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Metacogntive training add-on to esketamine treatment in TRD patients: effects on depressive rumination

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Introduction: Depressive rumination has been the subject of increasing clinical and research interest in recent years. Numerous studies have demonstrated its central role in the etiopathogenesis and maintenance of depressive disorders. It refers to the struggle to control repetitive and passive thoughts with a hyper-focus on depressive symptoms, their causes, meanings and consequences. It is, therefore, a process that is often active in people with depressive mood and that can exacerbate and prolong depressive symptoms by promoting their chronicity. It can therefore be argued that depressive rumination may contribute to treatment resistance. The metacognitive model of major depressive disorder and its derived treatment focuses on rumination supporting beliefs and on their modification, with the aim of reducing their negative effects.
Objectives: The aim of this study was to evaluate the improvement in depressive rumination using the metacognitive approach in TRD patients treated with intranasal esketamine.
Methods: Twenty-five patients (13F) with a mean age of 55.88 years (±11.31) diagnosed with treatment-resistant major depression (TRD) received an 8-session weekly metacognitive training (MCT) intervention in addition to the standard intranasal esketamine treatment protocol. Patients were assessed at baseline and after 3 and 6 months of treatment using the Penn State Worry Questionnaire (PENN) and the Ruminative Response Scale (RRS) to assess depressive rumination, and the Montgomery-Asberg Depression Rating Scale (MDRS) to assess depressive symptomatology.
Results: At baseline MADRS and RRS total scores did not differ significantly by gender or age. To assess the effect of MCT as an adjunct to esketamine therapy, a repeated measures ANOVA was performed comparing participants at different time points (T0, T3, T6). The analysis showed an effect of treatment on MADRS total score (η^2=0.45; F=18.22, p=0.001), MADRS item 9 (pessimistic thoughts) (η^2=0.18; F=4.85, p=0.02) and RRS total score. Post-hoc comparisons were significant for MADRS and RRS total scores, with progressive decreases between T0 vs T3, T0 vs T6 and T3 vs T6; for item 9, comparisons were significant between T0 vs T3 and T0 vs T6, with stability between T3 and T6. MCT treatment combined with intranasal esketamine resulted in significant improvements in depressive symptoms. It also reduced depressive rumination and maladaptive metacognitive beliefs.
Conclusions: These preliminary results show that MCT as an adjunct to esketamine treatment is effective for depressive rumination, with stable results up to 6 months after treatment. The generalisability of the results is limited by the lack of a control group and the relatively small sample size. Further studies in larger populations and comparing MCT with other psychotherapies or usual care are needed to confirm these findings.

Disclosure of Interest: None Declared

EPV0662

Brain Damage after ECT? No significant changes of Neurofilament Light Chain and Glial Fibrillary Acidic Protein in Cerebrospinal Fluid

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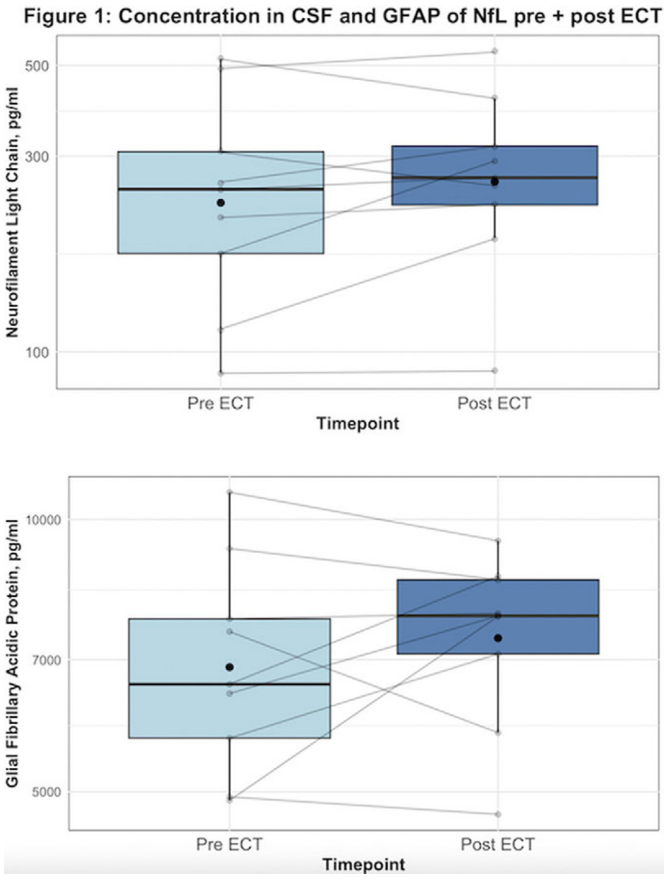
Introduction: Electroconvulsive therapy (ECT) is an effective treatment for major depressive disorder (MDD). Only few studies have measured CSF in patients undergoing ECT; thus far, no prognostic candidate biomarkers for treatment response have been found (Kranaster *et al.* Neuropsychobiology. 2019;77(1):13-22). Neurofilament light chain (NfL) is a protein found in the axons of neurons. If elevated in blood or cerebrospinal fluid (CSF), it is an indicator of neuroaxonal damage. A recent study including 15 patients with MDD who underwent ECT found no significant change in serum NfL concentrations after completion of treatment (Besse et al. Eur Arch Psychiatry Clin Neurosci 2024; 274(5):1187-95). The astrocyte marker glial fibrillary acidic protein (GFAP) is elevated in MDD and neuroinflammatory diseases. Serum GFAP levels in 40 MDD patients decreased after ECT compared to baseline (Xu *et al.* Psychiatry Clin Neurosci. 2023; 77(12):653-64). No studies measuring CSF levels of both markers have been performed.
Objectives: In this prospective study we aimed to measure changes in CSF of NfL and GFAP in patients undergoing an ECT series.
Methods: In a sample of 9 MDD patients undergoing bilateral ECT, CSF was analyzed before and after the 8th ECT session. Patients took antidepressant medication in a steady state over the course of ECT. A mixed-effects linear regression analysis was done using the log-transformed NfL and GFAP levels as outcome variables. The timepoint (pre-ECT, post-ECT) were entered as fixed effects, patient ID was included as a random effect to account for individual variability. We corrected for multiple testing and defined alpha = 0.05/2 = 0.025. Statistical analyses were performed using R version R-4.3.2.
Results: The mean age ± SD was 34 ± 11 years, 6 out of 9 patients (67%) were women. Mean elevations of NfL by 19,9 pg/ml (95% CI: -120.3 to 160.0) and GFAP by 445.8 pg/ml (95% CI: -1279.6 to 2171.4), there was no significant change in NfL (p = 0.213) or GFAP (p = 0.362) levels after ECT. Figure 1 shows concentrations of both NfL and GFAP pre and post ECT.

Image:



Conclusions: This study found no significant changes of NfL or GFAP levels in CSF after an ECT series, suggesting no evidence of neuroaxonal damage or brain damage through astrocyte activation related to ECT. However, the small sample size may have obscured potential effects. Future research with larger sample sizes is therefore essential.

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EPV0663

Measuring the efficiency of treatment with neurofeedback method in patients with Affective disorders

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Introduction: Affective disorders are in constant rise and they are a serious medical and social problem. All the latest studies suggest that the incidence of affective disorders is about 14%, which makes them one of the most common psychiatric disorders. Because of that, there is a need for alternative forms of treatment of affective disorders.

Objectives: The main goal of this study is to evaluate the effectiveness of the combined treatment of pharmacotherapy together with the Neurofeedback method in the treatment of affective disorders in adult individuals.

Methods: A prospective randomized study including a total of 100 outpatients from University Clinic of Psychiatry in Skopje. The subjects were randomly divided into 2 groups of 50 patients, of which the patients in the study group were treated with a combined treatment that includes the neurofeedback method as an augmentation to antidepressant therapy, while the control group with monotherapy with antidepressant medications. Subjects were examined for 2 months, with evaluation of despressive symptoms 2 weeks after the start of treatment, and then after 1 month, using the following psychodiagnostic instruments: psychiatric interview; short non-standardized sociodemographic questionnaire, CGI, HAMD, HAMA and Beck depression scale.

Results: Patients in the study group, treated with a combined approach of antidepressant therapy and the neurofeedback method, showed a significantly greater reduction in symptoms of depression and anxiety compared to patients in the control group treated with antidepressants as monotherapy. According to the HAMA anxiety scale, the mean score in the study group (SG) decreased by 2.86 points ($p<0.0001$), compared to a decrease of 0.84 points in the control group (CG) ($p=0.0017$). On the Beck Depression Scale, the mean score in the decreased by 2.08 points ($p<0.0001$), compared to a decrease of 0.44 points in the CG ($p=0.022$). On the HAMD depression scale, the average score in the study group (SG) decreased by 2.42 points ($p<0.0001$), while in the control group (CG) the decrease was 0.12 points ($p=0.63$), the CGI scale showed a significant reduction in global symptoms in (SG) ($p=0.0035$), which further confirms the positive effects of the combined treatment.

Conclusions: The research shows that neurofeedback treatment in addition to pharamcological therapy leads to significant improvement in depressive and anxiety symptoms.

Disclosure of Interest: None Declared