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Improving the assessment of everyday cognitive functioning in patients with epilepsy by means of proxy reports

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ABSTRACT

Objectives: The self-report of cognitive deficits by of patients with epilepsy is often poorly correlated with objective test performances but highly related to mood and personality. The aim of this study was to evaluate whether information obtained by close relatives of the patient shows higher correlations with the patients' objective test scores and thereby can be a complementary measure for ensuring a reliable basis for diagnostic decision-making.
Methods: Thirty-four patients and 29 relatives were asked to fill in a questionnaire about everyday cognitive deficits of the patient. All patients completed a neuropsychological test battery comprising measures of memory, attention, and executive functioning and questionnaires on anxiety, depression, and the personality trait neuroticism.
Results: Correlations between relatives' reports and patients' test performances were highly significant across all examined domains. By contrast, self-reports of the patients significantly correlated with none of the neuropsychological measures of memory and with only a subset of the objective measures of attention and executive functioning. Regression analyses additionally revealed a strong dependency of the patients' self-assessment on depression, anxiety, and neuroticism ($R^2 = 0.42$).
Conclusions: These results point out the risk of self-reports distorting reality and additionally recommend consulting a close relative of the patient to ensure reliable information about the patient's everyday cognitive functioning.

1. Introduction

In medical care of epilepsy, the patient's self-report of cognitive deficits is highly important for therapeutic decision-making and the evaluation of treatment success. It helps to assess the cognitive side effects of anticonvulsant medication (AEDs) and possible costs and benefits of epilepsy surgery. However, the self-perception of cognitive functioning frequently does not correspond with standardized neuropsychological test performances [1–6]. Patients complain about deficits that tests fail to detect or deny problems that seem likely in light of test scores.

Recent research indicates that one reason for this discrepancy may be a systematic distortion of the patient's subjective perception by intrapersonal factors such as depression, anxiety [2,6–9], and personality [9–11]. Taking this into account, the reliability and validity of the self-report as a basis for therapeutic decision-making are limited. However, the subjective report contains crucial information about everyday cognitive functioning and quality of life which is hard to access via laboratory tests.

One way to address this problem is to interview a close relative about his or her perception of the patient's cognitive abilities. This proxy assessment is supposed to be less influenced by intrapersonal variances and thereby can give more objective information about the patient's everyday cognitive functioning [12–14]. The present study sought to compare the correlations between patient and relative reports and the patient's objective neuropsychological test performance in order to evaluate whether the inclusion of proxy information can give a more accurate estimation of the day-to-day cognitive functioning of patients with epilepsy.

2. Methods

2.1. Subjects

Patients with epilepsy in an outpatient care center at the Department of Neurology of the University Hospital Dresden were invited to participate in the study. In addition, each patient was asked to recruit a relative. Thirty-four patients (aged 21 to 66) and twenty-nine relatives (aged 25 to 83) agreed to participate. All subjects gave written informed consent, and the study was approved by the Ethics Committee of the Dresden University of Technology. Diagnosis of epilepsy was made on

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the basis of clinical seizure characteristics and EEG. All patients were treated with prescribed AEDs and had been seizure-free for 24 h prior to testing. Exclusion criteria included neurological diseases apart from epilepsy and psychiatric background. Table 1 summarizes the characteristics of patients and relatives.

2.2. Measures

2.2.1. Questionnaires

Self-report of cognitive functioning was assessed by the questionnaire "Fragebogen zur geistigen Leistungsfähigkeit" (FLei) [15], asking for the subjectively observed frequency (scaled "never" to "very often") of deficits in memory, attention, and executive functioning. The questionnaire consists of 35 questions regarding everyday situations over the past 6 months. The patients' relatives were asked to fill in the proxy version of this questionnaire, which was developed for this study. In 12 cases, the relatives answered the questionnaire under controlled conditions at the Department of Neurology, while a further 17 relatives answered the questionnaire at home and returned it by mail. The analyses were based on the sum scores of the three domains, memory, attention, and executive functioning, and the total score as a sum of all domains (control items were excluded during analysis). High scores represent high perceived deficits.

In terms of controlling confounding variables, patients' anxiety and depression were assessed by the Hospital Anxiety and Depression Scale (HADS) [16], a 14-item questionnaire for emotional symptoms in people with physical health problems. In addition, the Big Five Inventory-10 (BFI-10) [17] was applied. This questionnaire consists of 10 items giving a basic assessment of the 5 dimensions of personality according to the five-factor model from which the trait neuroticism was taken for analyses.

2.2.2. Neuropsychological assessment

All patients completed a neuropsychological test battery comprising measures of memory, attention, and executive functioning to correspond to the domains of the self-report questionnaire.

Memory was assessed by the Wechsler Memory Scale—Revised (WMS-R, German version) [18], subtests Logical Memory I and II, which require the immediate (LM I) and delayed recall (LM II, after 30 min) of a short story.

Table 1
Characteristics of the sample.

	Patients ($n = 34$)	Relatives ($n = 29$)
Age (mean, *SD*)	41.2 (13.3)	48.1 (13.8)
Male (*n*, %)	7 (20.6)	19 (65.5)
Female	27 (79.4)	10 (34.5)
Education (mean, *SD*)	10.4 (1.4)	10.3 (1.6)
Relationship to the patient (*n*, %)		
Partnership		21 (72.4)
Parental		6 (20.7)
Other (sibling, close friend)		2 (6.9)
Joint household (*n*, %)		
Yes		20 (69.0)
No		9 (31.0)
Type of seizures (*n*, %)		
Simple partial seizures	2 (5.9)	
Complex partial seizures	20 (58.8)	
Simple partial and complex partial seizures	7 (20.6)	
Generalized seizures	5 (14.7)	
Duration of epilepsy (mean years, *SD*)	16.9 (13.6)	
Seizure frequency in the past 4 weeks (mean, *SD*)	3.7 (8.4)	
Number of AEDs (*n*, %)		
1 AED	12 (35.3)	
≥2 AEDs (polytherapy)	22 (64.7)	
Underwent epilepsy surgery (*n*, %)	9 (26.5)	

Attention and executive functioning were assessed by EpiTrack® [19,20], a screening tool for tracking the cognitive side effects of antiepileptic drugs. It consists of a Trail Making Test, a test of response inhibition, digit span backward, written word fluency, and a maze test.

Furthermore, tests of attention included the following:

- Trail Making Test (as a part of EpiTrack®), part A, measuring visual attention by calculating the time taken to connect 25 consecutive numbers on a sheet of paper.
- Parts of a Stroop Test (Farb-Wort-Interferenztest [FWIT], Farbwortlesen and Farbstrichbenennen) [21] which requires reading out loud a list of words (RLW) and naming the color of bars (NCB) as quickly as possible.

Executive functioning was additionally tested by the following:

- Trail Making Test (as a part of EpiTrack®), part B, a task-switching test in which the subject is asked to connect 25 consecutive targets alternating between numbers and letters.
- Parts of a Stroop Test (Farb-Wort-Interferenztest [FWIT], Interferenzversuch) [21] which requires the subject to name the color of a word that is displayed in a color different from the color it actually names (INT).

2.3. Statistical analysis

Statistical analyses were calculated by IBM(R) SPSS(R) Statistics 22. Pearson's correlation coefficient was used to assess the relationship between subjective perception of cognitive functioning and neuropsychological test performance. *T*-tests for dependent measures were calculated in order to compare self-report and relative report in the different domains. Group differences in control variables were assessed using *T*-tests for independent measures. In the case of nonparametric variables, the Spearman correlation coefficient was used for correlation analysis, and the Wilcoxon test (dependent variables) and the Mann–Whitney test (independent variables) were carried out for group comparisons, respectively. Additionally, a multiple regression analysis was performed, with the HADS sum score for anxiety and depression and the BFI-10 score for neuroticism as independent variables and the patient's overall subjective complaint score (FLei) as a dependent variable. The level of significance was set at 0.05.

3. Results

As shown in Table 2, the subjective rating given by the relatives was significantly correlated with all examined objective test scores except for WMS-R LM I, which barely missed the level of significance by $P = 0.68$. By contrast, the patients' self-rating showed significant correlations with only a subset of neuropsychological measures of attention and executive functioning and with none of the objective measures of memory. All correlation coefficients were lower than those for the proxy rating, showing a stronger relationship between subjective and objective measures for relatives.

A multiple regression analysis revealed that 42% ($P < 0.05$) of the variance of self-reported cognitive deficits can be explained by the patients' HADS score (anxiety and depression; $\beta = .36$, $P = .04$) and level of the personality trait neuroticism ($\beta = .37$, $P = .04$). By contrast, the self-report was not significantly correlated with any disease-specific variable (type of seizures, duration of epilepsy, seizure frequency, number of AEDs).

Table 3 shows comparisons of patient and relative ratings in the examined cognitive domains and the overall subjective complaint score. It becomes apparent that relatives rated smaller deficits in all domains. This difference was significant in the domains of memory and attention but not for executive functioning. The overall subjective rating shows a significant mean difference of $M = 8.90$ ($SD = 22.23$; $P = 0.04$) for patient and relative ratings.