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Prepared for pain? The impact of the nocebo effect on people with chronic pain

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People who have negative expectations about a treatment actually experience more pain. Merve Karacaoglu discovered in her Ph.D. research that anxious and pessimistic individuals are particularly susceptible to this nocebo effect. However, this sensitivity comes with a silver lining.

Causing someone pain in the name of science is hardly enjoyable, but it was essential for Merve Karacaoglu's research. She delved into the mechanisms behind the nocebo effect, where negative expectations lead to negative side effects. It's the kind of effect that makes you suddenly develop a headache after reading about it in a medication leaflet, or feel a dentist's needle sting a bit more sharply after hearing, "this might hurt a little." In essence, it's the negative counterpart to the better-known placebo effect.

Fibromyalgia

Karacaoglu focused her research on the nocebo effect in women with and without fibromyalgia, a condition characterized by chronic pain in muscles and connective tissue.

"This study is the first of its kind in this group, even though we know that the nocebo effect can reduce the effectiveness of pain treatments. That's why it's crucial to better understand which factors influence these patients' pain experiences and which interventions can counteract the nocebo effect."

On 4 September, she defended her dissertation, titled "Nocebo Hyperalgesia and Pain Progression: Prediction, Acquisition, and Recovery."

Both the healthy women and those with fibromyalgia were invited to the lab, where they were subjected to varying levels of pain. This was administered through a transparent cylinder that applied increasing or decreasing pressure on their thumbnail. "In other experiments, pain is often induced using ice water or heat, but we chose this cylinder because it mimics the connective tissue pain typically experienced by fibromyalgia patients."

Simultaneously, the participants were "treated" with an electronic device that did nothing—a so-called "sham device." "Beforehand, we told all participants that this device would intensify their pain. This is known as a closed-label instruction: you're essentially deceiving the participants. Although the device did nothing, it did vibrate when we pressed it, leading participants to believe that something was happening."

Nocebo stronger in healthy women

After receiving the instructions, all participants were subjected to varying levels of pain while the researchers turned the sham device on and off. "When participants saw the device light up, we increased the pressure in the cylinder. This heightened their expectation that the device would intensify the pain."

After a while, the same level of pain was applied, but this time with the sham device turned on. Those who experienced more pain under these conditions were considered more sensitive to the nocebo effect.

"We expected that women who typically suffer from chronic pain would be more affected by this nocebo effect. But, interestingly, the opposite was true: it was the healthy women who showed a stronger nocebo effect than those with fibromyalgia."

One possible explanation is that the healthy participants were less accustomed to experiencing pain and therefore entered the experiment with more anxiety. "We know that fear and nervousness amplify the nocebo effect," Karacaoglu explains.

"Women with fibromyalgia are already accustomed to chronic pain, which may make them less sensitive to anticipated pain in the controlled environment of the lab, where the pain was administered and then reduced in a safe, managed way.

"This is, of course, different from the spontaneous pain they often encounter in daily life. We do see that chronic pain patients do experience nocebo effects in a clinical setting, so further research is needed to translate that clinical environment as accurately as possible into the laboratory."

Fear increases sensitivity

In another experiment, the researchers invited only healthy participants to the lab. Beforehand, they completed a questionnaire assessing their levels of anxiety and pessimism. These participants were then subjected to pain using the cylinder, and once again, the sham device was brought out. However, this time the researchers were transparent about it.

"We explained that this was a sham device that technically would do nothing, but that they might still experience more pain due to the nocebo effect. This is known as an open-label instruction." In this experiment, they found that participants who were generally more anxious and pessimistic also reported feeling more pain during the experiment.

Interestingly, this group of participants also proved more responsive to the researchers' recovery attempts, known as counter-conditioning. "After initially instructing them that the sham device could worsen their pain, we then told them we would use the same device to reduce their pain. And those who were more anxious and pessimistic responded particularly well to this instruction. They actually experienced less pain."

"It's encouraging that we can help those most sensitive to the nocebo effect reduce their symptoms more effectively," says Karacaoglu. "This suggests that these individuals may respond well to interventions aimed at mitigating pain through learning-based interventions. This study is a good starting point, but I believe more fieldwork in clinical practice is needed to better understand these mechanisms."

More information: Read the thesis summary

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