# Carphology by A Fo Ben

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## PET THERE BE LIGHT

Figure 1 shows typical examples, from three French centres, of 18F-FDG PET images of patients with suspected long COVID-19. The left column shows patients with normal nuclear imaging. The middle column shows patients with mild-to-moderate long-COVID hypometabolic pattern and the right column shows patients with a severe long-COVID hypometabolic pattern. The white arrows are for the fronto-orbital olfactory regions, red arrows for the other limbic/paralimbic regions, grey arrows for the pons and yellow arrows for the cerebellum.
Eur J Nucl Med Mol Imaging. 2022;49(9):3197-3202.

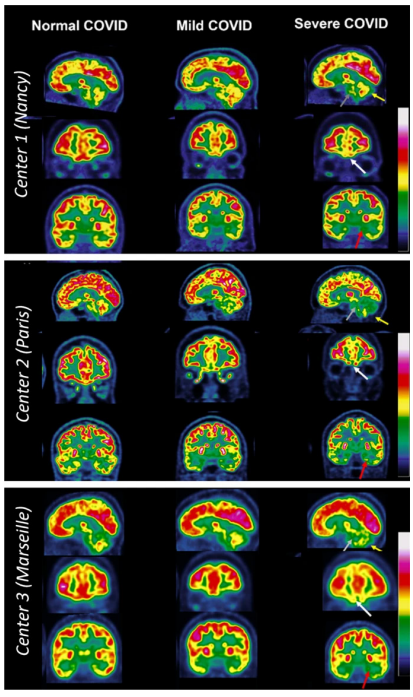


**Figure 1** 18F-FDG PET images of nine patients with long COVID. Republished with permission from Antoine Verger *et al*.

## FROM FLAT GUY TO FUN GUY WITH FUNGI

If your misspent youth included time playing Super Mario you will remember that a single encounter with the Mushroom would normally cause small Mario to transmogrify into his super form. A Fo Ben speculates that this is the subconscious rationale behind the randomised phase 2 double-blind trial of single dose psilocybin for people with treatment resistant depression. Change from baseline was measured at week 3 across three dosing groups, and the response was biologically plausible. Time will tell whether the responses can be sustained, as the 12-week remission data were not as promising as 3-week response. It also asks a philosophical question—what is an adverse event when you are dosing with magic mushrooms?
N Engl J Med. 2022;387(18):1637-1648.

## GENE GENIE

Some studies are too smart and sophisticated to be glibly summarised in Carphology, but that has never held me back. Precision medicine in genetic epilepsies relies on finding a specific cause and then developing a magic bullet—this is very clever, but time hungry and hard to scale up. Instead, could a modifying gene be provided to people—no matter the cause of their epilepsy—that changes brain characteristics? And could this be delivered on demand—meaning that the gene activity is focused mostly where neurones fire in an epileptic way? The *Fos* gene is upregulated when there are seizures, and this was used to drive the expression of a gene encoding an inhibitory protein, *Kcna1*. An adeno-associated virus vector encoding the *Fos* promoter and *Kcna1* was used to transfect neurones, which in turn leads to inhibition of neurones that participate in seizure activity. Seizures were not completely suppressed but as it is a closed loop system the treatment switches itself off once brain circuit activity has returned to baseline. Human studies next please!
Science 2022;3786619,:523-532.

## ORGAN(OID) DONOR

'Everything should be made as simple as possible, but no simpler' is attributed to Einstein, but like many bon mots this aphorism cannot be directly linked to the genius. So the benefits of self-organising neural organoids for researching human development and disease are many, but there are key limitations—particularly for advocates of xenotransplantation, as organoids lack the connectivity that exists in vivo, which limits maturation and makes integration with other circuits that control behaviour impossible. In Nature, a group from Stanford show that human stem cell-derived cortical organoids can be transplanted into the cortex of newborn rats and develop mature cell types that integrate into key circuits. Anatomical and functional tracings show that the transplanted organoids receive thalamocortical and cortico-cortical inputs, and in vivo recordings of neural activity show that these inputs produce sensory responses in human cells. This feels like a major step forward for the study of circuits in development and disease.
Nature. 2022;610 (7931):319–326.

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