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Higher ACE2 expression in the brains of individuals with Alzheimer's disease

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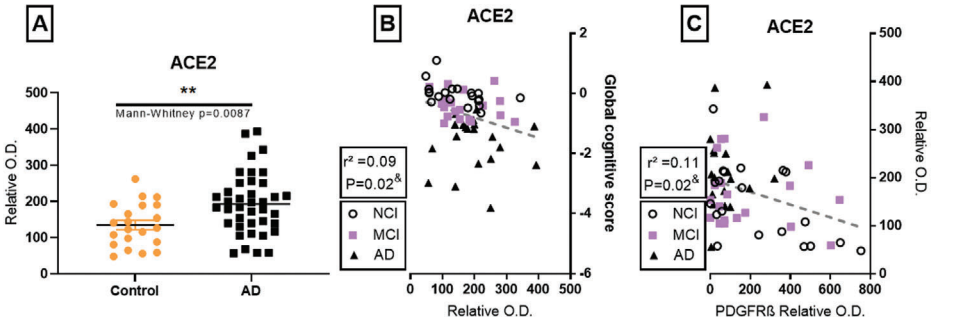
Abstract

Background: The emergence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a major cause of death, particularly in the elderly. The geriatric population in which cognitive decline due to Alzheimer's disease (AD) is frequent is disproportionately affected by the pandemic. In addition, central nervous system (CNS) manifestations have been reported in a significant subset of SARS-CoV-2 infected patients.

Method: Since the principal entry receptor utilized by SARS-COV-2 is Angiotensin-Converting Enzyme 2 (ACE2), we examined whether ACE2 protein and mRNA levels were altered *postmortem* in parietal cortex samples from two different AD cohorts, totalling 142 cases.

Results: Both immunoblot and RT-qPCR analysis revealed higher concentrations of ACE2 protein and mRNA in persons with a neuropathological diagnosis of AD, compared to age-matched controls. Brain levels of ACE2 were inversely correlated with *antemortem* cognitive scores. We found that ACE2 protein was highly enriched in microvessels of mice compared to brain parenchyma, but not in humans. Detachment of ACE2 from brain cell membranes was strongly associated with pericytes loss. No significant change of ACE2 protein was detected in the parietal cortex from the 3xTg-AD mouse model of AD neuropathology.

Conclusion: Our data suggest that cognitive impairment is associated with higher levels of ACE2 in the brain, which might contribute the higher risk of CNS SARS-CoV-2 infection in cognitively impaired individuals and AD patients.



A) Higher levels of ACE2 are associated with AD neuropathological diagnosis (ABC scoring), B) cognitive symptoms and C) lower PDGFRß in brain microvessels. Statistical analysis: Pearson correlation coefficient & $p<0.05$ Abbreviations: AD, Alzheimer, MCI, Mild cognitive impairment, NCI, No cognitive impairment, O.D., optical density.

FIGURE 1