A new study published in the August 2010 Arthritis & Rheumatism by Vitaly Napadow, Ph.D. and colleagues has shown that patients with fibromyalgia (FM) have a different degree of connectivity between specific brain networks as compared with healthy controls. The study, entitled “Intrinsic Brain Connectivity in Fibromyalgia Is Associated With Chronic Pain Intensity,” also demonstrated a relationship between the activity in these brain networks and perceived levels of spontaneous pain in those with FM.

Functional magnetic resonance imaging (FMRI) was used to gather information about the resting brain activity in 18 female patients with FM and 18 female age-matched healthy control subjects between the ages of 18 and 75. Subjects were first asked to rate the degree of pain they were in just prior to the FMRI and then “to rest comfortably without falling asleep” while FMRI data was gathered.

The researchers chose to examine the resting state of the brain because they were looking for neural correlates of the chronic endogenous pain or “spontaneous pain” that is characteristic of FM as opposed to the hypersensitivity that FM patients exhibit to external sources of pain (also known as hyperalgesia). Therefore, the researchers measured intrinsic brain connectivity which is the basic “ongoing neural and metabolic activity” that occurs while the brain is at rest and not responding to stimuli.

The researchers hypothesized that FM patients would have an altered level of resting-state connectivity in the default mode network (DMN) and the executive attention network (EAN) while the connectivity of the medial visual network (MVN) would be comparable to that in healthy controls. The DMN and EAN are both involved in cognitive processes that can be impaired in those with FM. The DMN is believed to be involved in self-referential thinking and is comprised of brain regions that have been shown to be deactivated by experimental pain, while the EAN is involved in working memory and attention. Conversely, the MVN is made up of the primary visual processing areas that are not known to be affected by FM. Thus, the MVN served as a negative control.

The researchers also controlled for age (as age and spontaneous pain were significantly positively correlated) and for physiological factors such as cardiorespiratory fluctuations, which can affect FMRI measurements of intrinsic connectivity.

In keeping with the given hypothesis, patients with FM exhibited greater DMN and EAN (specifically the right half of the EAN) connectivity than healthy controls. As predicted, there was no significant difference between the MVN connectivity levels in the FM patients and healthy controls. Patients with FM had a higher intrinsic DMN connectivity to other parts of the brain that are involved in pain processing such as the left anterior, middle, and posterior insula. Meanwhile, the FMRI results showed that these same patients also had greater intranetwork connectivity within the right EAN. Additionally, the researchers found that increased levels of connectivity between both the DMN and the right EAN and the insula were positively correlated with higher patient-reported pain levels.

These neural disparities between FM patients and healthy controls could serve as biomarkers that in turn could aid in diagnosis, help to validate chronic pain symptoms, and further our understanding of the physiological basis for these symptoms. For instance, the researchers speculated that the increased connectivity between the insula and the EAN during increased subjective feelings of pain could be causing interruption of the normal functions of the EAN (working memory and attention), which could help to explain some of the cognitive deficits (also known as “fibro fog”) experienced by patients with FM. Moreover, the abnormal functioning of these brain networks adds credence to the burgeoning theory that spontaneous pain associated with FM may be more closely linked to central nervous system hyperexcitability than to pathology of the nerves outside of the brain and spinal cord.

Interestingly, the authors, in this small study, attempted to separate out the potential overlap of depression with the pain associated with FM:

“In order to test for the influence of depression on any of our pain-related results, we also evaluated whether patients with FM classified as having a high level of depression…had greater ICN connectivity in any of the regions implicated…Based on our criteria, 7 patients had a high level of depression, while the remaining 11 patients were classified as having a low level of depression. We found no significant differences (all $P>0.2$) between these two FM subpopulations…in terms of ICN connectivity to regions of interest…Of particular interest, cognitive deficits in patients with FM are correlated more with their level of pain than with psychiatric comorbidities (e.g., depression, anxiety, or sleep disruption)…”

The importance of this study is summed up by the authors:

“In this study, we present the first direct evidence between elevated intrinsic brain connectivity

and spontaneous pain intensity in patients with FM…Furthermore, our data directly link ratings of self-reported spontaneous pain at the time of the scan to the degree of both right EAN and DMN connectivity to the insula. Our findings have implications for a better understanding of the underlying brain mechanisms of endogenous clinical pain in FM, potentially pointing toward biomarkers of disease progression…"

For those wishing to read the full study, it can be obtained at: http://www.nmr.mgh.harvard.edu/~vitaly/PDF/napadow_A&R_2010.pdf