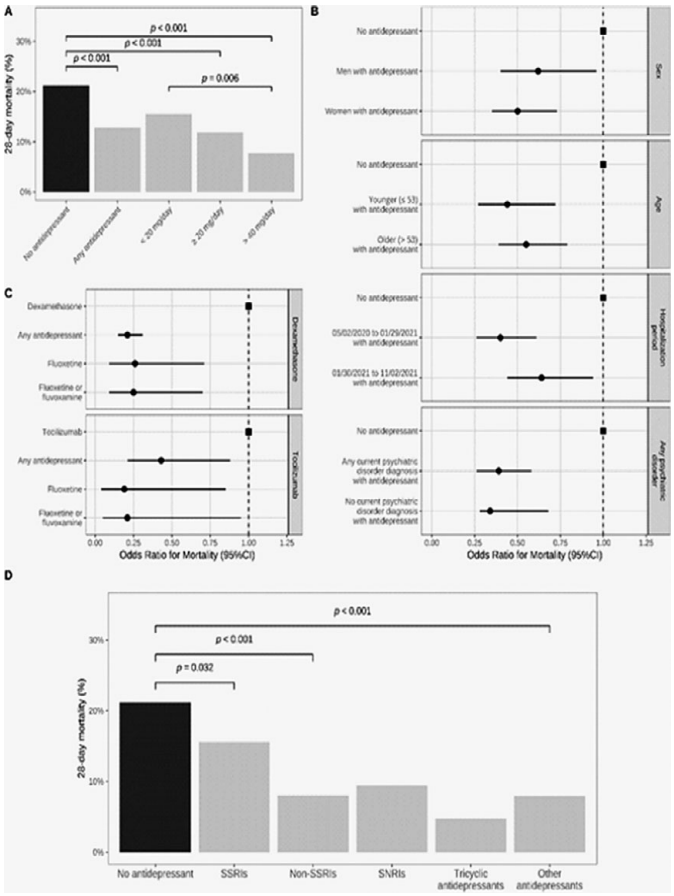
Image 3:



Conclusions: Antidepressant use is associated with a reduced likelihood of hospitalization in patients infected with SARS-CoV-2 and with a reduced risk of death in patients hospitalized with COVID-19. These associations were stronger for molecules with high FIASMA activity. These findings posit that prospective interventional studies of antidepressants with the highest FIASMA activity may be appropriate to help identify variant-agnostic, affordable, and scalable interventions for outpatient and inpatient therapy of COVID-19.

Disclosure of Interest: None Declared

O0115

Antiviral and Anti-Inflammatory Activities of Fluoxetine in a SARS-CoV-2 Infection Mouse Model

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Introduction: The coronavirus disease 2019 (COVID-19) pandemic continues to cause significant morbidity and mortality worldwide. Since a large portion of the world's population is currently unvaccinated or incompletely vaccinated and has limited access to approved treatments against COVID-19, there is an urgent need to continue research on treatment options, especially those at low cost and which are immediately available to patients, particularly in low- and middle-income countries. Prior in vitro and observational studies have shown that fluoxetine, possibly through its inhibitory effect on the acid sphingomyelinase/ceramide system, could be a promising antiviral and anti-inflammatory treatment against COVID-19.
Objectives: The aim of this sudy was to test the potential antiviral and anti-inflammatory activities of fluoxetine against SARS-CoV-2 in a K18-hACE2 mouse model of infection, and against several variants of concern in vitro, and test the hypothesis of the implication of ceramides and/or their derivatives hexosylceramides.
Methods: We evaluated the potential antiviral and anti-inflammatory activities of fluoxetine in a K18-hACE2 mouse model of SARS-CoV-2 infection, and against variants of concern in vitro, i.e., SARS-CoV-2 ancestral strain, Alpha B.1.1.7, Gamma P1, Delta B1.617 and Omicron BA.5.
Results: Fluoxetine, administrated after SARS-CoV-2 infection, significantly reduced lung tissue viral titres (Figure 1) and expression of several inflammatory markers (i.e., IL-6, TNFα, CCL2 and CXCL10) (Figure 2). It also inhibited the replication of all variants of concern *in* vitro. A modulation of the ceramide system in the lung tissues, as reflected by the increase in the ratio HexCer 16:0/Cer 16:0 in fluoxetine-treated mice, may contribute to explain these effects (Figure 3).
Image:

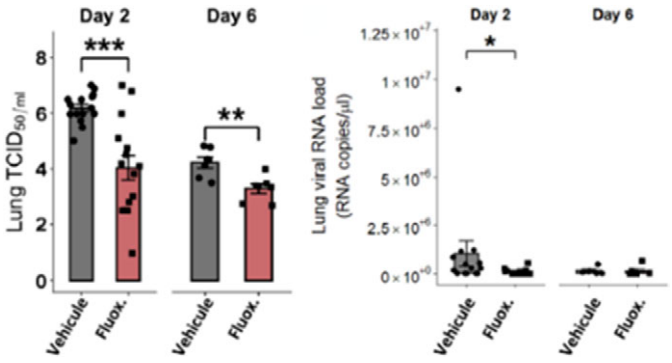


Image 2:

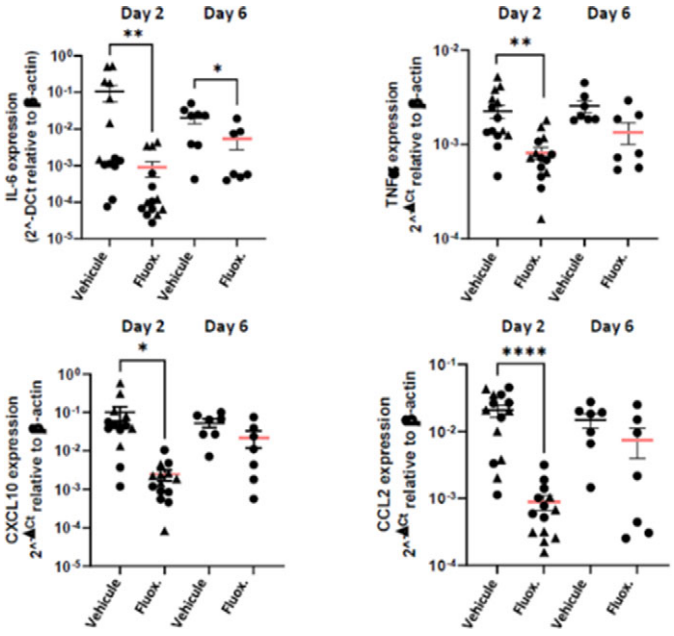
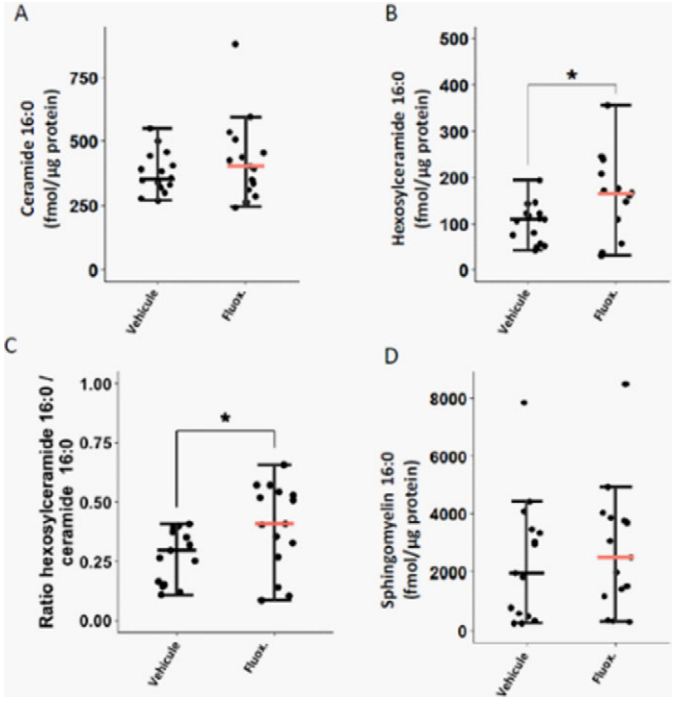


Image 3:



Conclusions: Our findings demonstrate the antiviral and anti-inflammatory properties of fluoxetine in a K18-hACE2 mouse model of SARS-CoV-2 infection, and its in vitro antiviral activity against variants of concern, establishing fluoxetine as a very promising candidate for the prevention and treatment of SARS-CoV-2 infection and disease pathogenesis.

Disclosure of Interest: None Declared

O0116

Brain correlates of perceived cognitive impairment after covid-19 infection: a multimodal MRI study.

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Introduction: Many different long-term neuropsychiatric sequelae of the novel Coronavirus have been described after the pandemic outbreak. One of the most common symptoms in the months following infection is related to "brain fog". This condition includes several signs of cognitive impairment like mental slowness, deficits in attention, executive functions, processing, memory, learning, and/or psychomotor coordination, which can be perceived on a subjective level and further confirmed by objective data. Since this kind of mental status has been documented in previous viral infections, and the SARS-COV-2 has been characterized by a worldwide diffusion, investigation into this condition in post-covid individuals is warranted. Currently, several hypotheses on its pathophysiology have been put forward, mostly hypothesizing a direct effect of the virus on the central nervous system or indirect consequences of the inflammatory response.
Objectives: The aim of our research is to analyze brain correlates of subjective cognitive complaints in Covid-19 survivors using multimodal brain imaging.
Methods: We performed a voxel-based morphometry (VBM) and a resting state functional connectivity analysis on 60 post-COVID-19 individuals recruited from the San Raffaele Hospital in Milan, that underwent a 3 tesla MRI scan. We assessed the perceived cognitive impairment both after the infection and at the time of the MRI scan through the PROMIS Cognitive Abilities scale. The difference of the two scores (delta PROMIS) was calculated as a measure of cognitive improvement over time.
Results: We found the perceived amelioration of cognitive abilities (delta PROMIS) to be positively associated to grey matter volumes in the bilateral caudate, putamen and pallidum (pFWE: <0.001). Moreover, in the resting state fMRI analysis, subjective cognitive status at MRI was found to be associated with functional connectivity between the right putamen and pallidum, and two clusters belonging to the attentional (pFWE: <0.001) and salience (pFWE: 0.02) networks.
Conclusions: This is one of the first studies investigating brain correlates of subjective cognitive impairment after COVID-19 infection; our main finding is the convergence of structural and functional results on brain areas located within the basal ganglia, implying their possible role in the pathophysiology of the condition. Moreover, this research could be interpreted as the first step toward understanding a very complex condition, with potential implications for the development of treatment and neurorehabilitative strategies.

Disclosure of Interest: None Declared