LONGITUDINAL COGNITIVE CHANGES IN MEDICALLY AND SURGICALLY TREATED PATIENTS WITH DRUG RESISTANT PARTIAL EPILEPSY

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The thesis is based on the following papers:

I. Andersson-Roswall L, Engman E, Samuelsson H, Sjöberg-Larsson C, and Malmgren K. **Verbal memory decline and adverse effects on cognition in adult patients with pharmacoresistant partial epilepsy: a longitudinal controlled study of 36 patients.** Epilepsy & Behavior (2004) 5:677-686.

II. Andersson-Roswall L, Engman E, Malmgren K, and Samuelsson H. **Verbal cognition and attention deficits do not explain the verbal memory decline associated with pharmacoresistant partial epilepsy.** Epilepsy & Behavior (2007) 11:413-420.

III. Andersson-Roswall L, Engman E, Samuelsson H, and Malmgren K. **Cognitive outcome 10 years after temporal lobe epilepsy surgery: a prospective controlled study.** Neurology (2010) in press.

IV. Andersson-Roswall L, Samuelsson H, Engman E, and Malmgren K. **Individual verbal memory outcome 10 years after temporal lobe epilepsy surgery: a prospective controlled study.** Manuscript.

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ABSTRACT

When this study was initiated, there were few published longitudinal studies on cognition in medically treated patients with refractory epilepsy, and none included reassessment data from healthy controls. At the time there were no long-term reports on surgically treated epilepsy patients. The rationale for this study was therefore to pursue a longitudinal study of cognitive changes in both medically and surgically treated epilepsy patients compared to controls. The aims were: in study I to explore the hypothesis that a cognitive decline across time would be disclosed; in study II to investigate whether verbal memory decline was influenced by verbal cognition or attention/processing speed; in study III to explore long-term cognitive changes after temporal lobe resection (TLR) for epilepsy and to investigate whether these relate to seizure outcome, and in study IV to describe individual changes in verbal memory after TLR and to explore specific risk factors for early and late decline.

Thirty-six medically treated patients with refractory partial epilepsy were tested twice, with a median test interval of 4.8 years (study I and II). Fifty-one patients with temporal lobe epilepsy (23 in the speech dominant temporal lobe, DTL; 28 in the non-dominant temporal lobe, NDTL) were tested preoperatively, 2 and 10 years after TLR (study III and IV). Thirty healthy controls were tested at baseline, and after 3 (25/30) and 10 (26/30) years (studies I-IV).

In medically treated patients a verbal memory decline in retention of word-pairs across time was found (study I). The decline could not be explained by performance in verbal cognition or in attention/processing speed (study II). Visuo-spatial memory and performance IQ (PIQ) (study I), and attention/processing speed (study II) were also found to be important correlates of epilepsy. In surgically treated patients, the main result was cognitive stability. In the DTL group there was a decline in verbal memory at the 10-year follow-up compared to the NDTL and the control group (study III). However, this decline was disclosed already at the 2-year follow-up after surgery, and no further decline occurred from 2 to 10 years. The verbal memory decline was not dependent on seizure outcome or antiepileptic drug treatment. At the individual level there was a profound variability in verbal memory outcome after TLR. Fewer patients in the whole TLR group showed decline at 10 (14%) compared to 2 years (28%) after surgery, while the proportion of patients with improvement was about the same at 2 (16%) and 10 (18%) years. Decline was more common in the DTL (2-year: 43.5%; 10-year: 26.1%) than in the NDTL group (2-year: 14.8%; 10-year: 3.7%), while improvement was more common in the NDTL (2-year: 18.5%; 10-year: 29.6%) than in the DTL group (2-year: 13.0%; 10-year: 4.3%). Intact verbal memory at baseline was identified as the strongest predictor of verbal memory decline 2 years after surgery, followed by dominant TLR, and older age at baseline, while only dominant TLR predicted verbal memory decline at 10 years (study IV). Less pronounced practice effects in PIQ were detected both in medically treated patients (study I) and after non-dominant TLR (study III). Continuing seizures was the most important correlate to inferior PIQ scores in surgically treated patients (study III).

In conclusion, our studies demonstrate that memory decline can be disclosed as early as within five years in medically treated epilepsy patients. The results also suggest a unique relationship with epilepsy for the verbal memory decline, since it could not be explained by any change in verbal cognition or attention/processing speed. After TLR the main result was cognitive stability from 2 to 10 years. The verbal memory decline in DTL patients found 2 years after epilepsy surgery was not progressive up to 10 years, and not dependent on seizure outcome. The individual variability in verbal memory outcome after TLR was considerable. A partial recovery seems to have occurred for some individuals, since fewer patients both in the DTL and NDTL group showed decline at the 10-year compared to the 2-year follow-up. Also, factors that are important predictors for verbal memory decline at earlier stages after surgery may be less important at later, since dominant TLR was the only remaining risk factor for verbal memory decline at the long-term follow-up. The results from these studies are relevant in the counselling process when epilepsy surgery is considered.

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