Resting State fMRI During Spinal Cord Stimulation

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Introduction:

Spinal cord stimulation (SCS) is currently a well-established treatment option for chronic neuropathic pain, specifically for neuropathic leg pain in patients with failed back surgery syndrome [1]. The neurophysiological basis for SCS and the related cortical processing of sensory information has so far been inadequately understood. However, resting state fMRI (rs-fMRI) is able to provide a tool to measure brain activation and cortical synchronization enabling the detection of changes in the functional brain network. Thus, the aim of this study is to investigate the sensitivity of rs-fMRI to detect changes related to the stimulator setting and the corresponding relief or pain level.

Methods:

Resting state functional studies were acquired from seven subjects. Each subject was fully implanted with thoracic epidural Medtronic Restore-family SCS for the treatment of chronic refractory neuropathic leg pain following failed back surgery syndrome. Pain quantification was based on the Visual-Analog Scale as reported by the subject during

Figure 1. The AAL atlas and the Cross correlation for the *Off*, *Low*, *Opt*, and *High* stimulator settings.

stimulation. Images were acquired using a 3 Tesla Philips Achieva MRI system (Cleveland, OH). The safety of the subjects for using this device and its risk related to the static and gradient magnetic field as well as RF heading was thoroughly investigated. Computer modeling and in-vitro testing were used to verify the safety for the specific implanted SCS devices and their leads. The risk of induced current and possible vibration due to the magnet and the gradient fields was extensively assessed. Transmit/Receive head coil was used to eliminate any potential for RF heating in the spinal cord or stimulator malfunction. A high resolution MPRAGE T1 weighted image was acquired with the parameters: TR/TE 7.8/3.8 ms, $1\times1\times1$ mm^3 voxel resolution. Functional scans were acquired using single-shot EPI sequence with an isotropic spatial resolution of 3.4 mm. The acquisition parameters are: TR/TE 2000/26 ms, 80° flip angle, 64×64 matrix size, 220×220 mm field of view, 30 slices. Four functional scans were acquired, each with a different state of the stimulator program setting i.e. with no pain or with different pain levels. The optimal stimulator setting with subject lying down was already known. The first functional scan was the only one with the stimulator turned off. The second, third, and fourth scans were with stimulator set at *below, at,* and *higher than* optimum levels respectively. Since it was not possible to change the stimulator settings inside the magnet during the study, the subjects were removed from the scanner between functional scans, the number of volumes acquired was 300 for the first three scans. However, 180 volumes were acquired for the fourth scan. The long scan time was selected

to ensure that the subjects were in a steady state. The time was reduced for the last scan due to the discomfort in that particular setting. The resting state images were analyzed using FSL and AFNI tools. The images were motion corrected, smoothed (5 mm^3) and band-pass filtered ($0.005<f<0.1$ Hz). The analysis was repeated for the first three scan sessions using successive windows of six minutes to check for consistency. The four scan settings are referred to as "*Off, Low, Opt*, and *High*".

Results:

The images were transformed to the MNI space and the AAL atlas [2] was used to segment 116 region of interest in the cortical and subcortical brain regions. Pearson cross correlation was applied to calculate the correlation between the nodes as seen in Figure 1. Graph characteristics of the network [3], including the network clustering coefficient and global efficiency were calculated as shown in Figure 2.

Figure 2. Upper: Group network strength for the *Off*, *Low*, *Opt*, and *High* stimulator settings. Lower: The network measures scaled to the *Off* setting.

Conclusions:

While the number of subjects is small, there is evidence that the brain network graph metrics are correlating with the stimulator settings. The global efficiency reduces from the *Off* to the *low* conditions (p<0.05). There is also a further small reduction during the optimal stimulator setting. A large increase is observed when the stimulator was set at above optimum. Although the subjects reported a pain level reduction, the discomfort introduced by the paresthesia may have been responsible for this change in these measures.

References: [1] Taylor RS, J Pain Symptom Manage. 2006 (4 Suppl):S13-9. [2] Tzourio-Mazoyer, Neuroimage 2002 15:273–2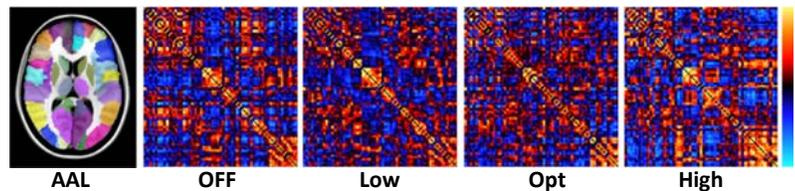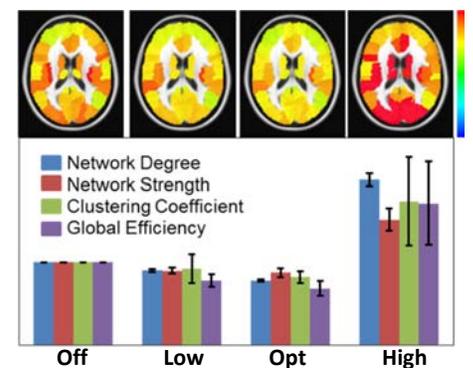89. [3] Rubinov and Sporns, 2010 Neuroimage 52:1059–1069.