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The influence of EPI parameter choice on reliability of sgACC-DLPFC functional connectivity

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Introduction

Resting-state fMRI (rs-fMRI) is increasingly used to derive functional TMS targets in clinical settings, e.g. in the treatment of Major Depressive Disorder (MDD, Weigand et al., 2018). Clinical treatment efficacy of TMS targets in the left DLPFC has been related to functional connectivity to the sgACC (Fox et al., 2012; Salomons et al., 2014; Cash et al., 2020). Close proximity of the stimulated target to the maximum anti-correlation with the sgACC strongly improves the treatment effects (Weigand et al., 2018). Quantifying the spatial variability of the subject-specific rs-fMRI guided target and network is important for understanding reliability and reproducibility of target definition strategies. Here we assessed the influence of echo time (TE) parameter choice on the reliability of the sgACC-DLPFC target network.

Results

Overall, the functional connectivity networks derived from the sgACC seed have similar network components (e.g. bilateral PFC, IPL, ACC) for both TE choices . However, connectivity maps acquired with TE = 38ms showed higher ICC values for these network components. Figure 1 shows the ICC reliability maps for both TE's on a whole brain level. The effect was more profound when a mask of the greater DLPFC area was applied to the ICC maps (see Figure 2). Specifically, the the distribution of ICC values of the voxels within the greater DLPFC area differed for both TE's (Figure 3). The distribution of ICC values was significantly higher ($p < 0.001$) for TE = 38ms (M = 0.4, SD = 0.15) compared to TE = 30ms (M = 0.24, SD = 0.19). Most voxels within the DLPFC for TE = 38ms had a reliability of moderate to good, while the reliability was mostly poor for TE = 30ms.

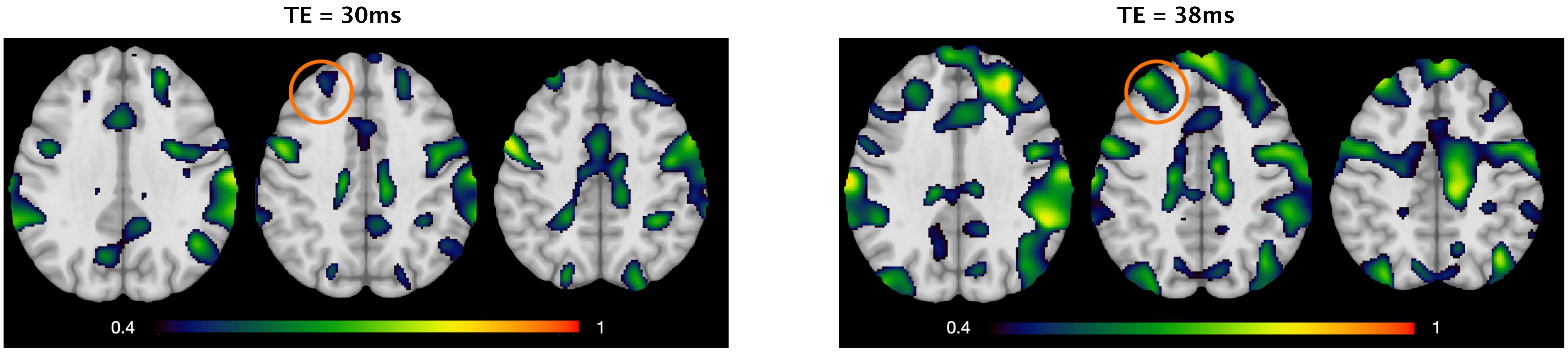

Figure 1. The improved test-retest reliability of the sgACC resting-state network for a longer echo time compared to a shorter echo time on a whole-brain level. There are clear differences in ICC values between TE = 30ms and TE = 38ms. The ICC values are higher for TE = 38ms. The results in the left DLPFC area are highlighted by the orange circle.

Methods

Fifteen healthy right-handed volunteers participated in this study. Data was acquired on a Siemens Prisma Fit 3T whole-body MR scanner using a 64-channel head coil with the CMRR multiband EPI (MB-factor 2) sequence (Moeller et al., 2010). We acquired resting-state data with two different echo times (TE), i.e. TE = 30ms and TE = 38ms while keeping other acquisition parameters equal (TR = 2000ms, flip angle 77, slice thickness 2mm, 170 volumes, 84 slices, voxel size = 1.8mm3). We acquired three runs per TE in a counterbalanced order, resulting in a total of six runs for each subject. All runs were acquired within one session. All analyses were performed on minimally processed data. The sgACC seed region was defined by a sphere with a 10mm radius centered around the mean MNI coordinates reported by Fox et al. (2012). The DLPFC was defined according to the method described in Cash et al. (2021). The resulting connectivity maps were spatially smoothed with a Gaussian kernel of 12mm as it has previously been shown to result in more stable and reliable target estimates (Ning et al., 2019). Intraclass Correlation Coefficients (ICC) were calculated for each run. ICC (3,1) was used in all analyses (Chen et al., 2018). 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 (Koo and Li, 2016).

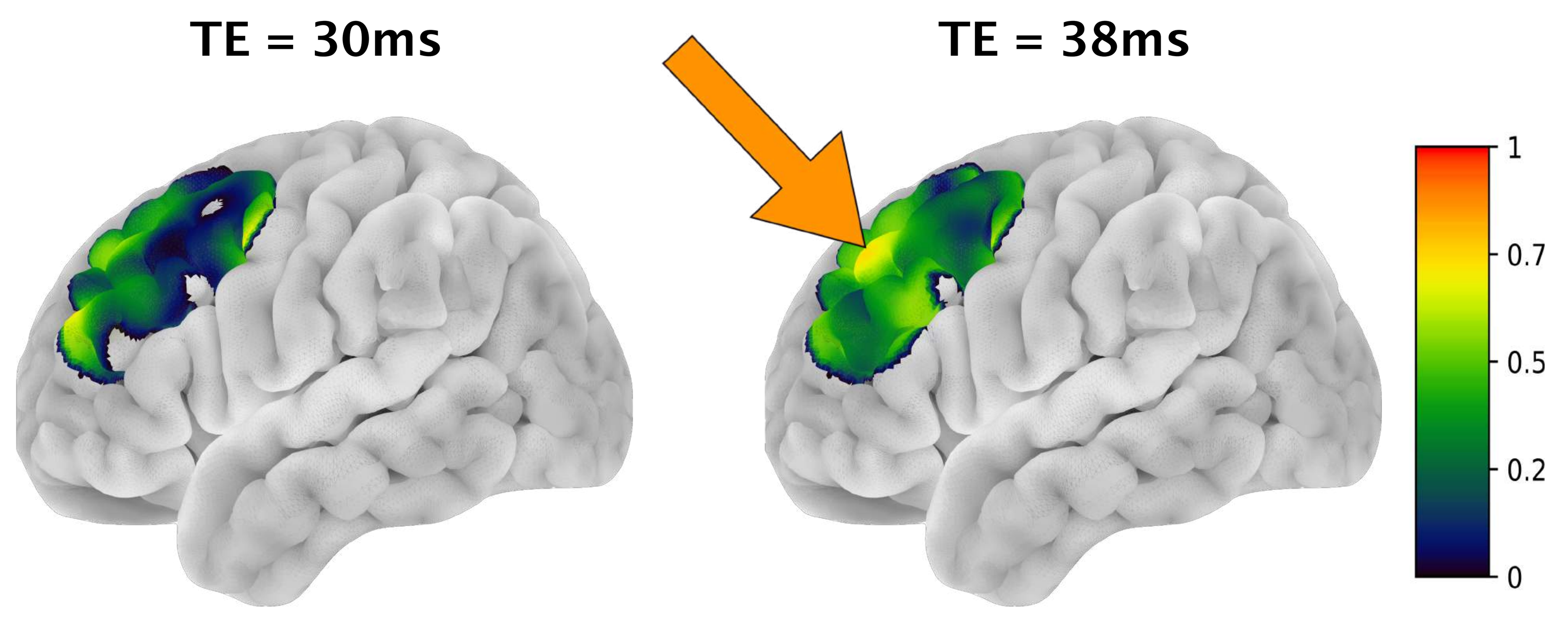

Figure 2. Higher ICC values for a longer echo time within the DLPFC component of the sgACC resting-state network. Thus far, no other groups have focused on optimization of the acquisition parameters for rs-fMRI guided localization methods. However, it is known that there are changes in the signal measures with different echo times. Here we show that these changes are relevant for the reliability of the functional sgACC-DLPFC network which is targeted in TMS treatment of MDD. The arrow points at the highest ICC values (good to excellent reliability) for TE = 38ms. The ICC maps are projected onto the cortical surface.

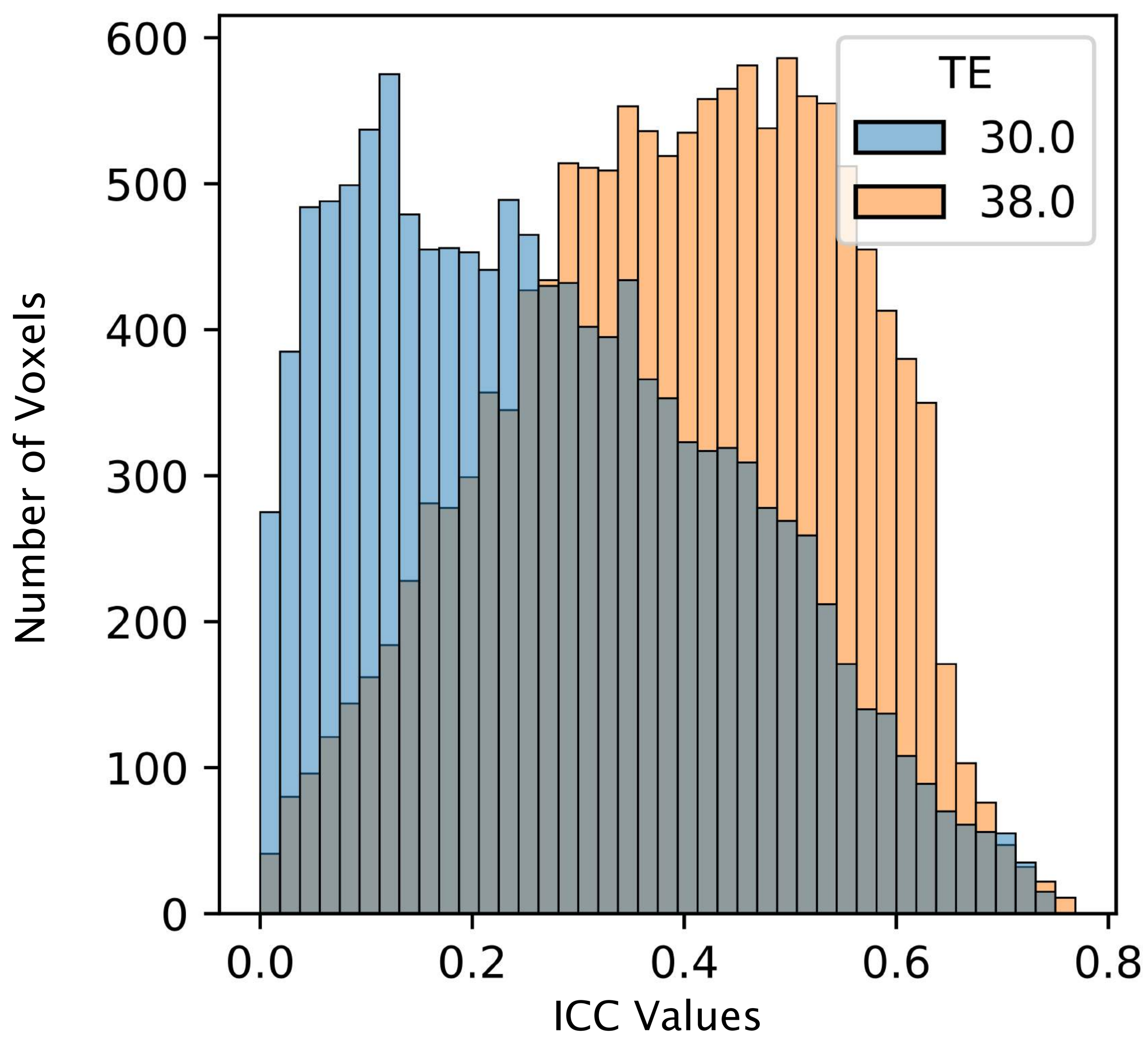

Figure 3. Histogram of test-retest reliability of voxels within the DLPFC for TE = 30ms and TE = 38ms. On the y-axis the number of voxels for each bin is depicted. For TE = 30ms most voxels within the DLPFC have an ICC value below 0.5, which indicates poor reliability. For TE = 38ms, more voxels have an ICC value above 0.5 (moderate to good) reliability.

Conclusion

Resting-state acquisition echo time affects the reliability of the resulting functional connectivity maps. This has an effect on TMS targeting approaches that base their DLPFC target on its functional connectivity to the sgACC. Our results clearly indicate that optimized acquisition parameters are beneficial for ensuring high-reliability resting-state acquisition protocols to be used for TMS targeting. The reliability of resting-state connectivity maps is not only important to improve clinical outcome, but also for the optimization of data acquisition and multi-center data analysis in these resting-state networks

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