CBT, Hypnosis Can Change Processing of Pain

BY KATE JOHNSON

FROM THE WORLD CONGRESS ON PAIN

MONTREAL – Psychological interventions such as cognitive-behavioral therapy and hypnosis can alter how the brain processes pain, thereby reducing patients' perception of pain, judging from findings from brain-imaging studies reported recently.

"This shows how mind and body can work in unison, and one can influence the other," said Dr. Magdalena Naylor, who works as a psychiatrist and lead investigator of one of the studies performed at the MindBody Medicine Research Clinic and Brain Imaging Program of the University of Vermont in Burlington.

The study, presented as a poster, used functional MRI (fMRI) to show that cognitive-behavioral therapy can alter dysfunctional neural circuitry associated with chronic pain.

Nine women with chronic pain resulting from low back pain or knee or hip osteoarthritis underwent fMRI before and after an 11-week CBT program for reducing pain and catastrophizing. The women's mean age was 57.5 years; their pain had an average duration of 11 years.

At baseline, amygdala reactivity in the subjects was different from that of healthy controls when they viewed emotionally upsetting photographs from IAPS (International Affective Picture System).

However, this difference disappeared after CBT, with the subjects showing reduced activity in somatosensory, frontal, and limbic areas that are associated with emotional and sensory processing, and increased activation in the left insula, Dr. Naylor said.

At the same time, the subjects reported decreased pain and better coping. Total Pain Experience scores decreased in correlation with decreased activation in the middle temporal gyrus and scores on the coping strategies questionnaire subscale of attention diversion.

VITALS

Major Finding: CBT produced changes on fMRI in patients with chronic musculoskeletal pain.

Data Source: Imaging study of nine people before and after they underwent CBT.

Disclosures: The researchers reported having no conflicts of interest.

Their score on the Beck Depression Inventory also improved in correlation with decreased activation in the superior frontal gyrus and postcentral gyrus. Dr. Naylor reported that her group has also recently published evidence of reduced pain symptoms and opioid use in a similar population (J. Pain 2010 July 8 [doi:10.1016/j.jpain.2010.03.019]).

"Our work shows that CBT decreases emotional vulnerability to negative emotions and pain, which go together," said Dr. Naylor in an interview.

"With CBT, these patients are not as emotionally dysregulated."

Her group is now examining brain structure – specifically thickness of cortices – with similar results.

"It's well documented that patients with chronic pain have thinner cortices, and this is correlated with the duration of pain.

"So we are very happy to see that with CBT we can reverse this structural damage."

Hypnosis is another psychological intervention that has been shown to alter pain processing and perception of pain, reported Dr. Marie-Elisabeth Faymonville during a workshop at the meeting.

Dr. Faymonville, who works as an anesthesiologist from the University Hospital Liège (Belgium), uses a technique called hypnosedation, which is a combination of hypnosis and local anesthesia, to help surgical patients avoid general anesthesia.

Findings from functional neuroimaging studies by her group and others have shown that patients under hypnosis show changes in neuronal activity in the presence of painful stimuli, Dr. Faymonville reported. In one recent study, her group showed that under hypnosis, painful stimuli failed to elicit cerebral activity in the pain network (Neuroimage 2009;47:1047-54).

"Increased functional connectivity between S1 and the prefrontal cortex may represent a top-down modulation of pain," she noted.

Although Dr. Faymonville's work demonstrates the impact of hypnosis on acute pain perception, another study presented as a poster at the conference showed the beneficial effect of hypnosis on chronic pain. The study included 41 patients with persistent idiopathic orofacial pain, "that is, pain in the mouth or face which cannot be explained by any kind of known disease,"Lene Baad-Hansen, D.D.S., the coinvestigator of the study, explained in an interview.

The subjects were randomized to five 1-hour sessions of active hypnotic intervention (22 subjects), which included progressive relaxation, guided imagery, and suggestions of controlling and changing pain perception, or to the same number of sessions but with progressive relaxation alone (19 subjects).

Quantitative sensory testing (QST) involving the subjects' ratings of psychophysical stimuli (such as cold, warm, tactile, and pin-prick) was performed on all subjects both before and after the intervention.

Subjective reporting showed that those who had undergone hypnosis reported a 33% reduction in orofacial pain, compared with a 3% reduction in the control group.

However, the QST tests showed no differences between the groups either before or after the intervention.

"Despite clear clinical pain relief, hypnosis does not influence somatosensory sensitivity, said Dr. Baad-Hansen of the department of clinical oral physiology in the dental school at Aarhus (Denmark) University. ■

Serotonin Synthesis Inhibitor Improves IBS Symptoms

BY AMY SCHONFELD

FROM NEUROGASTROENTEROLOGY AND MOTILITY 2010

BOSTON – LX1031, a novel, orally administered serotonin synthesis inhibitor, significantly improved overall irritable bowel syndrome symptoms in patients with nonconstipating IBS during a 4-week treatment period.

LX1031 is an investigational agent. The global response and improvement in stool form were significantly correlated with serotonergic inhibition, as indicated by the reduction of urinary levels of the serotonin metabolite 5-HIAA. Symptom improvement was greatest for those receiving high-dose LX1031 who had at least a 15% reduction in 5-HIAA levels, according to Dr. Joel P. Freiman, who presented the findings at the meeting.

"LX1031 acts locally on enterochromaffin cells in the GI tract to inhibit tryptophan hydroxylase, the rate-limiting enzyme in the synthesis of serotonin," explained Dr. Freiman, senior medical director of drug safety for Lexicon Pharmaceuticals Inc., manufacturer of LX1031.

"Reducing enteric 5-HT production via inhibition of TPH represents a mechanistically novel approach to the management of IBS symptoms," he said.

In a randomized, double-blind, placebo-controlled trial, patients with nonconstipating IBS were treated with low-dose LX1031 (250 mg q.i.d., 44 patients), high-dose LX1031 (1,000 mg q.i.d., 43 patients), or placebo (47 patients) for 28 days. The average age of participants was 48 years, and 84% were female.

At the 1,000-mg dose, patients reported "adequate relief from pain and discomfort" within 2 weeks at significantly greater levels than those reported by patients who received placebo, and this benefit was sustained through the fourth week of treatment ($P = .046$).

After 4 weeks of treatment, the urinary 5-HIAA level was reduced 31.4%, compared with those receiving placebo. The percentage change in urinary 5-HIAA over the 4-week treatment period was significantly correlated with the global response.

VITALS

Major Finding: LX1031 is a novel, orally administered serotonin synthesis inhibitor that produced a statistically significant improvement in IBS symptoms over a 4-week period in patients with nonconstipating IBS. There was a significant correlation between percent reduction in urinary 5-HIAA and global response, with the best responders to high-dose LX1031 showing at least a 15% reduction in 5-HIAA.

Data Source: A randomized, double-blind, placebo-controlled trial of 134 patients.

Disclosures: Lexicon Pharmaceuticals Inc. supported the study.

To further explore the link between response to LX1031 and serotonin inhibition, the researchers conducted a post hoc subset analysis on data from 24 patients who had received high-dose LX1031. The investigators used a 15% reduction from baseline in urinary 5-HIAA levels as the cut-off and found that 15 patients had a greater than 15% reduction while 9 patients had a smaller than 15% reduction.

The investigators also found that 73% of those in the greater than 15% reduction group reported adequate symptom relief (the high-responder group), compared with 11% of those who had a less than 15% reduction (the low-responder group).

The high responders reported significantly better scores regarding stool consistency and global improvement and trends toward better outcomes regarding measures such as pain, urgency, and bloating than did the low responders.

"Urinary 5-HIAA levels may be a biomarker that will serve as a potential guide to IBS therapy," Dr. Freiman commented.

He added that studies are planned to prospectively determine whether measuring changes in urinary 5-HIAA can predict which patients will respond best to LX1031.

Regarding safety and tolerability, most adverse events were mild, self-limited, and equally distributed among all the groups, Dr. Freiman said at the meeting, which was hosted by the American Neurogastroenterology and Motility Society.

The most common adverse events were nausea, diarrhea, vomiting, and headache. There was one serious adverse event, supraventricular tachycardia, that was thought to be unrelated to the study medication. Thirteen patients discontinued the medication, and of those, seven discontinued because of adverse events (one in the placebo group, four in the low-dose group, and two in the high-dose group). ■