New Research Confirms Spinal Cord Is Key to Chronic Pain

Pauline Anderson | Apr 15, 2013

Fort Lauderdale, Florida — For the first time, researchers have demonstrated the involvement of the spinal cord in chronic pain.

Using resting-state functional MRI of participants in whom central sensitization had been induced and who were not experiencing pain, researchers showed the spread of functional connectivity in the spinal cord.

Although this spinal cord component had been shown in animals, this was the first time that spinal involvement in pain has been shown functionally in the resting state in humans, said Brittney R. Reyes, research assistant in the laboratory that carried out the experiments. The lab is led by Sean Mackey, MD, PhD, professor, pain medicine, anesthesia, and chief, Pain Management Division, Stanford University, California.

The new study helps contribute to the "whole picture" of chronic pain, rather than just the brain component, said Reyes. "This is the start of what will likely be a lot of spinal cord research," she told Medscape Medical News. "I think that we’re going to find that the spinal cord is as important as the brain is in terms of pain."

She presented the findings here during the American Academy of Pain Medicine (AAPM) 29th annual meeting.

Whole Picture

The study included 2 groups, each with 8 healthy volunteers. In the first group, researchers induced central sensitization by first applying heat for 5 minutes to the left lower forearm of each participant, after which they measured the area of mechanical hyperalgesia. They then applied a cream with capsaicin (a substance that blocks a chemical involved in transmitting pain signals to the brain) to the forearm for 30 minutes. When the cream was removed, they administered the heat again for another 5 minutes and then remeasured the area of mechanical hyperalgesia.

"The spread in the mechanical hyperalgesia, or secondary hyperalgesia, was seen as a sign by us that we had induced central sensitization," said Reyes.

In another nonsensitized group, researchers applied heat to the left forearm of each participant for 30 seconds and followed this with 40 seconds of rest, repeating this process 7 times. Participants in this group did not receive the capsaicin cream.

All participants had 2 scans: a "heat pain" scan that was used to functionally define the dorsal horn and a "resting state" scan during which the participants were asked to lie in the scanner without completing a task. Participants in both groups reported having no pain before or during the resting-state scan.

The resting-state scans allowed the researchers to assess spontaneous low-frequency fluctuations in signals in the spinal cord. They were looking for functional relationships between regions, or areas that act similarly, that may reflect direct or indirect relationships between regions.

"The idea behind functional connectivity is that just because a subject isn't performing a task does not mean that communication between different regions or within the central nervous system ceases," said Reyes.
The task-related heat pain scans from the nonsensitized group defined the region of interest. Researchers used this region of interest to extract time courses from the resting-state scans. "We put these time courses into our analysis as a regressor, and basically asked our model to look for areas in the spinal cord that acted similarly to this original time course."

It's believed that areas that act similarly in the spinal cord indicate functional connectivity when the subject is at rest.

**Spreading Connectivity**

The analysis of resting-state scans showed that the functional connectivity in the nonsensitized group was limited to a specific area in the C6 region of the spinal cord. However, the functional connectivity in the sensitized group extended into adjacent spinal segments, spreading from C6 to C5 in regions of the dorsal horn. This was the spread that was measured the second time in this sensitized group.

"We found that central sensitization results in a spread in functional connectivity within the spinal cord, even when subjects report having no pain," said Reyes. "Given the incidence of hyperalgesia (hypersensitivity to pain) and allodynia (sensitivity to touch) experienced by patients with chronic pain, the implication for the role of the spinal cord is very important."

The lab at Stanford is among the first to do functional imaging in the spinal cord, said Reyes. "It took a lot of technological advancements to get to this point because it's difficult to image the human spinal cord."

After the presentation, Wally Smith, MD, professor, medicine, and chair, Division of Quality Health Care, Virginia Commonwealth University School of Medicine, Richmond, complimented the team for a study that he found was "elegant, complex, and meaningful."

However, Dr. Smith asked whether functional connectivity is "a basic human trait" or whether the mechanism differs depending on the presence and type of disease. Senior author Dr. Mackey responded that this is not yet known.

"These are just the first baby steps," he said. However, he added that the team will test patients with fibromyalgia to see whether they have the same type of enhanced synchrony and connectivity across spinal cord segments.

Asked how long it takes for get central sensitivity, Dr. Mackey noted that it probably occurs rapidly, judging by the nature of the capsaicin model causing mechanical hyperalgesia outside of where the cream is applied.

"I think that for the first time we're actually showing how and where it's occurring, and at least part of the mechanism behind it."

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