

## OPTIMIZED RESTING-STATE fMRI ACQUISITION STRATEGY FOR RELIABLE DLPFC TARGETING

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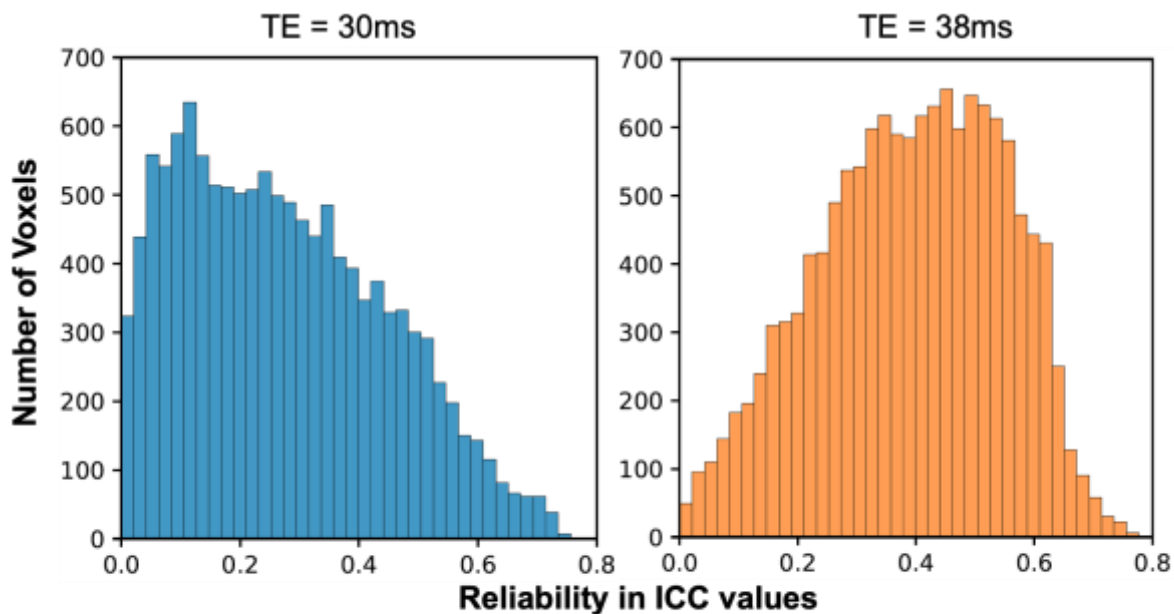
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**Introduction:** The sgACC resting-state network is highly relevant in clinical applications for determining brain stimulation targets in the left DLPFC. However, the effects of changes in resting-state fMRI acquisition parameters on the reliability and reproducibility of these functionally derived targets are largely unknown. Here, we quantify the effect of echo time choice and preprocessing strategies on the reliability of the resulting functional connectivity maps.

**Methods:** In a group of 15 healthy subjects, we performed single-session scanning at 3T acquiring six runs of rs-fMRI (three with TE=30 ms; three with TE=38 ms) each. Functional connectivity maps were calculated for each run, and correlations to a seed in the sgACC were computed. Smoothing kernel size (FWHM) was varied from 4 mm to 12 mm in steps of 2 mm. Intraclass Correlation Coefficients (ICC) were calculated for each run and for each smoothing kernel. Values below 0.5, between 0.5 and 0.75, 0.75 and 0.90, and greater than 0.90 are considered to indicate poor, moderate, good and excellent reliability, respectively.

**Results:** Overall, functional connectivity networks showed comparable distribution for both TE choices. However, connectivity maps acquired with TE=38 ms showed much higher ICC values within the DLPFC region. Specifically, the peak within the left DLPFC had a reliability value of 0.95 for TE=38 ms compared to 0.54 for TE=30 ms. Figure 1 shows the ICC reliability maps for both TEs using different smoothing kernels.



**Figure 1.** Histogram of test-retest reliability of voxels within the left DLPFC for TE = 38ms and TE = 30ms. On the y-axis the number of voxels for each bin is depicted. For TE = 30ms most voxels within the DLPFC have an ICC value below 0.5, which indicates poor reliability. For TE = 38ms, more voxels have an ICC value above 0.5, indicating moderate to good reliability.

**Discussion:** The choice of echo time has drastic effects on the reliability of the resulting functional connectivity maps. In addition, wider smoothing kernels could reduce the influence of local maxima within the correlation maps and increase the reproducibility. These findings highlight the value of exploring different acquisition and pre-processing strategies. Improved reliability of resting-state connectivity maps is important for improved outcome in clinical applications and for the optimization of data acquisition and multi-center data analysis in these resting-state networks.

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## SERT AVAILABILITY MODIFIED BY ACCELERATED HF-rTMS IN THE SUBGENUAL ANTERIOR CINGULATE CORTEX: A CANINE [<sup>11</sup>C]-DASB POSITRON EMISSION TOMOGRAPHY STUDY

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**Background:** Repetitive transcranial magnetic stimulation (rTMS) has been proven to be a useful tool for the treatment of several neuropsychiatric disorders by partly exerting the antidepressant effect through the serotonergic system. Accelerated high-frequency rTMS (aHF-rTMS) may have the potential to result in a similar but faster clinical improvement compared to the classical daily rTMS protocols. Given that delayed clinical responses have been reported, the neurobiological effects of accelerated paradigms remain to be elucidated. More, the optimal stimulation parameters need to be refined.

**Hypothesis** We hypothesized that [<sup>11</sup>C]-DASB binding alterations occurred in the regions with high SERT density. In line with antidepressant intake, we expected SERT decreases, more pronounced with the 20-sessions as compared to the 5-sessions protocol. No influences on any of the measurements following sham protocol were expected.

**Methods:** 10 dogs were allocated to the 5-sessions active group, 8 dogs were in the 20-sessions active group, 4 dogs were in the 20-sessions sham group. All dogs underwent four [<sup>11</sup>C]-DASB PET scans: baseline, 24 hours, 1 month, and 3 months after the last TMS session. A binding index (BI) was calculated for each region of interest (ROI) at each time point with the cerebellum (excluding the vermis) as the reference region.

**Results:** 5-sessions active protocol did not result in significant SERT BI changes at any time point. For the 20-sessions active protocol, one month after stimulation the SERT BI attenuated in the subgenual Anterior Cingulate Cortex (sgACC). No significant SERT BI changes were found after the 20-sessions sham protocol.

**Conclusion:** Our results suggest delayed decreased SERT binding by aHF-rTMS in the sgACC, a key region involved in the therapeutic response of antidepressant therapy after 20 sessions and not after 5 sessions of aHF-rTMS. These preliminary findings suggest that an intensified aHF-rTMS protocol may be preferred and that a similar working mechanism compared to pharmacotherapy may be the base of its treatment utility. Further research is needed to explore the exact pathways of the effects on the serotonergic system.

### References:

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