Functional MRI and deep-brain stimulation: Impact from distortion artifacts

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Target audience: Neuroscientists, neurologists and psychiatrists investigating mechanisms behind deep-brain stimulation; Researchers interested in fMRI and resting-state fMRI.

Purpose: Deep-brain stimulation (DBS) is a rapidly evolving neurosurgical strategy used to treat various debilitating neurological and psychiatric conditions; with continually emerging applications and novel stimulation targets. The striking therapeutic benefit of DBS therapy has been nevertheless established more or less empirically. This has opened entirely new horizons for further basic research and investigations. Several successful attempts to study neural circuitry of patients with fully implanted and active DBS hardware evidence experimental feasibility of functional MRI (fMRI) under strictly controlled safety standards. Here, we show that rigorous data analysis standards also need to be adhered to and highlight the associated caveats. In particular, we demonstrate that utmost caution should be exercised when analyzing fMRI data in the vicinity of the DBS electrode, due to severe geometric distortions and signal intensity drops, which may eventually culminate in false-positive findings.

Methods: Images were acquired at 1.5T on a MAGNETOM Symphony scanner (Siemens, Erlangen, Germany). Experiments included T1-weighted (T1w) and resting-state fMRI (rs-fMRI) scans: 200 volumes of T1w 3-dimensional (3D) data were collected using a gradient-echo planar imaging (EPI) sequence (TR/TE/TI = 2140/1100/3.93 ms/15°), consisting of 31 axial, 3 mm thick slices with a nominal in-place resolution of 3×3×3 mm3. Participants were instructed to follow a fixation-cross on a projector screen while remaining still in a supine position. T1w structural data were measured using a magnetization-prepared rapid acquisition gradient-echo (MP-RAGE; TR/TE/TI = 2140/1100/3.93 ms/15°). Functional images were realigned, co-registered with the structural images and resampled to 3×3×3 mm3. Both anatomical and functional data were normalized to the MNI template. In MR data shown in Figure 1, no spatial smoothing and no filtering were performed. The data were randomly selected from a patient with Parkinson's disease (PD) pre- and post-implantation of DBS electrodes targeted at the subthalamic nucleus (STN). Spherical region of interest (ROI) with a 15 mm diameter was formed around the electrode tips (STN) bilaterally. ROI voxel-value histograms were computed from temporally-averaged functional data. In addition, distributions of whole-brain voxel intensities were calculated. To emphasize the risk of potential false-positive results, rs-fMRI data from the same patient cohort were analyzed in various stages of their transition from levodopa (24 patients) to DBS treatment (13 patients). Pre-processing included spatially smoothing the functional data using an 8 mm full-width-at-half-maximum Gaussian kernel and filtering the fMRI time-courses using a band-pass filter (1/50 Hz-1/8 Hz). Left functional images were extracted from the ROIs (functional data), leaving out voxels exhibiting signal drops in the ROI compared to whole-brain intensity distribution and spatially larger signal drops in functional data compared to structural data are particularly noteworthy.

Results: Increased sensitivity of the fMRI signal to artifacts caused by the DBS leads is clearly visible post-implantation (Fig. 1). The intensity distribution within the ROI is broadened, with the majority of values shifted to the outlier range. In pre-surgery sessions (without electrodes), paired t-tests (dopaminergic medication on vs. off) revealed changes in functional connectivity of STN with thalamus and cerebellum (Fig. 2, a). Equivalent analysis (DBS on vs. off) on post-surgery sessions (electrodes in place) still yielded significant, yet ambivalent functional connectivity changes (Fig. 2, b; in particular cluster 2).

Discussion & Conclusion: Aforementioned artifacts are caused by the low bandwidth in phase-encoding direction of echo planar imaging (EPI) employed for fMRI. It is evident that extracting data from a structure around the electrode tip, despite adjusting the ROI using T1w data, can easily compromise consequent analysis. Functional connectivity changes in cerebellum and thalamus – regions involved in PD pathophysiology – were detected in response of patients to levodopa (without electrodes). In contrast, equivocal functional connectivity changes post-implantation in response to DBS (electrodes in place) demonstrate a possibility of obtaining a combination of false-positive and true effects, when selecting seed regions carefully. Presented work suggests particularly cautionary means of analyzing fMRI of patients with implanted DBS electrodes, and/or extremely careful interpretation of obtained results. We advocate excluding all fMRI voxels exhibiting signal drops from the analyses, until conclusive investigations quantifying the impact of aforementioned artifacts on the fMRI signal will be reported.

References: