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Research Article

A Comparison of Subjective and Objective Memory Deficits in Patients with Epilepsy Pre- and Post-Surgery

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Abstract

Objectives: Patients with epilepsy often report perceptions of cognitive deficits, especially memory decline. Previous research has demonstrated only a weak relationship between self-reported memory problems and memory impairments measured by neuropsychological tests, but quite a strong relationship with mood, especially depression. The present study investigated subjective memory complaints before and after epilepsy surgery and examined whether they contained information that accorded with neuropsychologically assessed memory deficits and reliable memory changes.

Methods: Twenty-one native German-speaking adult patients with focal refractory epilepsy, who were candidates for epilepsy surgery were investigated. They completed a standardized routine neuropsychological assessment pre-surgery and a six-month post-surgery. We correlated subjective and objective memory scores and their changes in the pre- to post-surgical assessment and compared the results of the impairment classifications.

Results: Change values indicated no closer relationship between subjective and objective memory scores when controlling for depressed mood. Post-surgery, there was a significant decrease in total verbal learning scores. One third of patients, who were classified as impaired in neuropsychological assessments or in change scores after surgery, reported no clinically relevant subjective memory complaints after surgery. Eighty-nine percent of the patients with clinically relevant subjective memory complaints post-surgery were classified as impaired in at least one neuropsychological assessed memory score or showed a reliable decrease in memory performance.

Conclusion: Clinically relevant subjective memory complaints appear to be an indicator of neuropsychologically assessed memory deficits in patients with epilepsy after surgery. A lack of subjective memory complaints potentially underestimates objective memory impairments but might be more reflective of emotional well-being post-surgery.

Keywords: *epilepsy, subjective cognition, subjective memory, FLei, epilepsy surgery*

Introduction

It is well-documented that subjective memory complaints differ from objective memory scores measured with neuropsychological assessments in patients with epilepsy [1-3]. Subjectively reported mood and anxiety related factors have consistently emerged as a significant influencing factor of perceived memory impairment [4-8]. This also applies to patients with different diagnoses such as cancer [9,10] or cardiovascular disease [11]. In addition to emotional factors, other cognitive domains, for example access to vocabulary [12] and attentional resources [13], have been considered to be involved in memory perception. Also, subjective memory seems to be negatively affected by the number of seizures and anticonvulsive medication [14]. Other authors [15] have pointed out that in most studies patients were examined at only one point in time. Therefore, intra-individual changes in cognitive functioning over time were not detectable. These longitudinal changes might influence the subjective evaluation of cognitive functioning and hide stronger associations between objective and subjective memory scores measured at one point in time. Until now, only a few authors have explored subjective and objective memory scores before and after epilepsy surgery. They found similar results to those of cross-sectional examinations in the sense of no or small associations [2,16-19]. It was therefore assumed that positive surgical outcomes reduced the perception of memory impairment [16], or that subjective and objective memory scores were based on different constructs [17]. Baxendale and Thompson [2] pointed out that the absence of a significant correlation should be considered in pre-surgical counselling, as seizure reduction affects subjective memory perception more than results in objective memory measures. Word finding problems and an increasing number of antiseizure drugs were considered to increase memory complaints [19]. Lineweaver et al. [18] also found no relationship between subjective and objective memory scores after surgery. However, when examining possible differences between patients with temporal and extratemporal lobe epilepsy, they observed a significant decrease in memory complaints after temporal surgery, but not after extratemporal surgery. In a subgroup of patients, who showed a decrease in memory performance after surgery, there was a correlation between subjective and objective memory scores when controlled for depression, indicating the importance of individual baselines for estimations and the relevance of perceived changes. However, the strength of the correlation was not stronger than in cross-sectional examinations (e.g., Grewe et al. [13]). We hypothesized a stronger relationship between objective and subjective memory assessments when including changes in memory performance and further focused on the clinical relevance of memory impairment.

Materials and Methods

Participants

The present study involved 21 patients in a retrospective approach with drug-refractory epilepsy who completed a comprehensive neuropsychological assessment during pre-surgical evaluation and again six months post-surgery. We included all patients with temporal or frontal lobe epilepsy surgery in our clinic, who were at least 18 years old, had an IQ above 80 and took part in the complete clinical pre-and post-surgical neuropsychological routine between 2016 and 2017. The sample consisted of 11 female and 10 male patients with a mean age of 39.90 years (SD = 11.77). All patients gave written informed consent for the use of data for research purposes and the study was approved by the local IRB and the STROBE guidelines were followed.

Measurements

Subjective memory complaints were operationalised using the “Fragebogen zur geistigen Leistungsfähigkeit” (FLei: Questionnaire for complaints of cognitive disturbances [20]). In 35 items, cognitive problems in everyday situations are described, and participants have to judge their experience with such difficulties on a 5-point scale (i.e., never, rarely, occasionally, frequently, and very frequently), with higher scores indicating more severe impairment. The FLei consists of 3 subscales (memory, attention, and executive functioning) and one control scale (5 items). Based on our hypothesis, we only considered the 10 items memory subscale. The FLei was already used in people with epilepsy in [13] study, which includes an English translation of the memory subscale.

Using a German adaptation of the Rey Auditory Verbal Learning Test [21] the Verbaler Lern- und Merkfähigkeitstest (VLMT [22], objective memory was assessed. Fifteen words had to be learned in five trials followed by one trial with 15 interference words. Subsequently there is an immediate recall and a free delayed recall 30 minutes later with an additional recognition trial. We focused on the change in the delayed free recall variable (VLMT DG7) and on the cumulative learning score (learning trail 1 to 5) (VLMT SUM) of the VLMT.

To estimate the mood of the participants, we used the German version of the Beck Depression Inventory, the Beck Depressions Inventar II (BDI-II [23]), which comprises 21 items.

The participants filled in the self-report questionnaires for memory (FLei) and mood (BDI-II) after they had taken part in the neuropsychological assessment (including the VLMT), but before they received feedback about their results in the neuropsychological assessments. The post-surgical evaluation was carried out approximately six months (with a range of three to seven months) after the surgery. Seizure frequency was determined by self-report, relatives' report and seizure diaries.

Statistical analysis

Statistical analyses were performed using SPSS (IBM® SPSS® Statistics Version 24). To describe the sample, frequency statistics were obtained. T-tests for paired samples or Chi-square-tests were computed to detect significant changes in the variables pre- vs. post-surgical assessment. To detect associations between clinical-demographic variables and the memory complaints we used Spearman rank correlations and Mann-Whitney-U tests. The change scores were obtained by subtracting the pre-surgical from the post-surgical score. A negative change score for the VLMT implied a decline in memory performance approximately six months after surgery. A negative change score for the self-reported measures (FLei, BDI-II) implied a decrease in reported memory/mood problems after surgery, that is, fewer complaints. We examined the impaired/unimpaired classifications for the measures. As cut-offs for the FLei and the VLMT we used one standard deviation (FLei memory Scale ≥ 20 points; VLMT DG7, VLMT SUM $z \geq -1$ age-corrected standard score). The test developers Helmstaedter et al. (2001) [22] defined a reliable change in the VLMT as a decrease of three words in the free delayed recall (VLMT DG7) and a decrease of nine words in the cumulative learning score (VLMT SUM). According to the authors we classified patients with such a decrease as reliably impaired. For the BDI-II we applied the critical value of a minor depression classification (>13 points). Possible differences between the subgroups of patients with frontal lobe and temporal lobe epilepsy were analysed by t-tests. The relationship between the objective and subjective memory scores were analysed using Spearman rank correlations. To assess the influence of mood, as measured by the BDI-II, we calculated a partial correlation between these measures and the BDI-II score as a control variable.

Results

Clinical-demographical variables

For the patients´ characteristics see Table 1.

Seizure frequency changed significantly from pre- to postsurgical with a decline of 8.58 seizures per month (SD=12.54, p=0.005). Because of the large number of seizure-free patients (n=15) approximately six months after surgery, we compared the groups with and without ongoing seizures. This revealed no significant differences in FLei scores between groups and no significant differences in VLMT and BDI-II scores.

Memory complaints and neuropsychological memory results

Regarding pre- to post-surgical assessments, 52.4% (n=11) of patients reported increased memory complaints in the FLei, while 47.6% showed a stable or reduced level of subjective memory scores. However, there was no significant change (FLei pre: M=16.67, SD=10.90; post: M=15.86, SD=8.39) in the means of the self-reported memory FLei score (t(20) =0.34; p=0.739). There were no significant differences in the delayed free recall (VLMT 7 pre: M=10.62, SD=3.14; post: M=9.91, SD=3.77), t(20)=1.04; p=0.311, and the BDI-II (pre: M=10.50, SD=7.75; post: M=8.25, SD=7.55) score; t(20)=1.10, p=0.284. The cumulative learning score of the VLMT changed significantly pre- to post-surgical (pre: M=53.29, SD=9.15; post: M=48.43, SD=11.47) with a decrease of 4.86 points (SD=10.16; Range: -29–14; t(20)=2.19, p=0.040, Cohen's d_z=0.478).

Table 1: Participants' demographic and clinical data

Participant characteristics	*M* (*SD*) / % / [range]
Age postsurgical	39.9 (11.8) [20-59]
Age at seizure onset	19.8 (13.3) [1-47]
Gender: female	52.4% (*n*=11)
Years of education	10.3 (2.0) [8-13]
Duration of epilepsy (years)	20.1 (15.5) [1-50]
Type of Epilepsy: TLE/FLE	76.2%/23.8%
Side of epilepsy left/right	52.4%/47.6%
Seizure frequency per month: presurgical postsurgical	9.0 (12.6) [0.3-53.3] 0.5 (1.4) [0-6.3]
Quantity of anticonvulsant medication Presurgical / Postsurgical: 0 1 2 3	 - / 9.5% 26.5% / 28.6% 52.4% /52.4% 19.1% / 9.5%
Antiseizure drugs (*n* presurgical/*n* postsurgical)	Levetiracetam (16/12), Lamotrigine (9/9), Brivaracetam (0/3), Lacosamide (3/2), Valproic Acid (1/1), Carbamazepine (6/4), Zonisamide (1/0), Topiramate (3/3)
M: Mean; *SD*: Standard Deviation; TLE: Temporal Lobe Epilepsy; FLE: Frontal Lobe Epilepsy	

Investigating possible differences in memory complaints between patients with frontal (FLE) versus temporal lobe epilepsy (TLE), we found no significant differences in change scores of memory complaints in the pre- *vs*. post-surgical assessment between groups (change FLei score: $t(19)=1.379$, $p=0.184$; Table 2).

Table 2: Mean and standard deviations of FLei in patients with TLE and FLE pre- and postsurgical

FLei score	Mean (*SD*)	*t(df)*	*p*
TLE: pre-surgical post-surgical	15.87 (10.58) 16.88 (8.80)	-0.585 (19)	0.565
FLE: pre-surgical post-surgical	19.20 (12.79) 12.60 (6.62)	0.995 (19)	0.332

Correlations between memory complaints and memory scores

Spearman rank correlations between objective and subjective memory variables were consistently high, ranging from $r=-0.47$ to $r=-0.58$, with the strongest correlation detected for the change in delayed free recall ($r=-0.581$; $p=0.006$). The relationship between the change scores of the Flei and the VLMT was comparable ($r=-0.511$; $p=0.018$). Significant correlations could be observed between memory complaints (FLei) and the BDI-II scores assessed after surgery, and especially between the change in BDI-II and in FLei scores ($r=0.63$; $p=0.003$). Further there was a relationship between a decrease in seizure frequency and a decrease in memory complaints ($r=0.44$, $p=0.044$). A partial correlation analyses between VLMT and FLei scores, controlled for the BDI-II score, revealed no significant results.

Classification as impaired/unimpaired

In the classification of the 21 patients, 12 (57%) patients showed at least one post-surgical VLMT score below the cut-off criterion. Four of those patients exhibited a reliable decrease in only one VLMT score after surgery, which was classified as impaired. Nine patients (43%) produced results above the cut-off in the FLei memory scale, indicating clinically relevant complaints. The proportion of patients classified as impaired by VLMT and the FLei differed significantly (χ^2 (df=1)=6.48, p=0.024). However, in the case of the subgroup of nine patients who were classified as impaired by the FLei, 89% were also classified as impaired in at least one memory score (VLMT), but only four (44%) in the BDI-II (Figure 1). With regard to the patients without clinically relevant memory complaints in the FLei (n=12), 95% (n=11) also reported no depressive symptoms in the BDI-II. See Table 3 for an overview.

Table 3: Number and percentage of patients classified as impaired postsurgical (n=21)

	FLei memory	**BDI-II**	**VLMT DG7**	**VLMT DG7 change**	**VLMT SUM**	**VLMT SUM change**	**VLMT ≥ 1 impaired variable**
***n*/% of patients**	9/42%	5/23%	8/38%	6/29%	7/33%	5/23%	12/57%
***n*/% patients with relevant FLei complaints**	-	4/44%	6/67%	4/44%	5/55%	4/44%	8/89%

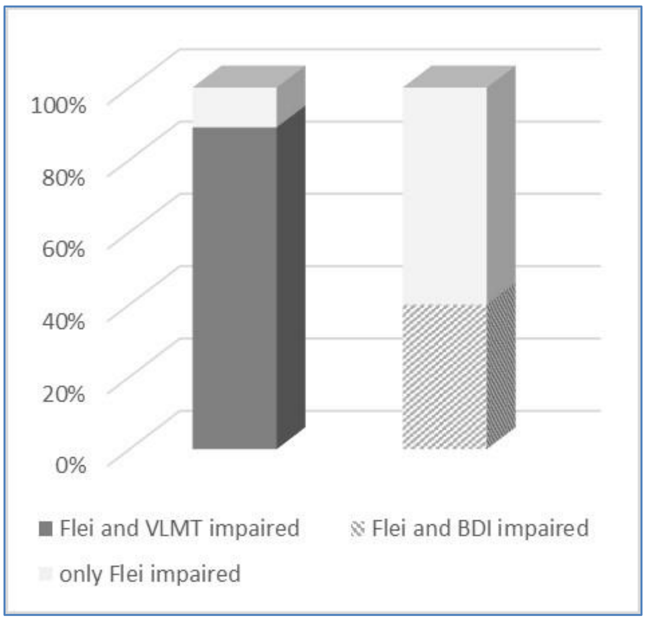

Figure 1. Percentage of patients (n = 9) classified as impaired by the FLei only and also by the VLMT or the BDI-II, postsurgical.

Note: FLei = Mental Capacity Questionnaire ("Fragebogen zur geistigen Leistungsfähigkeit"), VLMT = Verbal Learn and Memory Test ("Verbaler Lern- und Merkfähigkeitstest"), BDI-II = Beck Depression Inventory II (Beck Depressions Inventar II).

Discussion

The present study examined the relationship between subjective memory complaints (as measured by the FLei), and objective memory function (as measured by VLMT) in patients with focal temporal and frontal lobe epilepsy before and after epilepsy surgery.

Subjective memory reports and demographic variables

We found no significant relationship between memory complaints and sociodemographic variables. As with a previous study (Sherman et al. [24]), the mean values of the neuropsychological test scores showed a tendency to decline six months after epilepsy surgery. This was observed particularly in the VLMT learning score; the FLei score did not change significantly. In the case of possible differences in subjective memory scores between patients with temporal versus frontal lobe epilepsy, we could not replicate a previously described decline in complaints in TLE compared with FLE [18]. While in our sample no significant differences were detected, there appeared to be a tendency for FLE patients to report fewer memory problems after surgery. However, because of the small sample size, these findings should be treated with caution.

Correlations between subjective memory complaints and memory scores

We investigated the correlation between subjective and objective memory scores. Previous factor analyses identified depression as an important factor in memory perception (e.g., [14]). In our sample we found no significant correlation between subjective and objective memory scores when controlling for depressed mood. Grewe et al. [13], amongst others, noted a decreased, but still significant relationship between subjective and objective memory scores when controlling for mood. As was the case with previous research (e.g., [17]), change scores were not informative. They showed no stronger correlation between subjective and objective memory scores than the results examined at one point in time. Seizure frequency has been discussed as another influencing factor in the literature [14]. In our sample, the change in seizure frequency was related to the change in memory complaints. This appeared to be independent of depressed mood, as the correlation did not change after controlling for mood. However, the change in seizure frequency was not normally distributed, and one outliner was detected; otherwise, a trend could be observed (r=0.45, p=0.053). Larger sample sizes could be used to examine in more depth the relationship between change in seizure frequency and changes in subjective memory scores.

Classification of impairment vs. non-impairment

As a next step we examined the classification. Previous research showed at most weak correlations between subjective and objective memory scores (e.g., Hall et al. [15]). However, there was evidence that the associations became stronger when only patients with a decline in memory scores were examined [18]. In most neuropsychological assessments, the current state of memory function is evaluated, but the investigator has no information about possible changes in memory function up to the point of examination. Then, a change in memory can only be estimated based on anamnestic information given by the patients themselves. Even when a loss in memory function is examined at two different points in time, it is not immediately obvious whether the neuropsychological performance falls into the same classification (e.g., average, impaired) as in the preceding assessment. We focused on the classification accuracy including reliable change scores. Impairment was defined as a score below the cut-off criterion or a reliable decrease in objective memory scores. Out of the nine patients who were classified as impaired by the FLei, eight showed at least one impaired objective memory score. Of these, two exhibited impairment in the change scores, but not in the post-surgical assessment. Thus, the change score delivered important additional information that was in accordance with Lineweaver et al. [18]. In contrast with the correlation analysis, mood showed a lower association with memory complaints than objective memory scores. While ninety-five percent of the patients with an unimpaired FLei score reported also no depressive symptoms in the BDI-II. Only forty-four percent of patients who showed an impaired FLei score were also classified as depressed by the BDI-II. At an accuracy level of 89% clinically relevant subjective memory complaints emerged as an acceptable indicator of memory deficit in our sample. However, this did not apply the other way around, because one third of the patients with at least one score classifying them as impaired in the objective measures were not identified by the FLei. This suggests that the FLei underestimated the actual degree of memory deficit in our sample. Some researchers have reported an overestimation of memory problems in patients with epilepsy [25-27]. Others have described an underestimation of memory problems after epilepsy surgery [16,24]. In our sample, the memory scale of the FLei was able to point to memory deficits or reliable memory changes. However, it was not a suitable measure of cognitive functioning, because it missed too many patients with measurable memory impairment in our sample.

Limitations

The present study was limited by its small sample size. Larger studies are needed to differentiate better between subgroups (e.g., side and focus of lesion) and to investigate changes in other neuropsychological measures, such as attentional or executive functions, after surgery. It would especially be interesting to include a prolonged (e.g., >1 day) delayed recall, which would more accurately reflect participants' daily life memory experience. We also only examined patients with therapy-refractory epilepsy who were previously defined as good surgical candidates and who were expected to benefit from surgery. Even amongst patients with epilepsy, this group is relatively small, and so our findings cannot be generalised to other epilepsy patient groups. Future studies could include more non-cognitive variables, and these could be assessed directly, using, e.g., subjective standards of evaluation, or a wider concept of emotional well-being. Up until now, only Grewe et al. [13] have included those variables with a global psychological distress score (GSI of the SCL-90-R) in the examination of patients with epilepsy. Accordingly, the global distress score appeared to be the strongest predictor of memory complaints.

Conclusion

In line with the findings of previous research, we did not find a significant relationship between subjective and objective memory scores in patients with epilepsy after surgery. Two non-cognitive variables emerged as important factors in memory complaints. Depressed mood showed strong correlations with memory complaints, as did seizure frequency. Furthermore, 89% of patients with clinically significant memory complaints post-surgery showed at least one impaired objective memory score. However, one third of the patients, who classified as impaired by neuropsychological memory assessment, showed no elevated subjective memory complaints, i.e. (FLei) scores. Hence, clinically significant subjective memory complaints should warrant further examination of objective memory function in patients with epilepsy after surgery. A lack of subjective memory complaints potentially underestimates the occurrence of objective memory impairments but might be more reflective of emotional well-being post-surgery.

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