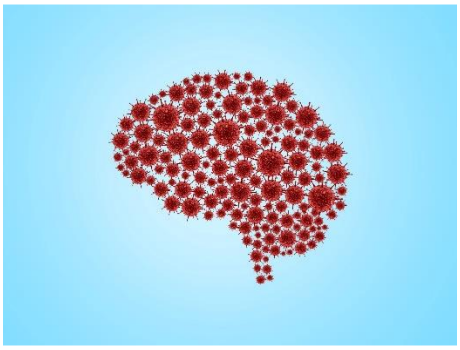
In Adolescents and Young Adults Mild COVID-19 Disrupts Brain Connectivity and Reduces Memory Function

Researchers used magnetic resonance imaging (MRI) and cognitive tests to examine brain structure, function, and cognition in adolescents and young adults with mild coronavirus disease 2019 (COVID-19) compared to healthy controls in a pandemic hotspot in Italy. They identified significant changes in brain regions related to olfaction and cognition, with decreased brain volume and reduced functional connectivity in areas like the left hippocampus and amygdala, which were linked to impaired spatial working memory. Notably, no significant differences were observed in whole-brain connectivity, suggesting that these changes were localized rather than widespread.



Study

The present study involved participants from the Public Health Impact of Metal Exposure (PHIME) cohort, a longitudinal investigation of adolescents and young adults in northern Italy. Between 2016 and 2021, 207 participants, aged 13 to 25 years, were included in a sub-study with MRI scans and cognitive tests. After COVID-19 restrictions were lifted, 40 participants (13 COVID+ and 27 COVID−) participated in a follow-up study, which replicated the MRI and cognitive assessments.

The mean age of participants was 20.44 years and 65% were female. COVID+ status was confirmed through positive reverse transcription polymerase chain reaction (RT-PCR) tests within 12 months of follow-up. Neuropsychological assessments used the Cambridge Neuropsychological Test Automated Battery (CANTAB) to evaluate spatial working memory.

MRI and functional MRI data were acquired using a 3-Tesla scanner, processed, and analyzed for structural and local functional connectivity using eigenvector centrality mapping (ECM) and functional connectivity (FC) metrics. Whole-brain functional connectivity metrics showed no significant differences between COVID+ and control groups, indicating that the observed changes were specific to key brain regions rather than generalized across the entire brain.

Statistical analysis involved the use of pairwise Student's t-tests, Kolmogorov–Smirnov test, linear regression, two-waves mediation analysis, negative binomial regression, and linear regression, all adjusted for covariates.

Findings and Discussion

Significant differences were observed in the two groups regarding the time between assessments, COVID-19 symptoms, and vaccine status. The research identified five localized functional connectivity hubs with significant differences between the two groups, including the right intracalcarine cortex, right lingual gyrus, left frontal orbital cortex, left hippocampus and left amygdala, which is vital for cognitive functions. Only the left hippocampal volume showed a significant reduction in COVID+ participants ($p = 0.034$), while whole-brain connectivity remained unchanged, reinforcing the localized nature of the brain changes.

The left amygdala mediated the relationship between COVID-19 and spatial working memory "between errors" ($p = 0.028$), a critical finding that highlights the indirect effect of amygdala connectivity on cognitive function in COVID+ individuals. This mediation analysis underscores the role of specific brain regions in influencing cognitive deficits, as only the indirect effect was statistically significant for spatial working memory errors. The orbitofrontal cortex, involved in sensory integration and cognitive functions, also showed decreased connectivity in COVID+ individuals, supporting previous findings of structural and functional changes in this region during COVID-19.

The study is limited by small sample size, lack of diversity, potential confounding factors due to the long interval between MRI scans, treatment of certain subjects as COVID-negative based on antibody testing beyond the 12-month threshold, and the possibility of non-significant findings in mediation analysis due to these factors.

Conclusion

In conclusion, the findings indicate persistent structural and functional alterations in specific brain regions of COVID-19-positive adolescents and young adults, including changes in gray matter volume and localized functional connectivity, which correlate with diminished cognitive function, particularly in working memory.

Further research is necessary to evaluate the longevity and potential reversibility of these brain and cognitive changes post-infection, enhancing our understanding of post-COVID outcomes and informing future interventions and treatments. The longitudinal design of this study, with pre- and post-COVID data, strengthens these findings by allowing direct comparisons over time, offering robust insights into the impact of COVID-19 on adolescent brain development.

Source:

https://www.news-medical.net/news/20241003/Mild-COVID-19-disrupts-brain-connectivity-and-reduces-memory-function-in-adolescents-and-young-adults.aspx