# COGNITIVE IMPAIRMENT IN POST-COVID-19 PATIENTS WITH MAJOR DEPRESSIVE EPISODES: A THREE-MONTHS STUDY ON THE EFFECT OF VORTIOXETINE

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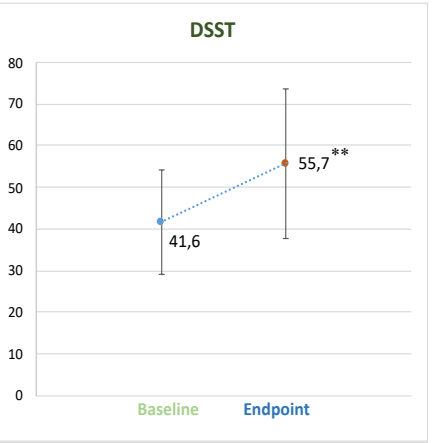
**Background.**
The COVID-19 pandemic has largely affected mental health worldwide. The occurrence of Major Depressive Episodes (MDE) following COVID-19 has been reported during all phases of the disease, including recovery [1]. MDE are generally characterized by low mood/anhedonia and additional physical and cognitive symptoms, such as impaired concentration, difficulty in decision-making, and memory and attention issues. Long-term cognitive dysfunctions have been extensively described in COVID-19 patients, with mild deficits reported even in asymptomatic cases [2]. The severity of cognitive impairment appears to correlate with depressive symptoms in patients recovering from SARS-CoV-2 infection [3], and alterations in the immune-inflammatory systems might underlie both manifestations. Vortioxetine is known to exert beneficial effects on cognitive performance in patients with depression [4], as well as showing anti-inflammatory and anti-oxidative activities [5]. Therefore, this retrospective study aimed to investigate the effect of vortioxetine on cognitive symptoms in post-COVID-19 MDE.

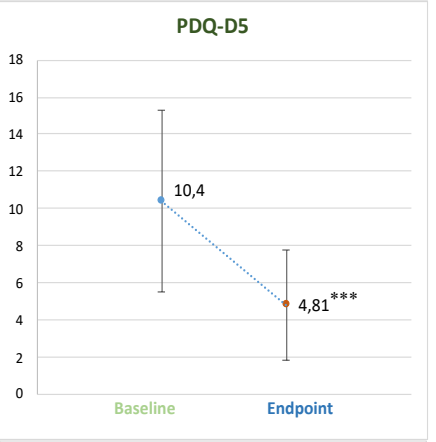
**Methods.**
Fifty patients with post-COVID-19 MDE (DSM-5 criteria), treated with vortioxetine (5-20 mg/d, flexibly dosed), were retrospectively evaluated at baseline and after three-months treatment (endpoint) through the following psychometric assessment: Hamilton Depression Rating Scale (HDRS); Perceived Deficits Questionnaire for Depression (PDQ-D5); Digit Symbol Substitution Test (DSST); Short Form-36 Health Survey Questionnaire (SF-36). SF-36 subdomain scores were aggregated into the summary measure Mental Component Score (MCS). Additionally, C Reactive Protein (CRP) levels and Systemic-Immune-Inflammatory Index (SII) were assessed to evaluate the effect of vortioxetine on inflammatory levels underlying post-COVID-19 MDE. Paired samples t-test was applied to detect pre- and post-treatment changes.

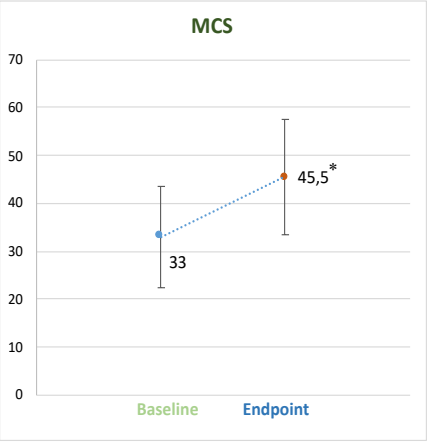
**Results.**
At baseline, all patients displayed moderate depression according to HDRS total score (>14, M±SD: 18.3±4.23) and impaired cognitive functioning, as detected by PDQ-D5 (10.4± 4.91), DSST (41.6±12.6) and MCS (33±10.6). Treatment with vortioxetine (mean dose: 9.54±3.80 mg/d) was safe and well tolerated by all patients. A significant improvement of cognitive symptomatology and functioning was detected according to PDQ-D5 (4.81±2.95, p<0.001), DSST (55.7±17.9, p=0.004), and MCS (45.5±12, p=0.019) scores, alongside with reduction of depressive symptoms, as for HDRS total score (5.92±3.45, p=0.007). CRP levels and SII showed a decreasing trend after treatment, yet not statistically significant.

**Conclusions.**
These preliminary results highlight that vortioxetine has beneficial effects on cognition in MDE in post-COVID-19 patients, who may experience an amplification of cognitive impairment in relation to SARS-CoV-2 infection, with detrimental effects on recovery. This compound, with a good safety/tolerability profile, might be a favorable therapeutic choice for treating this specific population. Consequences of COVID-19 are a public health concern because of high prevalence and clinical and socio-economic implications, and personalized interventions are crucial to allow full functional recovery. Further studies with larger samples are needed to confirm these findings and identify targeted, safe, and effective treatments.

| Characteristics *n, %; M ± SD* | N=50 |
|---|---|
| **Sociodemographic characteristics** | |
| **Age** (years) | 52.1 ± 17.6 |
| **Gender** | |
| Male | 24 (49.4) |
| Female | 26 (50.6) |
| **Educational level** (years) | 14.4 ± 3.44 |
| **Occupation** | |
| Unemployed | 14 (28.4) |
| Employed | 36 (71.6) |
| **Marital status** | |
| Unmarried | 21 (42.5) |
| Married | 29 (57.5) |
| **Clinical features** | |
| **Psychiatric diagnosis** | |
| New-onset depressive episode | 22 (44.3) |
| Recurrent depressive episode | 28 (55.7) |
| **Age at 1st MDE** (years) | 42.2 ± 16.4 |
| **Family history of psychiatric diseases** | 27 (54.7) |
| **Medical comorbidities** | 29 (58.8) |
| **Smoking** | 13 (26.2) |
| **BMI** | 25.5 ± 5.11 |
| **COVID-19 information** | |
| **SARS-CoV-2 vaccine** | |
| No | 15 (30.1) |
| Yes | 35 (69.9) |
| **COVID-19 duration (days)** | 24.7 ± 21.6 |
| **COVID-19 symptoms** | 45 (91.1) |
| Mild | 23 (50.7) |
| Moderate | 10 (22.5) |
| Severe | 12 (26.8) |
| **COVID-19 hospitalization** | 15 (29.5) |
| **Inflammatory levels** | |
| **PCR (mg/L)** | |
| **Baseline** | 14.1 (40.1) |
| **Endpoint** | 3.88 (3.9) |
| **SII** | |
| **Baseline** | 505 (372) |
| **Endpoint** | 372 (185) |




(* p < .05; ** p < .01; *** p < .001)

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