Are pandemic-related stressors impacting the brain health of uninfected people?

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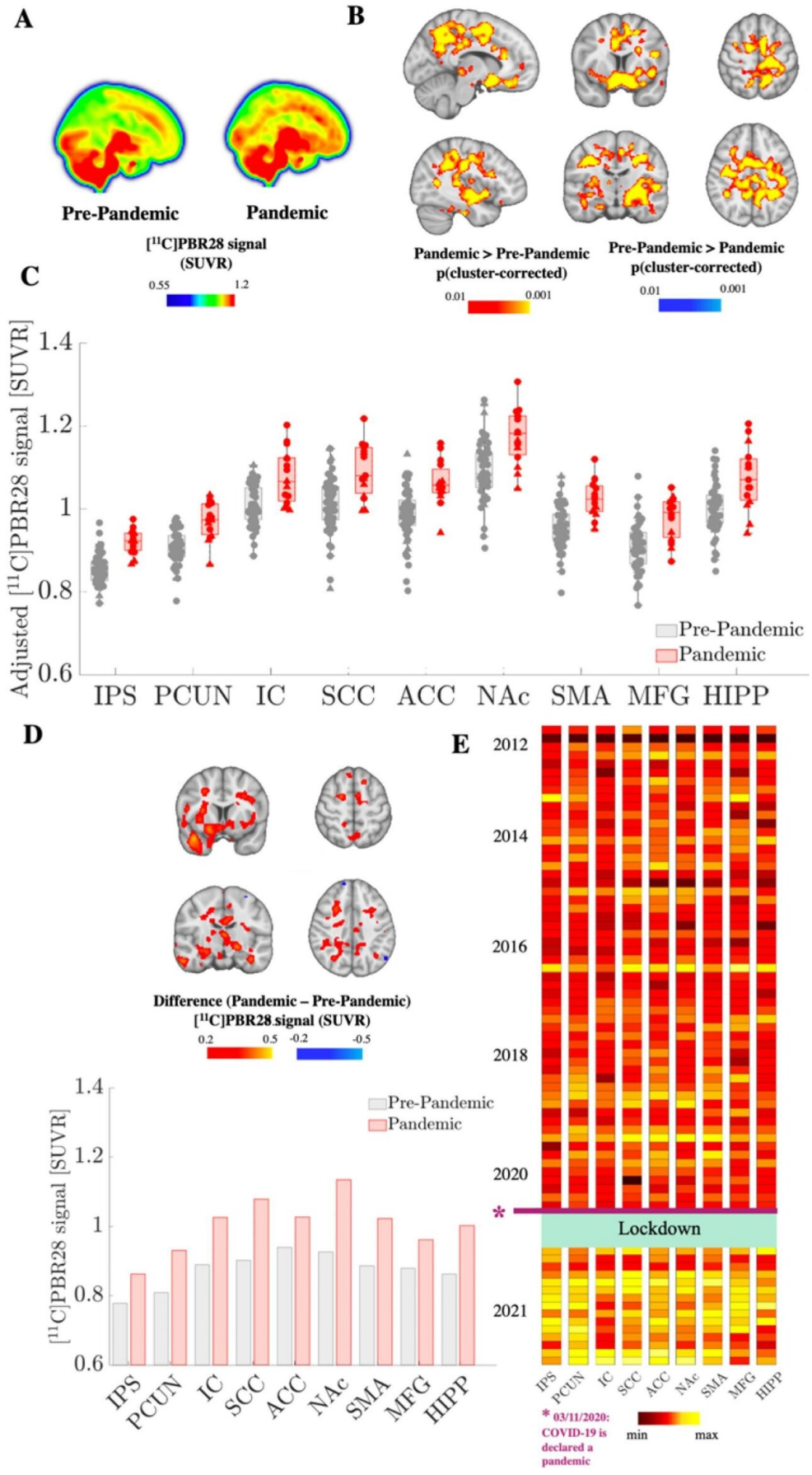
A
Pre-Pandemic
Pandemic
[11C]PBR28 signal (SUVR)
0.55
1.2
B
Pandemic > Pre-Pandemic p(cluster-corrected)
0.01
0.001
Pre-Pandemic > Pandemic p(cluster-corrected)
0.01
0.001
C
Adjusted [11C]PBR28 signal [SUVR]
1.4
1.2
1
0.8
0.6
IPS
PCUN
IC
SCC
ACC
NAc
SMA
MFG
HIPP
Pre-Pandemic
Pandemic
D
Difference (Pandemic – Pre-Pandemic) [11C]PBR28 signal (SUVR)
0.2
0.5
-0.2
-0.5
Pre-Pandemic
Pandemic
[11C]PBR28 signal [SUVR]
1.4
1.2
1
0.8
0.6
IPS
PCUN
IC
SCC
ACC
NAc
SMA
MFG
HIPP
E
2012
2014
2016
2018
2020
2021
*
Lockdown
IPS
PCUN
IC
SCC
ACC
NAc
SMA
MFG
HIPP
* 03/11/2020: COVID-19 is declared a pandemic
min
max

Fig. 1. [^{11}C]PBR28 PET signal elevations in the Pandemic group. (A) Mean images computed from 57 Pre-pandemic and 15 Pandemic subjects are displayed as maximum intensity projections. (B) Significant cluster from the Pandemic > Pre-Pandemic voxel-wise contrast is shown in a red–yellow color scale. There were no significant regions for the Pre-Pandemic > Pandemic contrast. (C) Visualization of mean [^{11}C]PBR28 SUVR extracted from sub-portions of the cluster statistically significant in A. IPS = Intraparietal Sulcus, PCUN = Precuneus, IC = Insular Cortex, SCC = Subcallosal Cortex, ACC = Anterior Cingulate Cortex, NAc = Nucleus Accumbens, SMA = Supplementary Motor Area, MFG = Middle Frontal Gyrus, HIPP = Hippocampus. Error bars denote 25th to 75th inter-quartile range. Triangles denote data from Scanner 1 and circles denote data from Scanner 2. (D) Case study of one subject scanned before- (September 2016) and during the pandemic (October 2020) in Scanner 1. Bar graph of mean [^{11}C]PBR28 SUVR are extracted from the cluster sub-portions in (C) and difference image (post-pre) are reported in red-yellow and cyan-blue color bars. E) Mean [^{11}C]PBR28 SUVR extracted from sub-clusters in (C) and sorted by scan date. The range of the color scale was set for each region independently to best illustrate the pandemic PET signal increase, for visualization purposes. Credit: DOI: 10.1016/j.bbi.2022.02.018

New research indicates that for some individuals—even those who have steered clear of becoming infected with SARS-CoV-2—societal and lifestyle disruptions during the COVID-19 pandemic may have triggered inflammation in the brain that can affect mental health. The study, which was conducted by a team led by investigators at Massachusetts General Hospital (MGH), is published in *Brain, Behavior, and Immunity*.

Beyond causing a staggering number of infections and deaths, the COVID-19 pandemic has led to significant social and economic disruptions that have impacted the lives of a large swath of the world's

population in multiple ways. Also, since the start of the pandemic, the severity and prevalence of symptoms of psychological distress, fatigue, brain fog, and other conditions have increased considerably in the United States, including among people not infected with SARS-CoV-2.

To obtain a better understanding of the effects of the pandemic on brain and mental health, researchers analyzed brain imaging data, conducted behavioral tests, and collected blood samples from multiple uninfected volunteers—57 before and 15 after lockdown/stay-at-home measures were implemented to limit the pandemic's spread.

After lockdowns, the study participants demonstrated elevated brain levels of two markers of neuroinflammation—translocator protein (measured using positron emission tomography) and myoinositol (measured using magnetic resonance spectroscopy)—compared with pre-lockdown participants. Blood levels of two inflammatory markers—interleukin-16 and monocyte chemoattractant protein-1—were also elevated in post-lockdown participants, although to a lesser extent.

Participants who reported a higher burden of symptoms related to mood and mental and physical fatigue showed higher levels of translocator protein in certain brain regions, compared with those reporting little or no symptoms. Also, higher post-lockdown translocator protein levels correlated with the expression of several genes involved in immune functions.

"While COVID-19 research has seen an explosion in the literature, the impact of pandemic-related societal and lifestyle disruptions on brain health among the uninfected has remained under-explored," says lead author Ludovica Brusaferri, Ph.D., a postdoctoral research fellow at MGH and Harvard Medical School. "Our study demonstrates an example of how the pandemic has impacted human health beyond the effects

directly caused by the virus itself."

Senior author Marco L. Loggia, Ph.D., co-director of the Center for Integrative Pain NeuroImaging at MGH and Harvard Medical School notes that acknowledging a role of neuroinflammation in the symptoms experienced by many during the pandemic might point to possible strategies to reduce them. "For instance, behavioral or pharmacological interventions that are thought to reduce inflammation—such as exercise and certain medications—might turn out to be helpful as a means of reducing these vexing symptoms."

Loggia adds that the findings also provide further support to the notion that stressful events might be accompanied by brain inflammation. "This could have important implication for developing interventions for a broad number of stress-related disorders," he says.

More information: Ludovica Brusaferri et al, The pandemic brain: Neuroinflammation in non-infected individuals during the COVID-19 pandemic, *Brain, Behavior, and Immunity* (2022). DOI: 10.1016/j.bbi.2022.02.018

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