Subjective memory complaints in patients with epilepsy: The role of depression, psychological distress, and attentional functions

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ABSTRACT

While objective memory dysfunctions have been thoroughly investigated in patients with epilepsy, assessment of subjective memory complaints (SMC) remains challenging. Former studies have demonstrated an impact of patients' depressive mood on SMC. However, the impact of more general psychological distress and cognitive functioning in non-memory domains on SMC has only received little attention so far. We therefore sought to determine the factors which may particularly predict SMC in a sample of patients with focal epilepsy ($n = 99$) who accomplished (1) a comprehensive neuropsychological assessment, (2) a subjective memory questionnaire, and (3) scales of self-rated depressive mood and psychological distress. General psychological distress (as measured by the Symptom Checklist- 90-Revised) accounted for a high proportion of SMC and, critically, explained more variance than depressive mood as a single factor (as measured by the Beck Depression Inventory II). Furthermore, SMC were predicted by recall measures of a verbal serial learning task, but also by measures of attention, importantly. Hence, our data firstly indicate that beyond the impact of depressive mood, SMC may be more accurately explained by psychological distress in a more general sense. Secondly, our study provides evidence that patients' estimation of subjective memory is not solely based on functioning in memory domains. Attentional resources may also be critical for patients' perception of everyday memory functioning.

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1. Introduction

A long-standing tradition of research has been dedicated to the investigation of memory functioning in patients with epilepsy (PWE) in neuropsychological tests or experimental paradigms. Apart from objective memory performance, more recent research has begun to consider subjective memory complaints (SMC) in PWE. Previous research has demonstrated poor correlations between objective episodic memory test performance and SMC (e.g., Baxendale and Thompson, 2005; Helmstaedter and Elger, 2000; Vermeulen et al., 1993). To predict patients' everyday functioning in a more reliable way, it will be of central relevance to understand and overcome this difference between SMC and objective performance. Likewise, it may help understanding patients' complaints which are still underestimated by many practitioners (McAuley et al., 2010).

Besides the role of episodic memory test performance, there is a lack of evidence on the specificity of SMC in PWE. In other words, it remains unclear if SMC actually reflect performance in objective tests of memory. It has been presumed that PWE might have a different psychological concept of memory and therefore base their subjective memory ratings on performance in non-mnemonic functions (Hall et al., 2009). Some studies could indeed demonstrate that SMC may be significantly predicted by patients' performance in language tests, such as word fluency or naming (Helmstaedter and Elger, 2000; O'Shea et al., 1996). Concerning the role of attentional functions there has been mixed results. While in an early report (McGlone, 1994) SMC were significantly related to neuropsychological tests of attention, two other studies could not replicate such a relationship (Piazzini et al., 2001; Vermeulen et al., 1993). However, due the frequent clinical observation that "memory deficits" reported by patients might in fact reflect a disturbance of attention (Howieson and Lezak, 2004) and the common neurocognitive mechanisms of memory and attention (Davidson et al., 2006; Naghavi and Nyberg, 2005) one may hypothesize that objective tests of attention may—at least to a certain degree—predict SMC in PWE.

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A further important factor which may moderate the correspondence between SMC and objective memory measures is patients' depressive mood (Au et al., 2006; Giovagnoli et al., 1997; Liik et al., 2009; Marino et al., 2009; Piazzini et al., 2001; Rayner et al., 2010). Accordingly, it has been suggested that this interrelationship might reflect common neurobiological mechanisms of epilepsy and depression (Rayner et al., 2010). However, there is some evidence that SMC may not solely be influenced by depression but by a wider range of psychological distress. Previous studies suggest that there may be a correlation of SMC and the number of psychiatric comorbid conditions (Pulsipher et al., 2006) or the severity of general psychological distress (Hermann et al., 2000) in PWE. One might therefore hypothesize that SMC may be influenced by a more broadly defined construct of psychological distress which—in addition to depressive symptoms—also reflects psychological dimensions such as anxiety, somatic symptoms, interpersonal thoughts, perception, or personality. So far, it has not been proven, whether SMC may be specifically related to depression or whether they may be more adequately explained by patients' general psychological distress which goes beyond depression as a single factor.

Based on the issues presented above, the aim of the present investigation was to analyze the association between SMC and objective test performance in well-characterized patients with chronic, pharmacoresistant focal epilepsy. We focused on the differential influence of self-reported mood versus psychological distress on the relationship between SMC and objective cognitive scores. Specifically, we assumed that the impact of general psychological distress would exceed the previously reported influence of depressive mood as a single factor. In addition to this, we intended to evaluate the role of non-mnemonic cognitive domains for patients' SMC. We particularly evaluated the hypotheses that SMC may be influenced by tests of attentional functions as patients may erroneously perceive concentration problems in everyday life as markers of memory problems. We predicted that after controlling for the influence of psychological distress measures of attentional functions would also contribute to SMC.

2. Material and methods

2.1. Participants

The study included 99 patients with focal epilepsy who attended our epilepsy centre for a presurgical video-EEG monitoring between May 2013 and October 2014 and who were consecutively included according to the following inclusion criteria: *(1)* diagnosis of focal epilepsy confirmed by EEG and seizure semiology, *(2)* participation in standard neuropsychological examination including self-rating of cognitive functioning with a standardized questionnaire (which is routinely given to all patients who attend to our video-EEG monitoring program), *(3)* age at examination of at least 16 years, *(4)* availability of both the Beck Depression Inventory II and the Symptom Checklist-90-Revised (which is routinely given to all patients who attend to our video-EEG monitoring program), and *(5)* general intellectual abilities sufficient to participate to standard neuropsychological examination and to fill in the self-report questionnaires. The sample consisted of 44 females and 55 males. Patients' mean chronological age at neuropsychological examination was 35.38 (*SD* = 12.8, *Min* = 17, *Max* = 70); patients' mean age at epilepsy onset was 18.05 (*SD* = 12.02) with a mean duration of epilepsy of 17.39 years (*SD* = 12.02). The majority of patients (*n* = 54; 54.5%) suffered from temporal lobe epilepsy (TLE), 15 patients (15.2%) had frontal lobe epilepsy, 7 patients (7.1%) had occipital-parietal epilepsy, 13 patients (13.1%) had multilobar epilepsy, and 10 patients (10.1%) had the diagnosis of focal epilepsy which could

not be further specified according to video-EEG monitoring and MRI findings. In 53 patients, seizures started in the right hemisphere, in 39 in the left hemisphere, and in one patient in either hemisphere independently; in 6 patients lateralization was unclear. Sixty-seven patients were on antiepileptic polytherapy, 26 were on monotherapy, and 6 patients were off antiepileptic medication at time of the neuropsychological examination. The study was carried out in compliance with the Code of Ethics of the World Medical Association (Declaration of Helsinki). No formal ethical consent was obtained because the procedures are regularly carried out during presurgical assessment in this centre for the sake of clinical diagnostics.

2.2. Self-report of cognitive functions

For estimation of subjective memory, we applied the "Fragebogen zur geistigen Leistungsfähigkeit" (Flei; Questionnaire for complaints of cognitive disturbances; Beblo et al., 2010). The Flei consists of 30 items which reflect typical and common everyday situations with demands on cognitive functions. For each of the 30 situations, the participant has to judge the frequency of disturbances she/he experienced in this respective situation during the last six months on the basis of a five point scale (i.e., "*never*", "*rarely*", "*occasionally*", "*frequently*", and "*very frequently*"). It covers three subscales (i.e., attention, memory, and executive functions) each consisting of 10 items. Scoring of each scale ranges from 0 to 40 points with higher scores reflecting more frequent subjective cognitive impairment; the Flei total score reflects the sum of all three cognitive scales and has a range from 0 to 120 points. An English ad-hoc version (translated by PG) of the German original version of the Flei can be found in Appendix A. Reliability of the Flei has been reported to be sufficiently high (*Cronbach's* $\alpha \geq 0.91$, $r_{split-half} \geq 0.87$) for all three subscales (Beblo et al., 2010). The Flei has been shown to detect subjective cognitive complaints in patients with schizophrenia and depression relative to healthy controls (Beblo et al., 2010). The original version of the Flei includes an additional set of five items adopted from a visual neglect questionnaire (e.g., "I ignore people on the left hand side") which intends to serve as a control scale. However, for our sample of neurological patients, we excluded this scale as ratings on these items may be confounded with patients' actual neurological deficits (Beblo et al., 2010). Based on our hypotheses presented above, we only considered the memory subscale for our analyses. The Flei was usually filled in by the patients after the standard neuropsychological examination, but before receiving potential feedback of the neuropsychological test results by the neuropsychologist or the neurologist.

2.3. Mood and psychiatric distress

Estimation of severity of patients' current depressive symptoms was based on the Beck Depression Inventory II (BDI; Hautzinger et al., 2006). In the BDI, the patient has to rate the severity of 21 depressive symptoms (e.g., sadness, guilt feelings, suicidal thoughts) according to his/her feelings during the last two weeks. The BDI has an acceptable sensitivity and specificity for the diagnosis of depressive disorders in patients with focal epilepsy (de Lemos Zingano et al., 2015). The reliability (*Cronbach's* α) of the German version of the BDI-II used in this study has been found to range from 0.89 to 0.93 for different clinical and non-clinical samples; the retest reliability in a non-clinical sample was *r* = 0.78 (Kühner et al., 2007). In the statistical analyses, we included the total score of the BDI-II as a continuous variable, which is the sum of the raw scores of the single items with higher scores indicating more severe and more frequent depressive symptoms.

Estimation of patients' overall psychological distress was based on the Symptom Checklist-90-Revised (SCL-90-R; Franke and