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### **Insight to Brain Connectivity in Chronic Low Back Pain Patients is Seen through a Novel Arterial Spin Labeling MRI Study**

February 24, 2012, Palm Springs, CA—Researchers at Harvard Medical School used arterial spin labeling, a novel functional magnetic resonance imaging (fMRI) technique, to show for the first time that brain connectivity in patients with discogenic chronic low back pain (CLBP) changes in proportion to the severity of their pain. The study was presented today at the 28<sup>th</sup> Annual Meeting of the American Academy of Pain Medicine.

Marco Loggia, PhD, Postdoctoral Research Fellow at Harvard Medical School, Massachusetts General Hospital and Brigham & Women's Hospital reported the results. The researchers used arterial spin labeling (ASL) to measure the cerebral blood flow to specific brain regions and assess the neural activity. In this particular study the authors performed sophisticated analyses on brain connectivity to determine how communication among areas is altered in CLBP patients.

After Institutional Review Board approval, 16 CLBP patients (average pain 4.8/10, average duration 6.2 years) and 16 matched healthy controls participated in two resting-state 6-minute ASL scans: one at baseline and one after the study subjects participated in clinical maneuvers

(such as straight leg raising, or pelvic tilt) that were painful to the CLBP group, inducing a clinically significant increase in ongoing pain (>30%), but not to the healthy control group.

Through the ASL images, the researchers found that at baseline the CLBP patients had a stronger connectivity between a particular brain region, the medial prefrontal cortex (MPFC), and a network of brain areas, the “Default Mode Network” (DMN), than the healthy controls. The results also showed that the more the DMN was connected to the MPFC, the less the pain experienced. This suggests that MPFC-DMN connectivity might be a pain-protective mechanism.

The analysis also showed that the connectivity between the MPFC and the DMN was reduced after the maneuvers in patients (but not in the controls). “Since painful maneuvers disrupt these connectivity patterns, we believe that the higher connectivity strength observed at baseline might reflect some type of a coping or compensatory mechanism, as if the patients, while at rest, are bracing for the next pain increase,” comments Dr. Loggia.

The authors also observed that the greater the pain, the more the DMN was connected to the insula, a region considered to be involved in pain processing. Furthermore, the greater the pain increased after the clinical maneuvers, the more the DMN-insula connectivity also increased. This was of particular interest to the researchers because a study published last year found similar results between the DMN-insula connectivity in fibromyalgia patients.<sup>1</sup> The researchers also believe that such fine tracking of the pain perception suggests that the DMN-insula connectivity might actually encode the perceptual aspect of the clinical pain. This appears to be a general feature of chronic pain that may cross over multiple pain conditions.

“Today there are no objective tests to evaluate the amount of pain experienced by a patient. The only way to assess it is simply to ask the patient, but of course self-report is a far-from-perfect measure, and cannot be obtained for everybody (e.g., preverbal children, patients with severe

dementia, etc). This study suggests that pain severity in a chronic pain population might be objectively measured by examining brain activity. One day, these methods may translate into clinical applications, and perhaps be used to improve the design of clinical trials,” comments Dr. Loggia.

“ASL is a promising tool to investigate the neural processing of chronic pain and provides a step forward in the quest for objective biomarkers in the study of chronic pain. Future studies should focus on linking such brain connectivity to changes in pain over time,” Dr. Loggia concludes.

1) Vitaly Napadow, PhD, Lauren LaCount, Kyungmo Park, PhD, Suzie As-Sanie, MD, Daniel J Clauw, MD, and Richard E Harris, PhD, Intrinsic Brain Connectivity in Fibromyalgia is Associated with Chronic Pain Intensity, *Arthritis Rheum.* 2010 August; 62(8): 2545–2555. doi:10.1002/art.27497.

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