CAPSI: Multimodal imaging in depression patients treated with psilocybin – exploring OPMs and conventional MEG

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Aims

1. Assess antidepressant effect of psilocybin 42 days after treatment.

2. Investigate P300 amplitude during auditory oddball paradigm after treatment.

3. Compare OPMs and conventional MEG during auditory oddballs and resting state recordings.

Background

Approximately one third of cancer patients develop depression, which adds to the burden of disease and medical costs. Recently, it has been found that in these patients, a single dose of psilocybin causes a rapid and prolonged antidepressant effect [1]. Psilocybin has been shown to induce synaptogenesis and neuroplasticity in preclinical models [2]. Depression is associated with lowered synaptic density [3]. To measure synaptic density changes after treatment, the patients in this study will undergo PET measurements with [^{11}C]UCB-J, in addition to (f)MRI measurements and MEEG recordings.

Methods

100 patients will be recruited at 4 centres in Sweden. At each site, patients will be randomised (2:1) to receive treatment (25 mg psilocybin) or active placebo (1 mg psilocybin). 50 patients will have multimodal imaging before and after treatment, with MRI, UCB-J PET and MEG-EEG. The other 50 patients will have EEG only.

The MEG-EEG recordings consist of resting state and an auditory oddball paradigm. In this paradigm, there are two oddballs (80/10/10), one higher and one lower pitch than the standard sound. For each of the two blocks the participant is instructed to press either on the high or low oddball, which changes for the second block. The P300 following oddball onset is expected to be lowered in depressed patients and to increase after treatment [4].

Study overview

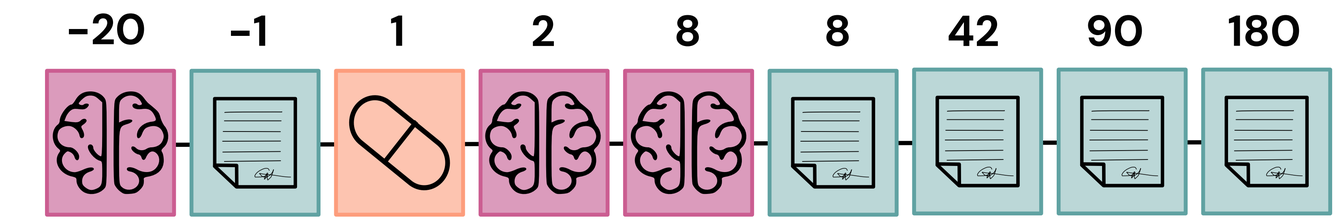

Figure 1: Schematic overview of imaging (purple), dosing (orange) and depression scores (blue) over the CAPSI project. The primary outcome of our study is antidepressant effect at +42 days. In fMRI we will record resting state and a social emotional learning task. In MEG with concurrent EEG in both a conventional system and a 128-channel OPM system, we have resting state and an auditory oddball paradigm.

Quality assurance

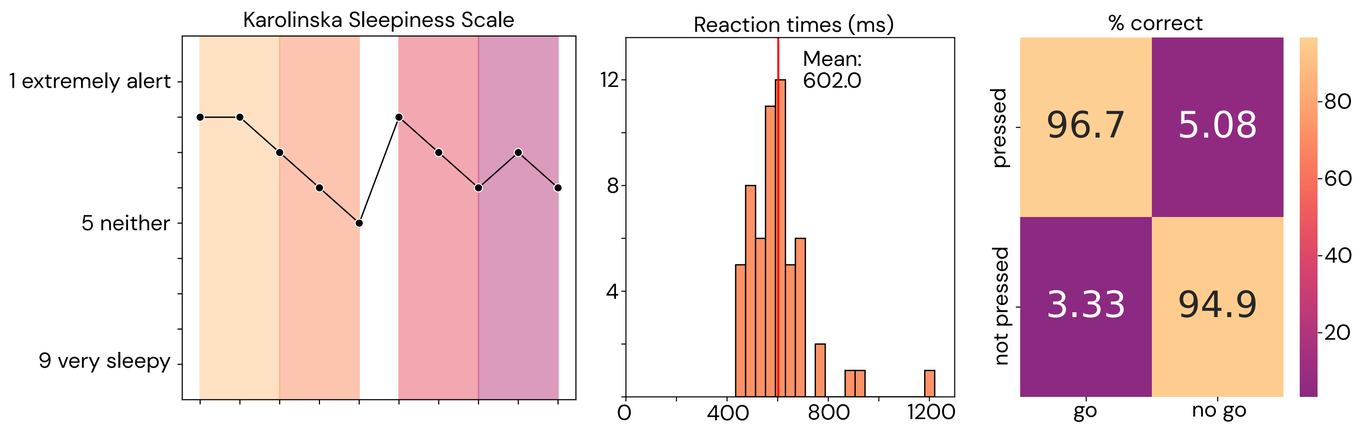

Figure 2: We use REDCap to collect all non-neuroimaging data and use several quality assurance steps. During our MEG-recordings, we monitor sleepiness. By considering sleepiness, reaction times and accuracy in the go-nogo task we can assess data quality. We also use RedCap to note noisy or flat channels, EEG cap size and other data that can help us spot systematic errors if they arise.

Global Field Potential pilot data

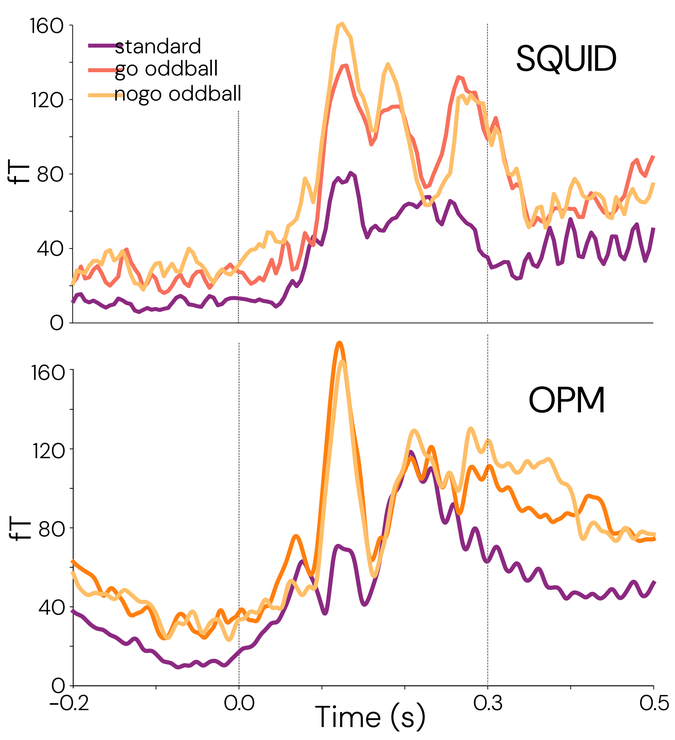

Figure 3: In our pilot data, we can separate standard and oddball stimuli at the 300ms post stimulus time point (P300). The shape of the GFP differs between SQUID MEG (top) and OPM (bottom). These figures represent minimally preprocessed data, only including filtering and homogenous field correction for OPM.

Source localisation pilot data

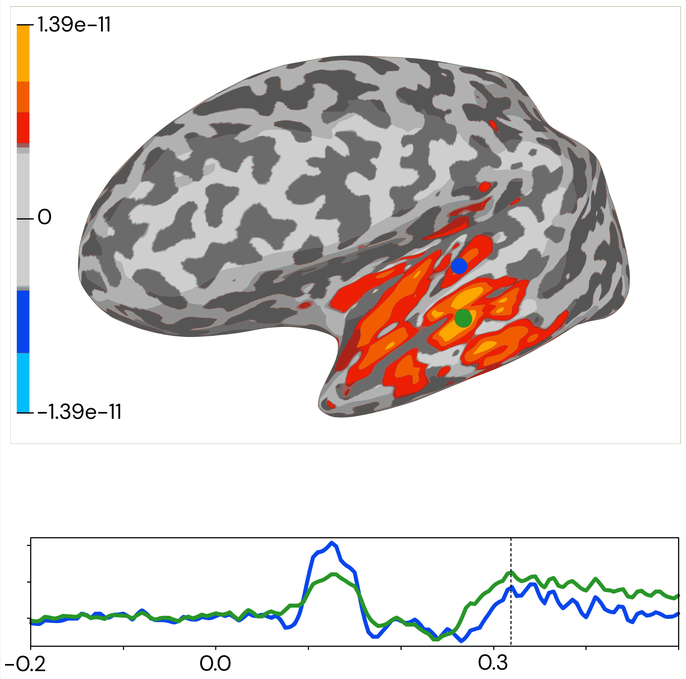

Figure 4: Source activity difference between all oddballs and standard stimuli at ~300ms post stimulus (top). Based on the activity difference, two locations were chose to represent the largest difference overall (blue) and largest difference at ~300ms (green). The time source activity of the blue and green sources can be seen in the bottom plot.

References

[1] Griffiths, R. R., et al 2016). Psilocybin produces substantial and sustained decreases in depression and anxiety in patients with life-threatening cancer: A randomized double-blind trial. Journal of Psychopharmacology, 30(12), 1181–1197. https://doi.org/10.1177/0269881116675513

[2] Ly, C., et al (2018). Psychedelics promote structural and functional neural plasticity. Cell Reports, 23(11), 3170–3182. https://doi.org/10.1016/j.celrep.2018.05.022

[3] Holmes, S. E., et al. (2019). Lower synaptic density is associated with depression severity and network alterations. Nature Communications, 10(1). https://doi.org/10.1038/s41467-019-09562-7

[4] Zhou, L., et al. (2018). Abnormalities of P300 before and after antidepressant treatment in depression: An ERP-sLORETA study. Neuroreport, 29(3), 160–168. https://doi.org/10.1097/WNR.0000000000000945