

## 75<sup>th</sup> AAN ANNUAL MEETING ABSTRACT

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**Abstract Title:** Anxiety and Depression Are Associated with Limbic Atrophy and Severe Disruption Of Brain Functional Connectivity After Mild COVID-19 Infection

**Press Release Title:** Can the Lingering Effects of a Mild Case of COVID-19 Change Your Brain?

*Study Finds Brain Changes in People with Anxiety, Depression Symptoms*

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**Objective:** To investigate gray matter atrophy (GMA) and alterations of functional connectivity (FC) associated with anxiety and depression after mild COVID-19 infection.

**Background:** Although anxiety and depression are frequently observed in long-COVID syndrome, little is known about correlated structural and functional brain changes.

**Design/Methods:** We evaluated 254 individuals after mild COVID-19 (177 women, median age of 41 years, median interval of 82 days from RT-PCR test) with 3T-MRI, BDI (Beck Depression Inventory), and BAI (Beck anxiety inventory). Patients were separated into asymptomatic (152, ASYMPT-group) and simultaneous groups (if presented with anxiety and depression symptoms simultaneously) (102 subjects, SIMULT-group, BAI>10 and BDI>13).

GMA was assessed with voxel-based morphometry (VBM, CAT12-TOOLBOX/MATLAB2019/SPM12), comparing the two groups of patients with 148 healthy controls. We reported results with  $p<0.05$  after Bonferroni adjustments.

The FC analysis included the ASYMPT-group (84 subjects), SIMULT-group (70 subjects), and 90 controls. We used UF2C/SPM12/MATLAB2019b to analyze 12 large-scale brain networks (NW; with 70 ROIs, regions-of-interest) with resting-state fMRI. We reported results with  $p<0.05$  after FDR adjustments.

**Results:** SIMULT groups exhibited functional and structural abnormalities, but the ASYMPT-group showed fewer functional alterations and no GMA. SIMULT-group presented a widespread, bilateral pattern of hyperconnectivity involving the 12 networks and GMA in the left cingulum (86 voxels) and the inferior frontal lobe (91 voxels). The ASYMPT-group showed hyperconnectivity involving only five networks (posterior salience, ventral and dorsal Default Mode Networks, and right and left executive control) and nine ROIs.

**Conclusions:** These findings indicate structural and functional alterations may occur even after mild infection. The combination of anxiety and depression is associated with atrophy of the limbic system and a severe pattern of abnormal cerebral functional connectivity. The magnitude of these changes suggests an association with cognitive dysfunction. Further analyses are necessary to yield specific treatment targets to prevent persistent deficits and improve quality of life.

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