HIgh-resolution Functional Connectivity Mapping of Eloquent Cortex Networks in Surgical Epilepsy Patients at 7T

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Target Audience: Clinically oriented researchers who study functional connectivity, presurgical mapping, and those interested in epilepsy.

Purpose: Neurosurgical resection of an epileptic lesion requires minimizing post-operative deficits while maximizing the resection itself. This is typically done with task-based functional mapping of eloquent cortex, including motor, language and memory tasks. This functional mapping is difficult in some patients due to the inability to perform a task either because they are too young or due to cognitive deficits. Therefore, we previously proposed a non-task method to localize eloquent cortex[1,2] and to determine the lateralization of cortical networks[3] based on functional connectivity. Improved sensitivity and resolution from advances in array coils and higher field strength allow for increased spatial resolution and partial volume dilution of the cortical connectivity[4] at the single subject level. The purpose of this study is thus to evaluate the feasibility of identifying, localizing and lateralizing eloquent cortex at ultra-high MRI field-strength (7T) using resting-state functional connectivity MRI (rs-fcMRI) at high spatial resolution and at a single subject level of patients with epilepsy.

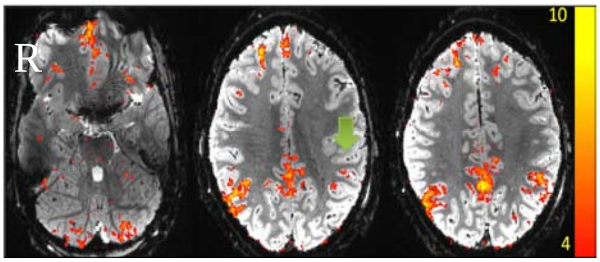

Figure 1: Single subject temporal connectivity maps of the Default Mode Network in a patient with left lobe epilepsy at a voxel size of 1.2mm isotropic. Note that in the DMN the absence of coupling in the lateral parietal lobe in this subject is right-hemisphere dominant (LI = 0.35).

Methods: We studied six patients with partial epilepsy with medically refractory seizures under a protocol approved by our institutional IRB. One had left-sided temporal lobe epilepsy, one had bi-temporal epilepsy, and the others had extra-temporal epilepsy. All subjects had a non-lesional 3T report and task-based language fMRI. Data acquired on a Siemens 7T MRI system (Siemens Healthcare, Erlangen, Germany) with an in-house built 32-channel head coil[5]. Resting-state time-series (no stimulus, subjects asked to relax with eyes open) were obtained using a single-shot gradient echo EPI sequence with TR/TE/flip = 5000ms/22ms/90°, 103 time-points and 90 slices covering the entire cerebral cortex at a high resolution of 1.2 mm isotropic voxel size. Data analysis was performed using FSL (FMRIB, Oxford, UK), and in-house software. Typical fMRI pre-processing was applied, including slice time, motion and drift correction as well as commonly used fcMRI preprocessing procedures; temporal filtering, estimation and regression of nuisance signals from motion parameters, white matter, and ventricular ROIs. Correlation maps were generated using the seed-based approach by computing the correlation between the 'seed' region and the time courses of all other voxels in the brain. The primary motor cortex, PCC (Post Cingulate Cortex), and Broca areas, were used as seeds for Motor, Default Mode and Language networks respectively. Correlation maps were then overlaid on the EPI data in each subject's native space. Based on the functional connectivity mapping of the language network, further quantitative analysis was performed to evaluate the language laterality by computing a laterality index (fcMRI-LI). The right and left frontal language ROIs comprising the dorsal lateral prefrontal cortex, including the *pars triangularis* and *pars opercularis,* was identified. The mean time course in this seed region was extracted and the correlation coefficient calculated between two pairs of points defined as: LI-fcMRI = [(LL – RL) – (RR – LR)]/[LL + LR + RR + RL], where LL is the number of voxels with a correlation coefficient equal to or great than 0.25 in the entire left hemisphere with seeding the left *pars triangularis* and *opercularis*, LR is the number of voxels above the threshold in the right hemisphere ROIs with seeding the left *pars triangularis* and *opercularis*; RL & RR was similarly calculated.

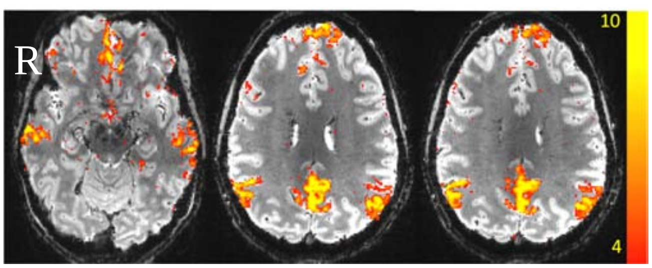

Figure 2: DMN network in patient with bi-temporal lobe epilepsy. Images are derived from the original unsmoothed 1.2mm isotropic EPI using the PCC as seed. Note that the DMN in this case is relatively symmetric (slight left preference).

Results: Fig. 1 shows the DMN from a single subject with left temporal lobe epilepsy illustrating the correlation between the seed area (PCC) and the whole brain when 1.2mm isotropic acquisitions with 2mm smoothing applied. Notice that in this subject there is clear asymmetry in the DMN, with decreased correlation of the DMN on the left). Fig. 2 shows the DMN for a different patient with bi-temporal lobe epilepsy. Fig. 3 shows the language network in a single subject. Notice that the language network, as identified by a highly correlated voxels in the angular gyrus and the superior temporal gyrus and the middle temporal gyrus, is much stronger in the left hemisphere. The LI-fcMRI were all left lateralized suggesting all were left-hemisphere dominant for language. This was congruent with the LI calculated from a semantic decision task-based fMRI at 3T (r=0.8, $p < 0.05$). The motor network was also identified and was symmetric in all subjects (ie, LI-fcMRI ~ 0.0).

Discussion: We were able to identify, localize and lateralize eloquent cortex in a series of patients with epilepsy including the motor cortex, a 'language' network, and the DMN. The motor next work was bilaterally symmetric and the language network was left lateralized in all subjects and correlated with their MEG lateralization scores. The DMN was more symmetric, but might clinically be related to the health of the hippocampal-cortical network (verbal and spatial memory).

Conclusions: In the patients with epilepsy, we show the feasibility of using ultra-high field strength MRI and high resolution acquisition to map clinically relevant resting state networks at a single subject level using a single short rs-fcMRI acquisition of ~8min. Abnormalities in the DMN were identified in one subject, consistent with his clinical diagnosis of left temporal lobe epilepsy.

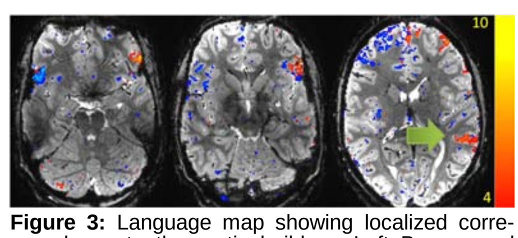

Figure 3: Language map showing localized correspondence to the cortical ribbon. Left Broca seed (red) and homologous right Broca seed (blue) are illustrated in the inferior frontal lobe. Left-sided Wernicke coupling (green arrow) which is absent in the right, denotes that the left hemisphere network is stronger than that on the right.

References: 1) Stufflebeam SM et al., J Neurosurg. 2011 Jun;114(6):1693-7, 2011 2) Liu H, et al., J Neurosurg. 2009 Oct;111(4):746-54, 1995 3) Liu et al., Proc Natl Acad Sci U S A. 2009 Dec 1;106(48):20499-50, 2009 4) Triantafyllou et al., ISMRM 2011 5) Keil B, et al., ISMRM 2010, # 6960**;** 6) Liao et al., Human Brain Map 2011.