

fMRI in patients with lumbar disc disease: A paradigm to study patients over time

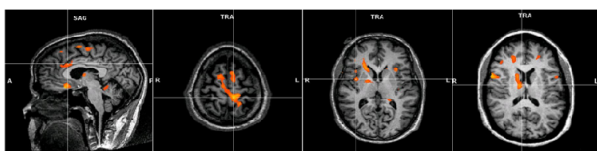
H. A. Sharma¹, R. Gupta², and W. Olivero³

¹Beckman Institute, University of Illinois at Urbana-Champaign, Urbana, IL, United States, ²University of Illinois College of Medicine, ³Neurosurgery, Carle Foundation Hospital

Introduction : Chronic pain affects millions of patients and the treatment options that are currently available are either limited, ineffective, or result in significant side effects. fMRI studies have made significant contributions to the understanding of how the brain processes pain. Using fMRI to study pain has revealed new information about how the brain responds to painful stimuli and what regions of the brain are activated during pain. Unfortunately, many of the paradigms that are used in fMRI studies either fail to replicate the subject's pain or painful stimuli is used in volunteers without pain. Moreover, longitudinal fMRI studies that follow patients who develop chronic pain from the acute phase of pain have not been performed. We developed an fMRI paradigm that reliably mimics a clinical pain syndrome in patients who have low back pain and leg pain from acute lumbar radiculopathy and lumbar degenerative disc disease. We believe this paradigm will allow performing longitudinal fMRI on patients as they progress from acute to chronic pain.

Methods : Lumbar radiculopathy patients were imaged in a 3T Siemens Allegra scanner using a single channel quadrature coil. The subjects signed a written consent form approved by the local IRB. A Block design was used for fMRI stimulus design. The blocks consisted of 20s task and 20s rest. Task included breathhold, dorsiflexion of right foot, muscle tensing of right foot, and right leg raise. A T2*-weighted EPI sequence (TR/TE/FA = 2000ms/30ms/77°) was used to acquire whole brain volumes (32 slices) at a voxel dimension of 3.8x3.8x4. High resolution T1-weighted anatomical images were acquired with an MPrage sequence.

Analysis : fMRI data were analyzed using Brainvoyager QX. The standard sequence of preprocessing steps were performed for the fMRI data, including slice scan time correction, high pass filtering and spatial smoothing. 3D head motion correction was performed to detect and correct for small head movements. Estimated translation and rotation parameters were inspected. The anatomical data was corrected for spatial intensity inhomogeneities. The data was then resampled to 1 mm resolution and transformed into ACPC and Talairach standard space. The fMRI data was co-registered with the subject's 3D anatomical data and then normalized so that the analysis could be done in the talairach space. For each subject block data, a Brainvoyager protocol file was derived representing the onset and duration of the tasks for the different conditions. In order to account for hemodynamic delay and dispersion, each of the predictors was derived by convolution of an appropriate boxcar waveform with a double gamma hemodynamic response function. Using hypothesis driven, voxelwise standard analyses (GLM), we tested for overall task related effects.



Figures 1-4 demonstrate the activated regions of the patients during the SLR maneuver. ($p < 0.05$, corrected). There is activation in the leg sensory-motor region S1, anterior cingulate gyrus, thalamus, caudate, and insular regions.

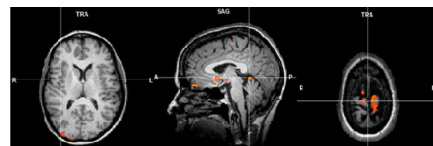


Figure 5-7. demonstrates no activity in the pain regions of the controls during the SLR maneuver. There is activation in the leg sensory-motor region S1 and anterior cerebellum ($p < 0.05$, corrected).

Results: The leg raise maneuver caused a two point or greater change on the VAS during the fMRI sessions and was the most likely maneuver to activate regions of the brain in the pain matrix. We report the group analysis results ($p < 0.05$, corrected) as figures that show the activated regions in the brain as a result of low back and leg pain. Figures 1-4 represent the summed data for the pain subjects during the leg raise maneuver. The images show activation in the anterior cingulate gyrus, bilateral insular regions, right thalamus and basal ganglia, sensorimotor regions (greater on the left side), and anterior cerebellar vermis. Figures 5-7 show that the activation regions in the controls during SLR are the sensorimotor region (representing the leg and back) and the cerebellar vermis.

Discussion : After inspecting the motion files from the fMRI data, we determined that the maneuvers we used to induce differential pain in the block design did not create motion artefacts that prevented analyses and interpretation. Any motion that was present was easily corrected by motion correction algorithm in Brainvoyager. We are now confident that these maneuvers can be used in the block design for the fMRI experiments to study acute and chronic pain. **References**: Apkarian, A.V., Bushnell, M.C., Treede, R.D., Zubieta, J.K., 2005. Human brain mechanisms of pain perception and regulation in health and disease. *Eur J Pain* 9, 463-484. Jeanmonod, D., Magnin, M., Morel, A., 1993. Thalamus and neurogenic pain: physiological, anatomical and clinical data. *Neuroreport* 4, 475-478. Functional magnetic resonance imaging, Huettel Scott A., Song Allen W.