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by ShARS Scale. We found that SSRIs were able to reduce anxiety level only on 25%25 in men or on 35%25 in women with the first MDD case after COVID-19 before treatment (p%26lt;0.05). Interestingly, MADRS Scale showed a similar improvement of the depressive manifestations in both men and women with the first GAD case after COVID-19 treated with SSRIs for 6 months (p%26lt;0.05). Also, women with the first GAD case after COVID-19 treated with SSRIs had the parameters of their affective profile that were similarly to those of control group. The reduction of depressive symptoms in women with the first GAD case after COVID-19 treated with SSRIs was associated with restoration of cortisol concentrations in the serum blood compared to the initial levels.

Conclusion: Thus, our pilot clinical study clearly demonstrated that SSRIs treatment have a beneficial effect on the depressive symptoms in patients of both gender with the first MDD or GAD cases after COVID-19. However, SSRIs therapy alone failed to produce the decrease of anxiety in the patients of both gender with the first MDD or GAD cases after COVID-19. In light of the demonstrated data, the importance of truly adequate treatment to the long-term neuropsychiatric outcomes of COVID-19 in patients of both gender, further randomized clinical trials involving new pharmacological therapies are needed in the future.

No conflict of interest

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P.0404
Rapid antidepressant response to first-line selective serotonin reuptake inhibitors in post-COVID-19 depression

M.G. Mazza1,2, M. Palladini1,2, R. Zanardi1, F. Benedetti1,2

1University Vita-Salute San Raffaele- Milan- Italy, Neuroscience, Milan, Italy; 1Psychiatry %26 Clinical Psychobiology Unit, Division of Neuroscience- IRCCS Scientific Institute Ospedale San Raffaele, Milano, Italy

Introduction: Depression was reported in 30-40% of patients at one, three, and six months following COVID-19 [1]. The host immune response to SARS-CoV-2 infection and related severe systemic inflammation seems to be the main mechanism contributing to the development of post-COVID depression. Emerging literature suggests anti-inflammatory and antiviral properties of antidepressants in the treatment of SARS-CoV-2 infection [2].

We hypothesized that post-COVID depression, triggered by infection and sustained by systemic inflammation, could particularly benefit from antidepressants. Thus, the present study aims to investigate the efficacy of SSRI in treating post-COVID depression.

Methods: We included 58 adults patients who showed depressive episodes in the six months following COVID-19. We excluded patients if they showed: other psychiatric comorbidities, ongoing treatment with antidepressants or neuroleptics, somatic disease and medications known to affect mood. The severity of depression was rated at baseline and after for four weeks from the start of the treatment on the Hamilton Depression Rating Scale (HDRS) and response was considered when the patients achieved a 50% HDRS reduction after treatment.

Statistical analyses to compare group means and frequencies (Student’s t-test, Pearson χ² test) were performed. To investigate changes in HDRS scores over time, repeated measures ANOVAs (according to sex, mood disorder history, and antidepressant molecule) were performed.

Results: We found that 53 (91%) patients showed a clinical response to antidepressant treatment. Age, sex, mood disorder history, and hospitalization for COVID did not affect the response rate.

Patients were treated with sertraline (n=26), citalopram (n=18), paroxetine (n=8), fluvoxamine (n=4), and fluoxetine (n=2). From baseline to follow-up, patients showed a significant decrease over time of HDRS score (F=618.90, p<0.001), irrespectively of sex (0.28, p=0.599), mood disorder history (F=0.04, p=0.834), and drug used (F=1.47, p=0.239).

Discussion: Common knowledge highlights that among antidepressant-treated patients, response rates are moderate (40-60%). On the contrary, we observed a rapid response to the first-line antidepressants in more than 90% of patients irrespectively of clinical variables, thus suggesting a higher antidepressant response rate in post-COVID depression.

The pathophysiology of post-COVID neuropsychiatric sequelae mainly entails severe systemic inflammation and subsequent neuroinflammation. In this context, we have previously found that one and three months after COVID-19, the severity of depression was predicted by the baseline systemic immune-inflammation index (SII) [3, 4]. Furthermore, we found a protective effect of the IL-1β and IL-6 receptor antagonist against post-COVID depression possibly associated with their effect in dampening SII [5].

Mounting evidence suggests that antidepressants may a) decrease markers of inflammation; b) may inhibit acid sphingomyelinase preventing the infection of epithelial cells with SARS-CoV-2; c) may prevent the COVID-19 related cytokine storm by stimulating the a-1 receptor; d) may exert antiviral effects via lysosomalotropic properties; e) may inhibit platelets activation [2].

In conclusion, we hypothesized that post-COVID depression could particularly benefit from antidepressants since this molecules have anti-inflammatory and antiviral properties, pass the BBB and accumulate in the CNS, thus preventing the neuro-inflammation triggered by SARS-CoV-2 and associated with post-COVID depression.
No conflict of interest

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P.0405 Enhanced inflammatory response in the brain of suicide victims is associated with a weakening of the AMPK/CREB signaling pathway

M. Sowa-Kućma 1, P. Pańczyszyn-Trzewik 1, G. Nowak 2

1 Institute of Medical Sciences- Medical College of Rzeszow University, Department of Human Physiolog, Rzeszow, Poland; 2 Maj Institute of Pharmacology- Polish Academy of Sciences, Department of Neurobiology, Krakow, Poland

Background: Suicide is a global phenomenon that particularly affects the young adult population [1]. Increasing number of studies points to the significant role of oxidative stress and neuroinflammation in the development of depressive and/or suicidal behavior [1,2,3]. It’s suggested that the 5’AMP-activated protein kinase (AMPK; an intracellular energy sensor) may be important in the regulation of oxidative stress and inflammatory processes in the brain, especially via cAMP-response element-binding (CREB) protein [1]. To verify this hypothesis, the levels of proinflammatory cytokines - interleukin-1α/β (IL-1α/β) were examined. On the other hand, AMPK and CREB activity (evaluated by its phosphorylation at threonine residue 172; p-T172-AMPK or serine residue 133; p-S133-CREB, respectively) was studied.

Methods: Post mortem brain tissues [Hippocampus (Hp) and Frontal Cortex (FCx) - Brodmann area 10] were collected from two groups: non-diagnosed psychiatrically suicide victims (n=14) and unexpected sudden death controls (n=8) at the time of autopsy in the Department of Forensic Medicine, Jagiellonian University Medical College [approved by Ethics Committee (2001-2004)] and stored at −80°C until the start of biochemical analysis. Among the 22 study subjects were 8 females and 14 males. The mean age (± SEM) in the suicides (29.21 ± 3.594) had no significant differences from the control group (31.0 ± 4.89). According to available medical history, both suicides and controls included in the study were not treated for any chronic central nervous system disorders. They do not take any medication permanently (including psychotropic) as well. The levels of inflammatory parameters were assayed by commercially available ELISA kits (RayBiotech). The levels of AMPK (AMPK, p-T172-AMPK) and CREB (CREB, p-S133-CREB) proteins were investigated using Western blotting (all the proteins were normalized to the density of the β-actin). Group differences were assessed using unpaired Student’s t-test. p<0.05 was considered as statistically significant.

Results: There was a statistically significant increase in IL-1α level both in FCx (by 89 %) and Hp (by 70%) of the suicide victims relative to the control group (t(17)=2.879, p=0.0104 and t(19)=2.143, p=0.0478, respectively). Moreover, in Hp (but not in FCx) an increase (by 82%) in the IL-1β level was observed (t(20)= 2.811, p=0.0108). These alterations were associated with statistically decrease in the p-T172-AMPKα1 in the both studied brain structures [FCx: ↓21%, t(20)=2.400, p=0.0262; Hp: ↓35%, t(20)=2.911, p=0.0084] of suicides. Interestingly, a statistically significant reduction in the p-S133-CREB protein level was also revealed [FCx: ↓34%, t(20)=3.530, p=0.0021; Hp: ↓28%, t(20)=2.767, p=0.0119] in the suicide group with regard to controls. On the other hand, the total AMPKα1/2 and CREB protein levels were not statistically different from the control group, both in FCx and Hp.

Conclusions: The obtained results strongly confirm the importance of neuroinflammation in the development of suicidal behavior. Furthermore, our findings, provide evidence, for the first time, that an increased inflammatory response as well as oxidative stress (revealed in our previous study) in the brains of suicides may be a consequence of decreased activity of the AMPK/CREB signaling pathway.

Conflict of interest

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