MAPPING HIGHER-ORDER BRAIN FUNCTION AND RESTING-STATE NETWORKS WITH DIFFUSE OPTICAL TOMOGRAPHY

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Purpose: Traditional functional neuroimaging, with positron emission tomography (PET) or functional magnetic resonance imaging (fMRI), cannot be used when applications require portability, or are contraindicated because of ionizing radiation (PET) or implanted metal (fMRI). Optical neuroimaging offers a noninvasive alternative that is radiation free and compatible with implanted metal and electronic devices (e.g., pacemakers). However, optical imaging technology has heretofore lacked the combination of spatial resolution and wide field-of-view sufficient to map distributed high level brain functions. Herein, we present integrative advances in high-density diffuse optical tomography (HD-DOT[1]) imaging arrays, large field-of-view instrumentation, and anatomical head modeling. Mapping of higher-order, distributed brain function was tested by imaging four hierarchical language tasks and multiple resting-state networks (RSNs[2]) including the dorsal attention, fronto-parietal control, and default mode networks.

Methods: To test the capability of the HD-DOT system to map higher-order brain function over an extended FOV, we followed a classic PET imaging study of single word processing[3] that used a hierarchy of tasks to isolate responses to the sensory (visual and auditory), motor, and sematic aspects of language. Four task conditions reflected a three-level hierarchy in processing: sensory tasks (reading and hearing words), a simple output task (imagined speaking of words), and an association task (generating verbs). To calculate the magnitude of response, voxel-wise contrasts were calculated comparing: the sensory conditions to fixation, imagined speaking of words to covert reading, and covert verb generation to imagined speaking of words. In each case, random effects t-statistics were calculated across subjects. Imaging RSNs using functional connectivity analysis on 10 minutes of resting state data provides a comprehensive and stringent test of HD-DOT against fMRI. Functional connectivity (FC) maps are created by computing the correlation between the time courses of particular seed regions and the time courses of all other voxels in the imaging domain. The spatial patterns of functional connectivity are highly sensitive to the location of the seed region of interest. We generated maps of multiple key RSNs using a seed-based correlation approach with spherical seeds (5 mm radius) defined by the co-registered anatomy and 10 minutes of resting-state DOT or fMRI data.

Results: Subjects were instructed to either listen quietly to words presented through room speakers (HD-DOT) or through headphones (fMRI) **(Fig. 1a)**; to quietly read each word (covert reading; **Fig. 1b**); to imagine themselves saying the word out loud (imagined speaking words; **Fig. 1c**); or to covertly generate a verb associated with each word (covert verb generation; **Fig. 1d**). Contrasting the hierarchical tasks (e.g., covert verb generation vs. covert reading) revealed strong HD-DOT activations (including in left-lateralized prefrontal Broca's area) that were spatially congruent with the fMRI responses.

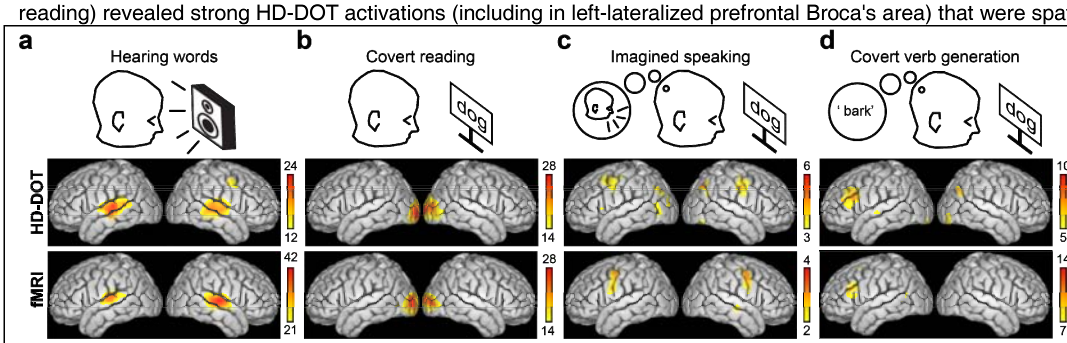

Figure 1: Evaluation of higher-order brain function mapping by imaging hierarchical language processing. Differential responses were detected throughout the FOV in response to language tasks including **(a)** hearing, **(b)** reading, **(c)** imagined speaking, and **(d)** generating words. Non-concurrently recorded fMRI in a subject-matched population (N = 5) shows excellent agreement. All maps are t-maps thresholded at 50 percent maximum.

The sensory and motor sub-networks (**Fig. 2**) displayed robust inter-hemispheric functional connectivity with homotopic regions in the opposite hemisphere. Quantitative functional connectivity DOT (fcDOT) vs. fcMRI comparisons were computed as the spatial correlation between the functional connectivity maps obtained by the two modalities (Vis: r = 0.84; Aud: r = 0.77; Mot: r = 0.77). Seeding the higher-order RSNs revealed intra- as well as inter-hemispheric functional connectivity patterns (**Fig. 2**) comparable to the maps obtained with fMRI (DAN: r = 0.73; FPC: r = 0.83; DMN: r = 0.72).

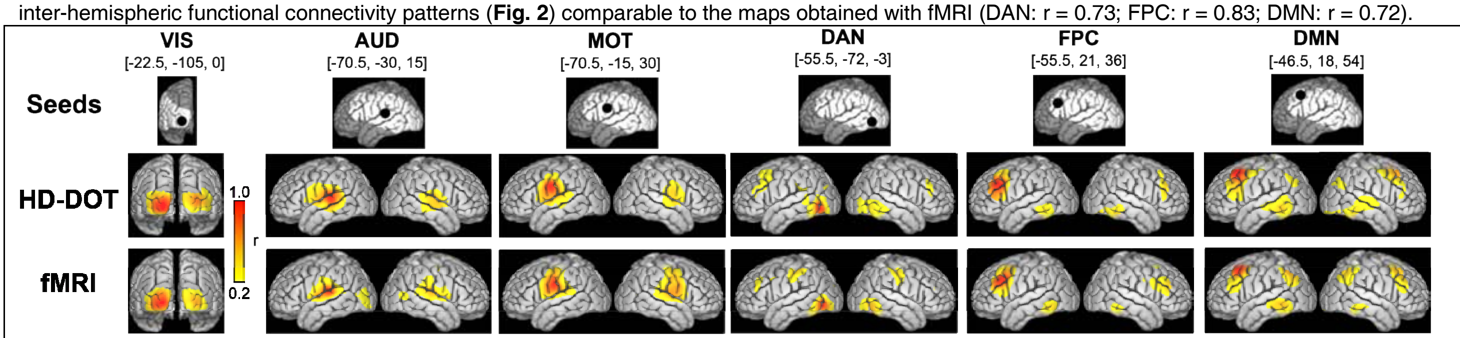

Figure 2: Mapping the functional connections of distributed brain networks. Maps (N=8 subjects) of functional connectivity (Fisher z) were generated from seeds adapted from the literature, representing three sensory-motor networks: visual (VIS), auditory (AUD), motor (MOT), and three higher-order networks: dorsal attention (DAN), fronto-parietal control (FPC), and default mode (DMN). The anatomical location of the seed (black dot on the highlighted FOV of the study) and MNI coordinates are shown above the maps.

Discussion: Collectively these maps of tasks and resting state function in adult humans clearly indicate that high-density DOT can be a practical and powerful tool for functional brain mapping. Apart from compatibility with implanted electronic devices, HD-DOT offers several advantages in comparison to fMRI. First, DOT provides a more ecologically natural scanning environment. Noise within the bore of an MRI scanner can exceed 120 dB whereas DOT is effectively silent. Subjects can sit in a chair and listen to speakers rather than headphones, thereby permitting for more nuanced language studies and even natural social interactions. These advantages might be especially useful in studies of autism spectrum disorder (a population that is especially sensitive to the imaging environment). Second, the potential portability of HD-DOT systems opens the door to bedside monitoring, for example of preterm infants, patients in intensive care, or patients in the operating room.

References:

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