# Research highlights

### Three-photon microscopy

## Imaging in freely moving mice

Three-photon head-mounted microscopes are used to record neuronal activity. Their technical limitations include imaging depth, interference with animal behavior when changing focal plane, and the inability to image in a lit environment. Klioutchnikov, Kerr, and colleagues developed a head-mounted three-photon excitation microscope that can image activity at single-neuron resolution from all cortical layers in freely moving mice in a lit environment. The authors designed a lightweight microscope with remote focusing, extended *z*-range, and high resolution. The setup allowed proper animal mobility and head orientation. The authors imaged neurons expressing a calcium indicator, and they imaged vascular structures with a label-free approach. They performed repeated measurements of neuronal activity in layers 4 and 6 over several days with minimal or no photobleaching or photodamage. A two-channel detector system allowed the authors to increase the light collection efficiency, which enabled imaging in both dark and lit environments without significant changes in signal detection and with no artifacts in the transition between the two conditions. Layer 4 and layer 6 neurons were active in lit and dark environments, respectively, with sparse neuronal activity when the light conditions were switched. The developed imaging setup enables recording under natural conditions.

**Elisa Floriddia**

*Nature Neuroscience*

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### Neuroimaging biomarkers

## fMRI signatures of social perception

Functional MRI (fMRI) studies that have outlined specific brain regions involved in processing social information have often relied on study-specific stimulus designs and experimenter-labeled conditions that could influence the results. As social perception is known to be subjective, Varrier and Finn examined the contributions of experimenter labels and participants' self-reports of social versus non-social conditions using data from the Human Connectome Project's social cognition task to find a potentially more reliable signature of social perception. Participants were biased towards reporting animations as social regardless of an animation's social or non-social experimental design. fMRI analyses revealed 70 social perceptual regions throughout the brain, with a subset of temporal, occipital, and subcortical areas showing a graded response to the amount of perceived social information. Among these brain regions, the authors could discern when and where social versus non-social percepts emerged. Individuals with higher internalizing scores had a stronger bias towards perceiving social interactions and a lower neural response to social animations.

**Jean Mary Zarate**

*Nature Neuroscience*

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### Neuroinflammation

## COVID-19 and brain aging

Severe COVID-19 has been associated with cognitive impairment and changes in the frontal cortex. In a study published in *Nature Aging*, Mavrikaki, Lee et al. performed RNA sequencing on frontal cortex samples from 21 individuals with severe COVID-19, 22 age- and sex-matched uninfected controls, and 9 uninfected people who had received intensive care or ventilator treatment. The authors found almost 7,000 differentially expressed genes (DEGs) in the patient samples compared to controls. Upregulated DEGs were enriched for genes involved in immune-related pathways, and downregulated DEGs were enriched for genes involved in synaptic activity, cognition and memory — a profile of transcriptional changes that resembles those previously observed in aging brains. Direct comparisons between frontal cortex samples from young and old individuals confirmed this overlap. Application of tumor necrosis factor, interferon-β or interferon-γ to cultured human primary neurons induced transcriptional changes similar to those seen in patients with severe COVID-19. As no SARS-CoV-2 RNA was detected in the patient samples, these data suggest that the transcriptomic changes in frontal cortex of patients with severe COVID-19 were due to neuroinflammatory processes rather than a direct effect of the virus.

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*Nature Neuroscience*

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