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## Verbal cognition and attention deficits do not explain the verbal memory decline associated with pharmacoresistant partial epilepsy

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#### **Abstract**

The aim of this study was to explore whether change in verbal memory with time in patients with epilepsy is influenced by performance on tasks assessing verbal cognition or attention/processing speed. Thirty-six patients and twenty-five healthy controls were tested twice with median retest intervals of 4.8 and 3.1 years, respectively. Aspects of verbal memory, verbal cognition, and attention/processing speed were assessed. Decline in one verbal memory variable (Cronholm–Molander Memory Test Paired Associates—Delayed Recall) was the strongest correlate of epilepsy. The second strongest correlate was a decrease in one attention/processing speed variable (Digit Symbol). The relationship between decline in verbal memory and epilepsy was not influenced by the decline in attention/processing speed, and the results did not support the notion that limited mental reserves as reflected in impaired verbal cognition or attention/processing speed can explain the relationship between verbal memory and epilepsy.

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#### 1. Introduction

Memory impairment is common in people with epilepsy [1–6]. Deficits in new learning are commonly reported, especially in patients with temporal lobe epilepsy, and impaired verbal episodic memory is the most consistent finding in left temporal lobe epilepsy [7]. Whether the memory impairment is progressive or not has been a matter of debate for many years. Although several earlier longitudinal studies of memory reported cognitive stability in patients with continuing seizures [8–12], recent studies have reported memory decline [6,13–15].

Deficits in attention have also been reported in epilepsy populations [2,3,5,16,17], and deterioration with time in various attention variables was observed in three longitudinal studies [8,14,18]. However, little is known about whether these changes in attention interact with the decline in memory in patients with epilepsy, although this is sometimes assumed. Kälviäinen et al. suggested that memory difficulties may be related to an attention dysfunction leading to impaired or slowed initial encoding of memory trace and, also, to a deficit in the storage process [2].

The level of verbal cognition may also be of importance in relation to performance on tasks assessing verbal memory. Verbal cognition, as measured by Verbal IQ (WAIS-R) or its subtests, is often impaired in patients with epilepsy [5,19–21]. This low level of performance is usually stable with time [6,10,11,13]. It has been suggested that a low intellectual level (IQ level) reflects reduced mental capacity and that such a reduction is indicative of an increased risk

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for memory decline due to a reduced compensatory reserve [5,13,22,23]. If this is so, one might expect that low-level performance on tasks assessing verbal cognition would predict a decline in verbal memory in patients with epilepsy.

In an earlier longitudinal, controlled study of cognition in patients with pharmacoresistant epilepsy, we could disclose an adverse effect on verbal memory in the patient group over time when compared with the longitudinal changes in an adequate control group [6]. In the present study, the same data set has been further analyzed, with the aim of testing the hypothesis that performance on tasks assessing verbal cognition and attention has a confounding influence on the relationship observed between epilepsy and decline in verbal memory.

#### 2. Methods

#### 2.1. Subjects

The patient cohort consisted of a consecutive series of patients with pharmacoresistant partial epilepsy who had undergone presurgical evaluations between 1987 and 1994 but had not undergone an operation. The inclusion criteria were as follows: (1) seizure frequency of at least one complex partial or secondarily generalized seizure per month at the time of follow-up; (2) no progressive neurological disease. Furthermore, it had to be possible for the patients to travel to the hospital and participate in the testing in 1 day (for three patients, this was not possible). Thirty-one patients fulfilled these criteria and were asked to participate in the study; 27 accepted. Nine patients who eventually underwent epilepsy surgery but who had undergone two serial neuropsychological assessments preoperatively (i.e., for the purpose of this study both baseline and follow-up assessments) were also included. (None of the other patients had been serially assessed with respect to epilepsy surgery before the baseline neuropsychological examination.) In total, 36 patients were included (64% male), and the median test interval was 4.8 years (range: 1.4–9.3, Quartile 1; Quartile 3: 2.5;7.3). Medical and demographic data are detailed in Table 1.

All patients had localization-related partial epilepsy. Half of them (n = 18) had secondarily generalized tonic-clonic seizures as well as partial seizures; the other half had partial seizures only between the assessments. Seizure onset was left-sided in 12 patients, right-sided in 14, and bilateral in 8; for one patient, lateralization of seizure onset was not possible. With respect to type of seizures at onset, of the 27 nonsurgical patients, 9 had temporal lobe, 3 had frontal lobe, 4 had parietal or occipital, and 8 had frontal and temporal lobe seizures; for 3 patients, seizure type at onset could not be adequately determined. The reasons why these patients were not operated varied: some patients refused surgery, whereas others were rejected due to multilobar or bilateral seizure onset or seizure onset in eloquent cortex. Of the 9 patients who eventually were operated, 6 had temporal lobe, 1 had frontal lobe, 1 had both frontal and temporal lobe, and 1 had parietal seizures at onset. There were no statistically significant differences between the 9 patients who were eventually operated upon and the 27 patients who did not undergo epilepsy surgery with respect to medical, sociodemographic, or neuropsychological variables.

A control group consisting of 25 neurologically healthy persons (60% male) was assessed twice with a median testing interval of 3.1 years (range: 2.8–3.3, Quartile 1; Quartile 3: 2.9; 3.2). The controls were recruited among the patients' friends, working mates, and spouses, that is, persons in similar sociocultural circumstances. Demographic data for the control group are also detailed in Table 1.

#### 2.2. Test procedures

#### 2.2.1. Neuropsychological variables

The test instruments used in the present study (baseline and follow-up) were part of a comprehensive standard neuropsychological assessment battery for epilepsy surgery. The same tests were used for patients and controls. The tests are listed below and also summarized in Table 2. Test–retest reliability coefficients calculated for all tests based on the results from the control group are also listed in Table 2.

2.2.1.1. Verbal memory. The Claeson–Dahl Learning and Retention Test (CD) (cf. Table 2) assesses acquisition/learning and retention of a word list [24,25]. The test consists of 10 (8 abstract and 2 concrete) words. The stimuli are presented verbally, with a maximum of 10 separate recall trials, each

Table 1 Medical and demographic variables for patients (N = 36) and controls (N = 25)

	Baseline			Follow-up		
	Median	Range	Q1;Q3	Median	Range	Q1;Q3
Age at epilepsy onset (years)						
Patients	14.0	0.4-39.0	6.8;19.2			
Controls	NA	NA	NA			
Monthly seizure frequency						
Patients	8.5	1-1050	5.1;48.8	8.0	1-150	3.0;30.0
Controls	NA	NA	NA	NA	NA	NA
Number of antiepileptic drugs						
Patients	2.0	0-3	2.0;2.2	2.0	0-4	2.0;3.0
Controls	NA	NA	NA	NA	NA	NA
Age (years)						
Patients	33.0	18.0-47.0	28.0;40.7	39.5	23.0-55.0	33.0;45.2
Controls	36.0	22.0-51.0	27.0;41.0	38.0	25.0-54.0	30.0;44.0
Length of education (years)						
Patients	11.0	7.0-17.0	9.0;13.0	11.0	7.0-17.0	33.0;45.3
Controls	11.5	6.0-16.0	11.0;12.0	12.0	6.0-16.0	11.0;12.5
Test interval (years)						
Patients				4.8	1.4-9.3	2.5;7.3
Controls				3.1	2.8-3.3	2.9;3.2

Q1 = 25th centile, Q3 = 75th centile. NA, not applicable.

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