 315-316.

Grote, C.L., Pierre-Louis, S.J.C., Smith, M.C., Roberts, R.J., & Varney, N.R. (1995). Significance of unilateral extinction on the dichotic listening test. *Journal of Clinical and Experimental Neuropsychology, 17,* 1-8.

Haettig, H., Burckhardt, K., Bengner, T., & Meencke, H.J. (2003). Differential effects of temporal-cortical and hippocampal lesions on dichotic listening. (Abstract). *Epilepsia, 44,* Suppl. 8, 65.

Halstead, W.C. (1947). *Brain and Intelligence: A Quantitative Study of the Frontal Lobes.* Chicago: University of Chicago Press.

Harden, C.L., Kossoy, A., Vera, S., & Nikolov, B. (2004). Reaction to epilepsy in the workplace. *Epilepsia, 45,* 1134-1140.

Hauser, W.A. (1997). Incidence and prevalence. In J. Engel Jr. & T.A. Pedley (Eds.) *Epilepsy. A Comprehensive Textbook* (pp. 47-57). Philadelphia: Lippincott-Raven.

Hauser, W.A. & Hesdorffer, D.H. (1990). *Epilepsy: Frequency, Causes and Consequences.* New York: Demos Press.

Heaton, R.K., Miller, S.W., Taylor, M.J., & Grant, I. (2004). *Revised Comprehensive Norms for an Expanded Halstead-Reitan Battery: Demographically Adjusted Norms for African American and Caucasian Adults.* Lutz, FL: Psychological Assessment Resources, Inc.

Hellige, J.B. & Sergent, J. (1986). Role of task factors in visual field asymmetries. *Brain and Cognition, 5,* 200-222.

Helmstaedter, C. (2001). Behavioral aspects of frontal lobe epilepsy. *Epilepsy & Behavior, 2,* 384-395.

Helmstaedter, C., Grunwald, T., Lehnerz, K., Gleissner, U., & Elger, C.E. (1997). Differential involvement of left temporolateral and temporomesial structures in verbal declarative learning and memory: Evidence from temporal lobe epilepsy. *Brain and Cognition, 35,* 110-131.

Helmstaedter, C., & Kurthen, M. (2002). Validity of the WADA test. *Epilepsy & Behavior, 3,* 562-563.

Helmstaedter, C., Sonntag-Dillender, M, Hoppe, C., & Elger, C.E. (2004). Depressed mood and memory impairment in temporal lobe epilepsy as a function of focus lateralization and location. *Epilepsy & Behavior, 5,* 696-701.

Hermann, B.P. (1991). Contributions of traditional assessment procedures to an understanding of the neuropsychology of epilepsy. In W.E. Dodson, M. Kinsbourne, & B. Hiltbrunner, (Eds.), *The Assessment of Cognitive Function in Epilepsy* (pp. 1-22). New York: Demos Publications.

Hermann, B.P., Seidenberg, M., Schoenfeld, J., & Davies, K. (1997). Neuropsychological characteristics of the syndrome of mesial temporal lobe epilepsy. *Archives of Neurology, 54,* 369-376.

Hermann, B.P., & Whitman, S. (1986). Psychopathology in epilepsy: a multietiologic model. In S. Whitman, & B.P. Hermann, (Eds.), *Psychopathology in Epilepsy: Social Dimensions* (pp. 5-37).New York: Oxford University Press.

Hesdorffer, D.H. & Verity, C.M. (1997). Risk factors. In J. Engel Jr. & T.A. Pedley (Eds.) *Epilepsy. A Comprehensive Textbook* (pp. 59-67). Philadelphia: Lippincott-Raven.

Hilkevitch, R.R. (1946). A study of the intelligence of institutionalized epileptics of the idiopathic type. *Journal of Orthopsychiatry, 16,* 262-270.

Horton, A.M. Jr. (2000). General Neuropsychological Deficit Scale sans IQ. *International Journal of Neuroscience, 103,* 127-130.

Hugdahl, K. (1995). Dichotic listening: probing temporal lobe functional integrity. In R.J. Davidson & K. Hugdahl (Eds.). *Brain Asymmetry* (pp. 123-156). Cambridge: The MIT Press.

Hugdahl, K. (2000). Lateralization of cognitive processes in the brain. *Acta Psychologica, 105,* 211-235.

Hugdahl, K. (2003). Dichotic listening in the study of auditory laterality. In K. Hugdahl & R.J. Davidson (Eds.). *The Asymmetrical Brain* (pp. 441-475). Cambridge: The MIT Press.

Hugdahl, K. & Andersson, L. (1986). The "forced-attention paradigm" in dichotic listening to CV-syllables: a comparison between adults and children. *Cortex, 22,* 417-432.

Hugdahl, K., Carlsson, G., Uvebrant, P., & Lundervold, A.J. (1997). Dichotic-listening performance and intracarotid injections of amobarbital in children and adolescents. Preoperative and postoperative comparisons. *Archives of Neurology, 54,* 1494-1500.

Hund-Georgiadis, M., Lex, U., Friederici, A.D., & von Cramon, D.Y. (2002). Non-invasive regime for language lateralization in right- and left-handers by means of functional MRI and dichotic listening. *Experimental Brain Research, 145,* 166-176.

Jacoby, A., Snape, D., & Baker, G.A. (2005). Epilepsy and social identity: the stigma of a chronic neurological disorder. *Lancet Neurology, 4,* 171-178.

Jansen, A., Flöel, A., Menke, R., Kanowski, M., & Knecht, S. (2005). Dominance for language and spatial processing: limited capacity of a single hemisphere. *NeuroReport, 16,* 1017-1021.

Jokeit, H., & Ebner, A. (2002). Effects of chronic epilepsy on intellectual functions. *Progression in Brain Research, 135,* 455-463.

Jung-Beeman, M. (2005). Bilateral brain processes for comprehending natural language. *Trends in Cognitive Science, 9,* 512-518.

Jäncke, L., & Steinmetz, H. (1993). Auditory laterality and planum temporale asymmetry. *NeuroReport, 5,* 169-172.

Kane, R.L. (1991). Standardized and flexible batteries in neuropsychology: an assessment update. *Neuropsychological Review, 2,* 281-339.

Kimura, D. (1961). Some effects of temporal-lobe damage on auditory perception. *Canadian Journal of Psychology, 15,* 156-165.

Kimura, D. (1966). Dual functional asymmetry of the brain in visual perception. *Neuropsychologia, 4,* 275-285.

Kimura, D. (1967). Functional asymmetry of the brain in dichotic listening. *Cortex, 3,* 163-178.

King, T.Z., Fennell, E.B., Bauer, R., Crosson, B., Dede, D., Riley, J.L., Robinson, M.E., Uthman, B., Gilmore, R., & Roper, S.N. (2002). MMPI-2 profiles of patients with intractable epilepsy. *Archives of Clinical Neuropsychology,17,* 583-593.

Kinsbourne, M. (1970). The cerebral basis of lateral asymmetries in attention. *Acta Psychologica, 33,* 193-201.

Kinsbourne, M. (1975). The mechanisms of hemispheric control of the lateral gradient of attention. In P.M.A. Rabbit & S. Dornic (Eds.). *Attention and Performance. V.* New York: Academic Press.

Kinsbourne, M., & Hiscock, M. (1983). Asymmetries of dual-task performance. In J.B. Hellige (Ed.) *Cerebral Hemisphere Asymmetries: Method, Theory and Applications.* New York: Praeger.

Klöppel, S., & Büchel, C. (2005). Alternatives to the Wada test: a critical view of functional magnetic resonance imaging in preoperative use. *Current Opinion in Neurology, 18,* 418-423.

Kløve, H. (1963). Clinical neuropsychology. *Medical Clinics of North America, 47,* 1647-1658.

Kløve, H. (1974). Validation studies in adult clinical neuropsychology. In R.M. Reitan, & L.A. Davison (Eds.). *Clinical Neuropsychology: Current Status and Applications.* New York: John Wiley & Sons.

Kløve, H., & Matthews, C.G. (1966). Psychometric and adaptive abilities in epilepsy with differential etiology. *Epilepsia, 7,* 330-338.

Kobau, R., & DiIorio, C. (2003). Epilepsy self-management: a comparison of self-efficacy and outcome expectancy for medication adherence and lifestyle behaviors among people with epilepsy. *Epilepsy & Behavior, 4,* 217-225.

Langfitt, J.T. (1995). Comparison of the psychometric characteristics of three quality of life measures in intractable epilepsy. *Quality of Life Research, 4,* 101-114.

Lavados, J., Germain, L., Morales, A., Campero, M. & Lavados, P. (1992). A descriptive study of epilepsy in the district of El Salvador, Chile, 1984-1988. *Acta Neurologica Scandinavica, 85*, 249-256.

Lavidor, M., Brinksman, V., & Gödel, S.M. (2004). Hemispheric asymmetry and the mental number line: comparison of double-digit numbers. *Neuropsychologia, 42,* 1927-1933.

Lazarus, R.S., & Folkman, S. (1984). *Stress, Appraisal and Coping.* New York: Springer-Verlag.

LeDoux, J.E. (1996). *The Emotional Brain: The Mysterious Underpinnings of Emotional Lift.* New York: Simon & Schuster.

Lee, G.P., Loring, D.W., Varney, N.R., Roberts, R.J., Newell, J.R., Martin, J.A., Smith, J.R., King, D.W., Meador, K.J., & Murro, A.M. (1994). Do dichotic word listening asymmetries predict side of temporal lobe seizure onset? *Epilepsy Research, 19,* 153-160.

Leone, M.A., Beghi, E., Righini, C., Apolone, G., & Mosconi, P. (2005). Epilepsy and quality of life in adults: A review of instruments. *Epilepsy Research, 66,* 23-44.

Levin, R., Banks, S., & Berg, B. (1988). Psychosocial dimensions of epilepsy: a review of the literature. *Epilepsia, 29,* 805-816.

Lezak, M.D., Howieson, D.B., & Loring, D.W. (2004). *Neuropsychological Assessment* (4th ed.). Oxford, NY: Oxford University Press.

Livneh, H., Wilson, L.M., Duchesneau, A., & Antonak, R.F. (2001). Psychosocial adaptation to epilepsy: the role of coping strategies. *Epilepsy & Behavior, 2,* 533-544.

Loring, D.W., Meador, K.J., & Lee, G.P. (2004). Determinants of quality of life in epilepsy. *Epilepsy & Behavior, 5,* 976-980.

Luerding, R., Boesebeck, F., & Ebner, A. (2004). Cognitive changes after epilepsy surgery in the posterior cortex. *Journal of Neurology, Neurosurgery and Psychiatry, 75,* 583-587.

MacLeod, J.S., & Austin, J.K. (2003). Stigma in the lives of adolescents with epilepsy. A review of the literature. *Epilepsy & Behavior, 4,* 112-117.

Mashal, N., Faust, M., & Hendler, T. (2005). The role of the right hemisphere in processing nonsalient metaphorical meanings: application of Principal Component Analysis to fMRI data. *Neuropsychologia, 43,* 2084-2100.

Matthews, C.G., & Kløve, H. (1967). Differential psychological performances in major motor, psychomotor and mixed seizure classifications of known and unknown etiology. *Epilepsia, 8,* 117-128.

Matthews, C.G., & Kløve, H. (1968). MMPI performance in major motor, psychomotor, and mixed seizure classifications of known and unknown etiology. *Epilepsia, 9,* 43-53.

Matthews, C.G., Shaw, D.J., & Kløve, H. (1966). Psychological test performance in neurologic and "pseudo-neurologic" subjects. *Cortex, 2,* 244-253.

Mazzucchi, A., & Parma, M. (1978). Responses to dichotic listening tasks in temporal epileptics with or without clinically evident lesions. *Cortex, 14,* 381-390.

Mazzucchi, A., Visintini, D., Magnani, G., Cattelani, R., & Parma, M. (1985). Hemispheric prevalence changes in partial epileptic patients on perceptual and attentional tasks. *Epilepsia, 26,* 379-390.

Moskovitch, M. (1979). Information processing and the cerebral hemispheres. In M.S. Gazzaniga (Ed.). *Handbook of Behavioral Neurobiology: Neuropsychology.* New York: Plenum. Vol 2.

Nelson, L.T., Elder, J.T., Groot, J., Tehrani, P., & Grant, A.C. (2004). Personality testing and epilepsy: comparison of two MMPI-2 correction procedures. *Epilepsy & Behavior, 5,* 911-918.

Oestreicher, J.M., & O`Donnell, J.P. (1995). Validation of the General Neuropsychological Deficit Scale with nondisabled, learning-disabled, and head-injured young adults. *Archives of Clinical Neuropsychology, 10,* 185-191.

O`Leary, D.S. (2003). Effects of attention on hemispheric asymmetry. In K. Hugdahl & R.J. Davidson (Eds.). *The Asymmetrical Brain* (pp. 477-508). Cambridge: The MIT Press.

Orsini, D.L., & Satz, P. (1986). A syndrome of pathological left-handedness. Correlates of early left hemisphere injury. *Archives of Neurology, 43,* 333-337.

Penfield, W., & Milner, B. (1958). Memory deficit produced by bilateral lesions in the hippocampal zone. *AMA Archives of Neurology and Psychiatry, 79,* 475-497.

Penfield, W, & Mathieson, G. (1974). Memory. Autopsy findings and comments on the role of hippocampus in experiental recall. *Archives of Neurology, 31,* 145-154.

Pollmann, S., Maertens, M., von Cramon, D.Y., Lepsien, J., & Hugdahl, K. (2002). Dichotic listening in patients with splenial and nonsplenial callosal lesions. *Neuropsychology, 16,* 56-64.

Prpic, I., Korotaj, Z., Vlasic-Civaric, I., Paucic-Kirincic, E., Valerjev, A., & Tomac, V. (2003). Teachers` opinions about capabilities and behavior of children with epilepsy. *Epilepsy & Behavior, 4,* 142-145.

Rasmussen, T., & Milner, B. (1977). The role of early left-brain injury in determining lateralization of cerebral speech functions. *Annals of New York Academy of Science, 299,* 355-369.

Reed, J.E. (1996). Fixed vs. flexible neuropsychological test batteries under the Daubert standard for the admissibility of scientific evidence. *Behavioral Science and Law, 14,* 315-322.

Reitan, R.M. (1974). Methodological problems in clinical neuropsychology. In R.M. Reitan, & L.A. Davison (Eds.). *Clinical Neuropsychology: Current Status and Applications.* New York: John Wiley & Sons.

Reitan, R.M., & Davison, L.A. (Eds.) (1974). *Clinical Neuropsychology: Current Status and Applications.* New York: John Wiley & Sons.

Reitan, R.M., & Wolfson, D. (1992a). *Neuropsychological Evaluation of Older Children.* Tucson, AZ: Neuropsychology Press.

Reitan, R.M., & Wolfson, D. (1992b). *Neuropsychological Evaluation of Young Children.* Tucson, AZ: Neuropsychology Press.

Reitan, R.M., & Wolfson, D. (1993). *The Halstead-Reitan Neuropsychological Test Battery. Theory and Clinical Interpretation* (2nd ed.). Tucson, AZ: Neuropsychology Press.

Reitan, R.M., & Wolfson, D. (1997). Emotional disturbances and their interaction with neuropsychological deficits. *Neuropsychology Review, 7,* 3-19.

Reminger, S.L., Kaszniak, A.W., Labiner, D.M., Littrell, L.D., David, B.T., Ryan, L., Herring, A.M., & Kaemingk, K.L. (2004). Bilateral hippocampal volume predicts verbal memory function in temporal lobe epilepsy. *Epilepsy & Behavior,5,* 687-695.

Rolls, E.T. (1999). *The Brain and Emotion.* New York: Oxford University Press.

Rose, K.J., Derry, P.A., & McLachlan, R.S. (1996). Neuroticism in temporal lobe epilepsy: assessment and implications for pre- and postoperative psychosocial adjustment and health-related quality of life. *Epilepsia, 37,* 484-491.

Russell, E.W., Neuringer, C., & Goldstein, G. (1970). *Assessment of Brain Damage: a Neuropsychological Key Approach.* New York: Wiley-Interscience.

Russell, E.W., Russell, S.L.K., & Hill, B.D. (2005). The fundamental psychometric status of neuropsychological batteries. *Archives of Clinical Neuropsychology, 20,* 785-794.

Sass, K.J., Sass, A., Westerveld, M., Lencz, T., Novelly, R.A., Kim, J.H., & Spencer, D.D. (1992). Specificity in the correlation of verbal memory and hippocampal neuron loss: dissociation of memory, language and verbal intellectual ability. *Journal of Clinical and Experimental Neuropsychology, 14,* 662-672.

Sawrie, S.M., Martin, R.C., Knowlton, R., Faught, E., Gilliam, F., & Kuzniecky, R. (2001). Relationships among hippocampal volumetry, proton magnetic resonance spectroscopy, and verbal memory in temporal lobe epilepsy. *Epilepsia, 42,* 1403-1407.

Scoville, W.B., & Milner, B. (1957). Loss of recent memory after bilateral hippocampal lesions. *Journal of Neurology, Neurosurgery and Psychiatry, 20,* 11-21.

Schwarzer, R. (1993). Measurement of perceived self-efficacy. Psychometric scales for cross-cultural research. *Forschung an der Freien Universität Berlin,* Berlin.

Sequeira, S.D., Woerner, W., Walter, C., Kreuder, F., Lueken, U., Westerhausen, R., Wittling, R.A., Schweiger, E., & Wittling, W. (2006). Handedness, dichotic-listening ear advantage, and gender effects on planum temporale asymmetry - A volumetric investigation using structural magnetic resonance imaging. *Neuropsychologia, 44,* 622-636.

Sherer, M., & Adams, R.L. (1993). Cross-validation of Reitan and Wolfson`s Neuropsychological Deficit Scales. *Archives of Clinical Neuropsychology, 8,* 429-435.

Sparks, R., & Gescwind, N. (1968). Dichotic listening in man after section of neocortical commisures. *Cortex, 4,* 3-16.

Spilker, B. (Ed.) (1996). *Quality of Life and Pharmacoeconomics in Clinical Trials.* Philadelphia: Lippincott-Raven.

Spreen, O., & Strauss, E. (1998). *A Compendium of Neuropsychological Tests: Administration, Norms and Commentary* (2nd ed.). New York: Oxford University Press.

Strauss, E., Gaddes, W.H., & Wada, J. (1987). Performance on a free-recall verbal dichotic listening task and cerebral dominance determined by the carotid amytal test. *Neuropsychologia, 25,* 747-753.

Strauss, E., Satz, P., & Wada, J. (1990). An examination of the crowding hypothesis in epileptic patients who have undergone the carotid amytal test. *Neuropsychologia, 28,* 1221-1227.

Swinkels, W.A.M., Kuyk, J., van Dyck, R., & Spinhoven, P. (2004). Psychometric properties of the Dutch version of the Washington Psychosocial Seizure Inventory. *Epilepsia, 45,* 844-848.

Temkin, O. (1971). *The Falling Sickness.* Baltimore: Johns Hopkins Press.

Thomsen, T., Rimol, L.M., Ersland, L., & Hugdahl, K. (2004). Dichotic listening reveals functional specificity in prefrontal cortex: an fMRI study. *NeuroImage, 21,* 211-218.

Thorbecke, R., & Fraser, R.T. (1997). The range of needs and services in vocational rehabilitation. In J. Engel Jr. & T.A. Pedley (Eds.) *Epilepsy. A Comprehensive Textbook* (pp. 2211-2245). Philadelphia: Lippincott-Raven.

Toga, A.W., & Thompson, P.M. (2003). Mapping brain asymmetry. *Nature Reviews Neuroscience, 4,* 37-48.

Tomson, T., Beghi, E., Sundqvist, A., & Johannessen, S.I. (2004). Medical risks in epilepsy: a review with focus on physical injuries, mortality, traffic accidents and their prevention. *Epilepsy Research, 60,* 1-16.

Trenerry, M.R. (1996). Neuropsychologic assessment in surgical treatment for epilepsy. *Mayo Clinic Proceedings, 71,* 196-200.

Trenerry, M.R., Jack, C.R.Jr., Ivnik, R.J., Sharbrough, F.W., Cascino, G.D., Hirschorn, K.A., Marsh, W.R., Kelly, P.J., & Meyer, F.B. (1993). MRI hippocampal volumes and memory function before and after temporal lobectomy. *Neurology, 45,* 1800-1805.

Trenerry, M.R., Hermann, B.P., Barr, W.B., Chelune, C.J., Loring, D.W., Perrine, K., Strauss, E., & Westerveld, M. (1996). MMPI scale elevations before and after right and left temporal lobectomy. *Assessment, 3,* 307-315.

Upton, D., & Thompson, P.J. (1992). Effectiveness of coping strategies employed by people with chronic epilepsy. *Journal of Epilepsy, 5,* 119-127.

van den Broek, M., & Beghi, E. (2004). Accidents in patients with epilepsy: types, circumstances, and complications: a European cohort study. *Epilepsia, 45,* 667-672.

van Empelen, R., Jennekens-Schinkel, A., van Rijen, P.C., Helders, P.J., & van Nieuwenhuizen, O. (2005). Health-related quality of life and self-perceived competence of children assessed before and up to two years after epilepsy surgery. *Epilepsia, 46,* 258-271.

Waaler, P.E., Blom, B.H., Skeidsvoll, H., & Mykletun, A. (2000). Prevalence, classification, and severity of epilepsy in children in western Norway. *Epilepsia, 41,* 802-810.

Wada, J., & Rasmussen, T. (1960). Intracarotid injection of sodium amytal for the lateralization of cerebral speech dominance. Experimental and clinical observations. *Journal of Neurosurgery, 17,* 266-282.

Wallston, K.A., Wallston, B.S., & DeVellis, R. (1978). Development of the Multidimensional Health Locus of Control (MHLC) scales. *Health Education Monographs, 6,* 160-170.

Watson, D., & Clark, L.A. (1991). *Preliminary manual for the PANAS-X: Positive and Negative Affect Schedule - Expanded Form.* Dallas: Southern Methodist University.

Wechsler, D. (1955). *Wechsler Adult Intelligence Scale. Manual.* New York: The Psychological Corporation.

Wiebe, S., Rose, K., Derry, P., & McLachlan, R. (1997). Outcome assessment in epilepsy: comparative responsiveness of quality of life and psychosocial instruments. *Epilepsia, 38,* 430-438.

Wilkus, R.J., & Dodrill, C.B. (1989). Factors affecting the outcome of MMPI and neuropsychological assessments of psychogenic and epileptic seizure patients. *Epilepsia, 30,* 339-347.

Wolfson, D., & Reitan, R.M. (1995). Cross-validation of the General Neuropsychological Deficit Scale (GNDS). *Archives of Clinical Neuropsychology, 10,* 125-131.

Wood, R.L. (2005). Cognitive and behavioural interactions as late sequelae of head injury. Lecture given at the Annual Congresss of the European Federation of Neuropsychiatry, München, 16-18 November.

Zatorre, R.J. (1989). Perceptual asymmetry on the dichotic fused words test and cerebral speech lateralization determined by the carotid sodium amytal test. *Neuropsychologia, 27,* 1207-1219.

Zhu, D., Jin, L., Xie, G., & Xiao, B. (1998). Quality of life and personality in adults with epilepsy. *Epilepsia, 39,* 1208-1212.