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Subjective perception of cognition is related to mood and not performance

S.E. Marino [a,*], K.J. Meador [b], D.W. Loring [b], M.S. Okun [c,d], H.H. Fernandez [c,d], A.J. Fessler [e], R.P. Kustra [f], J.M. Miller [f], P.G. Ray [g], A. Roy [h], M.R. Schoenberg [i], V.J. Vahle [j], M.A. Werz [k]

[a] Experimental and Clinical Pharmacology, University of Minnesota, 717 Delaware Street SE, Room 517, Minneapolis, MN 55414, USA
[b] Department of Neurology, Emory University, Atlanta, GA, USA
[c] Department of Neurology, University of Florida, Gainesville, FL, USA
[d] Movement Disorders Center, University of Florida, Gainesville, FL, USA
[e] Department of Neurology, University of Rochester, Rochester, NY, USA
[f] GlaxoSmithKline, Research Triangle Park, NC, USA
[g] Department of Neurology, Medical College of Georgia, Augusta, GA, USA
[h] Department of Statistics, University of Nebraska—Lincoln, Lincoln, NE, USA
[i] Department of Psychiatry & Behavioral Science, University of South Florida College of Medicine, Tampa FL
[j] St. Louis College of Pharmacy, St. Louis, MO, USA
[k] Department of Neurology, University Hospitals Case Medical Center and Case Western Reserve University School of Medicine, Cleveland, OH, USA

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ABSTRACT

Objective: Clinicians monitor cognitive effects of drugs primarily by asking patients to describe their side effects. We examined the relationship of subjective perception of cognition to mood and objective cognitive performance in healthy volunteers and neurological patients.
Methods: Three separate experiments used healthy adults treated with lamotrigine (LTG) and topiramate (TPM), adults with epilepsy on LTG or TPM, and patients with idiopathic Parkinson's disease. Correlations were calculated for change scores on and off drugs in the first two experiments and for the single assessment in Experiment 3.
Results: Across all three experiments, significant correlations were more frequent ($\chi^2 = 259$, $P \leqslant 0.000$) for mood versus subjective cognitive perception (59%) compared with subjective versus objective cognition (2%) and mood versus objective cognitive performance (2%).
Conclusions: Subjective perception of cognitive effects is related more to mood than objective performance. Clinicians should be aware of this relationship when assessing patients' cognitive complaints.

1. Introduction

Practitioners commonly rely on patient self-report of perceived difficulties with memory, attention, concentration, and language when assessing how much a disease state or its treatment might be affecting day-to-day cognitive functioning. Similarly, self-accounts of cognitive performance are often sought from participants in clinical research trials to monitor the safety, efficacy, and side effects of the therapy or drug being studied. Therefore, the extent to which subjective perceptions of cognitive functioning correspond to objective measures of cognitive performance is crucial in determining whether or not self-reports should be considered valid appraisals of neuropsychological status on which diagnostic, treatment, research, or regulatory decisions should be based.

As subjective memory complaints may serve as an indicator of more general cognitive decline [1], the relationship between the subjective perception of memory impairment and objective measures of memory function has been studied extensively, especially in the elderly. In a number of cross-sectional studies of patients without dementia, subjective memory complaints were more highly correlated with measures of mood, especially depression and anxiety, than with objective measures of cognitive performance [2–7].

Memory is also negatively impacted by epilepsy [8], and patients with epilepsy are apt to report more significant memory disturbances than individuals without epilepsy [9]. Not only are self-reported memory problems by patients with epilepsy weakly correlated with standard memory and neuropsychological measures [10,11], but patients with subjective memory complaints are more likely to be depressed or anxious than those who report no memory difficulties [10,12–14].

Using the Quality of Life in Epilepsy Inventory (QOLIE-89) to measure subjective perceptions of domains known to affect daily living as well as the Profile of Mood States (POMS), Perrine et al. [15] found that mood significantly correlated with self-reported QOLIE-89 cognition sub-scales for memory, attention/concentration, and language, as well as the overall QOLIE-89 score. They also reported smaller, but significant correlations between the objective

* Corresponding author. Fax: +1 612 626 0148.
E-mail address: marin007@umn.edu (S.E. Marino).

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neuropsychological tests and the three-self reported QOLIE-89 cognition subscale measures, suggesting that self-reports of memory impairment by persons with epilepsy may be a function of both mood and objective memory functioning. However, the degree to which neuropsychological measures used in these studies reflect the types of memory problems experienced in day-to-day living has been called into question [12,16]. Elixhauser et al. [17] sought to address this issue by using the Rivermead Behavioural Memory Test (RBMT), a measure explicitly designed to assess everyday memory function, and found similar associations between everyday behavioral memory performance, subjective perception of memory difficulties (QOLIE-89), and self-reported mood (POMS) in patients with epilepsy. Similar to Perrine et al. [15], Elixhauser et al. [17] found a strong association between mood and perceived cognitive function, but a smaller, yet significant, correlation between objective memory performance and perceived cognitive function, regardless of whether neuropsychological tests or measures of everyday performance were used.

Investigations into the validity of self-reports of cognitive function in patients with epilepsy have employed subjects whose seizures were controlled by antiepileptic drugs (AEDs). A cross-sectional study by Uijl et al. [18] attempted to tease out the contribution of AEDs in the number of subjective complaints that patients with epilepsy conveyed to their physician. Sixty-seven percent of the 173 patients with well-controlled epilepsy reported moderate to severe complaints, most often regarding cognitive dysfunction. The two factors most closely associated with the number and severity of these complaints were high scores on Psychoneuroticism (Symptom Check List-90) and AED polytherapy. These results support the influence of mood on the subjective perception of cognitive impairment, but Uijl et al. [18] did not validate those complaints by objective neuropsychological testing. In fact, there are no studies in the literature that have examined the direct effect of drug treatment on subjective perception of cognitive function and its relationship to both mood and objective performance despite the fact that this is the primary method of assessing cognitive side effects of drugs in clinical settings and in clinical trials for regulatory approval of drugs.

We previously published two double-blind studies that compared the effects of two AEDs on neuropsychological function in healthy volunteers [19] and in patients with epilepsy [20]. In this article, we reanalyzed those data to investigate the relationship of subjective perception, mood, and objective cognitive performance as a function of effects of treatment with AEDs, that is, lamotrigine (LTG) and topiramate (TPM). We hypothesized that changes in perception of cognition across drug/nondrug conditions would be more related to changes in mood than to changes in objective cognitive performance.

As the number of studies that have examined the validity of subjective perception of cognitive performance in patients with neurological diseases remains limited, we also examined the robustness of the relationship between subjective perception of cognition and mood in a new cross-sectional study, which is the first to examine this association in patients with Parkinson's disease.

2. Materials and methods

All studies were conducted under the principles of the Helsinki Accords and were approved by the local ethics committees.

2.1. Experiment 1: Healthy volunteer AED cognition study

Methodology and prior results have been described in detail elsewhere [19] and are outlined below.

2.1.1. Study design and prior results

This was a randomized, double-blind, repeated-measures, crossover investigation. As previously reported, subjects had significantly better performance on 80% of the neuropsychological variables for LTG compared with TPM; there were no variables that exhibited superior performance for TPM [19].

2.1.2. Subjects

Forty-seven healthy paid volunteers (19 men, 28 women; mean age = 37 years) without a history of neurological or psychiatric diseases including drug abuse completed this study.

2.1.3. Procedure

Subjects were treated with each AED in monotherapy for a 12-week period (7 weeks of dose escalation followed by 4 weeks of maintenance, and then a 1-week taper off of AED) followed by a 4-week washout period off AED. Target dose was 300 mg/day for both drugs. Subjects underwent neuropsychological testing on four occasions: two AED conditions and two nondrug conditions. The mean (range) blood level for LTG on the day of neuropsychological testing was 4.7 μg/mL (1.6–7.0) and for TPM was 9.3 μg/mL (2.8–15.8). The mean LTG dose was 298 mg/day and the mean TPM dose was 300 mg/day.

2.1.4. Neuropsychological tests

The test battery to assess AED neuropsychological effects consisted of 17 tests.

2.1.4.1. Cognitive performance measures

1. Attention/vigilance: Continuous Performance Task, Digit Cancellation Test, Visual Serial Addition Test.
2. Memory: MCG Paragraph Memory, Selective Reminding Test.
3. Language: Controlled Oral Word Association Test (COWA), Boston Naming Test, Semantic Fluency Test.
4. Cognitive and motor speed: Lafayette Grooved Pegboard, Choice Reaction Time.
5. Other cognitive tests: Stroop Color–Word Test, Symbol Digit Modalities Test (SDMT).

2.1.4.2. Behavioral measures. Profile of Mood States (POMS—adjective checklist to assess mood; subscales include Tension/Anxiety, Depression, Anger/Hostility, Vigor, Fatigue, and Confusion/Bewilderment), and subjective cognitive function rating scales (i.e., attention, language, and memory) from the Quality of Life in Epilepsy-89 (QOLIE-89).

The A-B Neurotoxicity Scale, Adverse Events Profile, Side Effects and Life Satisfaction (SEALS), and SF-12 (generic 12-item quality of life scale) were also administered but were not included in the present analysis. Thus, a total of 14 tests with 33 variables were used in the present analysis including three subjective perception of cognition, seven mood, and 23 objective cognitive performance measures for each of the two AED conditions.

2.2. Experiment 2: Patients with epilepsy AED cognition study

Study methodology and prior results have been described in detail elsewhere [20] and are outlined below.

2.2.1. Study design and prior results

This was a randomized, double-blind, repeated measures, parallel-group investigation. As previously reported, cognitive performance at the end of the maintenance phase was better for LTG than TPM when using a combined summary score reflecting performance on all neuropsychological measures (415 vs 315, $P < 0.001$) [20].