Can prefrontal theta cordance differentiate between depression recovery and dissimulation?

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Abstract
We present a case report of a 37-year old woman diagnosed with depressive disorder, first episode, who was admitted into a psychiatric hospital after a failed suicidal attempt. She responded to antidepressant therapy, as evidenced by a >50% reduction in MADRS total score. She was discharged after 4 weeks of treatment, denying any suicidal ideations. The following day the patient committed suicide; she burned herself to death. It is very likely that the patient dissimulated her symptoms and ideations. Subsequently, her quantitative EEG records were retrospectively analyzed. An increase of prefrontal theta cordance value after the first week of mirtazapine therapy was found. Recently three small studies have revealed that decrease of prefrontal theta cordance after 1 week of antidepressant administration can predict clinical response in patients with unipolar depression. In our previous study the absence of a decreased theta prefrontal cordance was associated with lack of treatment response with NPV 1.0 (Bares et al., 2007). Thus, we hypothesize that prefrontal theta cordance could become an objective marker of change of depressive symptoms, independent of patients’ compliance and symptom dissimulation, more precise than objective and self-rated depression rating scales.
INTRODUCTION

Until now, no clinically useful laboratory markers for diagnosis of depressive disorder or objective prediction of treatment response have been available. A new promising method to predict antidepressant effect is prefrontal cordance [8]. Cordance is a relatively new application of QEEG. The cordance combines complementary information from the absolute and relative power of EEG spectra to yield values that have a stronger correlation with regional cerebral perfusion than either measure alone [14]. Three small studies have revealed that a decrease of prefrontal theta cordance after 1 week of antidepressant administration can predict clinical response in patients with unipolar depression [1,2,5,6]. Our group found a significant increase in prefrontal cordance value after the first week of antidepressant therapy in patients who did not respond to a 4-week antidepressant trial. In our sample of 51 patients with resistant depression, only one showed an increase of prefrontal cordance associated with response to antidepressant therapy (reduction of ≥50% in total MADRS score). We present a case report of this patient and discuss potential usefulness of prefrontal theta cordance in identification and verification of patient’s clinical status.

CASE REPORT

37-year old woman diagnosed with severe depressive disorder without psychotic features, first episode of depression in her lifetime, was admitted to the Prague Psychiatric Centre (PPC) after a failed suicidal attempt with a combination of alcohol and drugs. The patient was married and had two daughters. Psychiatric symptoms manifested as insomnia, anxiety, and marital problems and first occurred two years ago at the age of 35 years. However, fully expressed symptoms of clinical depression had lasted for two months before the admission. She felt worthless and guilty and experienced working incapacity. After the suicidal attempt, the patient was treated for 2 days in an emergency unit where antidepressant treatment was initiated (mirtazapine 15 mg/day) After her transfer into the PPC the patient signed an informed consent with QEEG assessments. We recorded her EEG data after 2 days of mirtazapine treatment and rated her clinical status using MADRS [15], CGI [7] and BDI-SF [3]. She scored a total of 35 in MADRS, 6 and 26 in CGI and BDI-SF, respectively. The dose of mirtazapine was increased up to 45 mg/day and alprazolam added to control her anxiety. A second EEG assessment and evaluation of clinical status were performed one week after the first assessment (9th day of mirtazapine and alprazolam treatment). The total MADRS score decreased down to 30, CGI to 5 and BDI-SF to 19. She was granted two weekend passes to visit her family, during which time she did not indicate any signs of worsening of depression or suicidal ideations. Her final MADRS score after 4-week of mirtazapine therapy was 16, CGI 3 and BDI-SF 10. She underwent a last EEG assessment. Upon questioning by an experienced psychiatrist prior to the discharge, the patient denied any suicidal ideations. She was clearly less anxious, her depressive symptoms improved, including mood, appetite, and sleep. The patient was rated as clinically improved. A day after the hospital discharge, she walked approximately 1 km to a gas station where she bought a container and some gasoline.

Then she returned to her apartment, locked the door, poured gas all over the place, set the fire and burned herself to death.

We analyzed retrospectively her QEEG records to evaluate the change of theta prefrontal cordance during antidepressant therapy. We used the same algorithm as Leuchter et al. [13,14]. A detailed description of cordance calculation was presented recently elsewhere [1]. Theta prefrontal cordance value was 0.55 before starting treatment with the higher dosage of mirtazapine and 0.72 after week 1 and 0.70 after week 4 of therapy, respectively.

DISCUSSION

The patient was assessed as a responder based on the reduction of the MADRS total score following a 4-week antidepressant therapy. Despite the fact that she reached the criterion of response, denied any suicidal ideations, guilty feelings or psychotic symptoms during the final clinical assessment, she committed suicide the day after her discharge. Considering her previous clinical symptoms, we presume that the patient dissimulated the severity of depressive symptoms and that her suicide was not an impulsive act.

Moreover, we did not detect a theta prefrontal cordance reduction, supposedly an early biological predictor of antidepressant response [1,2,5,6]. In our previous study the absence of a decreased theta prefrontal cordance was associated with lack of treatment response with NPV 1.0 [1,2]. On the contrary, the patient displayed an increase of this parameter. Thus, we suggest that increase of theta prefrontal cordance could be an objective marker of the real severity of depressive symptoms, which is not affected by dissimulation, unlike depression rating scales. Such objective measures may be clinically useful, especially in patients with a high risk of suicide who are often not able to describe their symptoms reliably.

We are aware of the case study limitation; as well as the fact that the patient had her first EEG assessment after 2 days of drug administration and not before the

**Abbreviations**

- BDI-SF: Short Form of Beck Depression Inventory
- CGI: Clinical Global Impression scale
- EEG: electroencephalography
- MADRS: Montgomery-Åsberg Depression Rating Scale
- NPV: Negative predictive value
- QEEG: quantitative electroencephalography
- SSRI: selective serotonin reuptake inhibitor
- rTMS: repetitive transcranial magnetic stimulation
initial treatment as in the previous studies [1,2,5,6]. In a pooled analysis of 54 subjects from three studies across investigative teams, decreases in prefrontal cordance yielded an overall accuracy of 78% [11], so our results could be limited by accuracy of method. On the other hand, only this patient showed an increase of theta prefrontal cordance associated with response to antidepressant therapy in our larger sample with 51 patients. Also, there may be an alternative explanation for the observed results. For example, placebo responders showed an early significant increase of prefrontal cordance values not detected in antidepressant or placebo nonresponders [13]. Placebo response could be transient and may explain a discrepancy between decrease of depressive symptoms and sudden occurrence of depression relapse.

Nevertheless, the data from our case report should draw attention to a more extensive research of prefrontal theta cordance in patients with depressive disorder to further elucidate its role as a potentially objective biological marker of depression. It is important for clinical practices to know i) if EEG cordance prediction is valid to antidepressant therapy in general (i.e. rTMS, ECT, augmentation [10]), not only to antidepressant ii) if we can use it in sequencing antidepressants prediction too. We recently published a case report in which decreased prefrontal theta cordance predicted response to rTMS monotherapy and two cases which suggest that prefrontal theta cordance could be used repeatedly during sequencing antidepressant therapy [10]. iii) If we can use it in the whole spectrum of depressive disorder [16]. When our expectations are validated, we could use EEG cordance in a similar way as microbiologists use cultivation to find the best antibiotic. Another potential usefulness of EEG cordance could be to test other drugs that could be effective in some subtypes of depressive disorder [4].

Another recent study demonstrated that frontal QEEG can predict changes in suicidal ideation during SSRI treatment [9] which further supports potential usefulness of the QEEG in patients with depressive disorder.

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