How do we experience the pain of other people?

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A new study from the Netherlands Institute for Neuroscience recorded the neurons of human patients to show that the pain of others is directly mapped onto neurons in the insula—a brain region critical for our own emotions.

Sharing the distress of others is considered key to empathy and our motivation to help others. With people greatly differing in their ability to empathize, and some psychiatric patients lacking the ability to empathize, understanding how our brain makes the pain of others feel painful is key to understanding the origin of these individual differences.

So far, we have had to rely on fMRI studies to identify brain regions that become activated while we perceive the pain of others. Unfortunately, fMRI cannot directly measure the activity of neurons. Instead it measures changes in blood-flow that help pinpoint brain regions that are associated with empathy.

To understand where in the brain neurons help us share the distress of others, we would need to insert electrodes into the brain, and directly measure the electrical activity through which neurons process information. For obvious reasons, this is not possible in humans, or is it?

Epilepsy patients

In certain cases of epilepsy that cannot be treated using pharmacological treatments, surgeons implant electrodes directly into the brain of patients, to localize the origin of the epilepsy.

The patients then have to stay in the hospital for about a week, while the surgical team records their brain activity and waits for an epileptic event to occur. To add purpose to this waiting, some patients volunteer a unique opportunity to better understand the human mind: they engage in psychological tasks while their brain activity is measured through these medical electrodes.

In a new paper published in *eLife*, a collaboration between NIN researchers Efe Soyman, Rune Bruls, Kalliopi Ioumpa under the supervision of professors Christian Keysers and Valeria Gazzola leveraged this unique opportunity to test the notion that neurons in brain regions involved in our own pain, like the insula, contain neurons with activity that directly mirrors the pain of others.

They showed patients short video-clips of a woman experiencing various levels of pain, and measured how strongly neurons in the insula—a brain region involved in the patient's own pain experiences—respond to the pain they observe the woman in the video-clip to experience.

Specifically, they could measure intracranial local field potentials, which measure the activity of some hundreds of insula neurons close to the electrode, from 7epilepsy patients. In addition, they could zoom into the activity of individual neurons in the insula of 3 epilepsy patients.

Background: The insula and our own emotions

The insula, a brain region hidden inside of the brain, is known to play a critical role in our own emotions. It can sense the state of our body through input from our inner organs and skin, and integrates this information with what we see, hear and smell, and is thought to give rise to these conscious feelings we call emotions. In particular, it has also been shown to contain many neurons that respond when we experience pain in or on our own body, with the level of its activity scaling with how unpleasant we find this pain.

The novelty: Coding the pain of others

The team therefore explored whether neurons in this region would also represent the level of pain experiences by others. Because the movies they showed participants varied in how much pain the actress in the movies was experiencing, the team could explore whether movies in which the patients perceived others to be in more pain would be movies in which the insular neurons would show more activity—serving as a mirror for other people's pain.

This is exactly what they found: throughout the insula, they could record electrical activity that scaled with the pain the people reported perceiving in the movies. This was true in the local field potentials, and even in individual neurons, providing the first evidence, that a brain region involved in our own pain, contains a fine-grained representation of how much pain others experience.

Using advanced data analysis methods, the team could take the level of electrical activity in the insula during each movie, and predict how the patient would respond to the question: "how intense do you think the pain was that the person in the movie experienced".

By offering the unique opportunity to directly record from their brain, the patients thus provided us with a key insight into human empathy: it really looks as though we empathize with the pain of others because our brains are wired to transform their pain into activity in regions involved in our own pain.

How do we perceive the pain of others?

The team provided further insights into how we perceive the pain of others. In half the videos, the camera was focused on the facial expression of the actress, which was seen to unfold from a neutral expression to one of varying degree of pain in a period of about one second.

Analyzing the electrical responses in the insula and the muscle movements of the actress in the movies revealed that what the brain appears to use to perceive the pain of others was not the movement per se, but simply how contracted the eyes of the actress ended up being. In the other half, the camera was focusing on the hand of the actress, and showed a belt hitting the hand. In that case, the brain appeared to deduce the amount of pain from processing how much the hand was moving under the action of the belt.

Together, this revealed intricate details of how flexibly the human brain transforms what we see others do into a fine-grained perception of their inner states.

While this study focused on a single brain region, the insula, that fMRI studies had suggested to be important for empathy, future research of the team will aim to combine the data from all recorded electrodes. They can then develop a map of where in the brain, the pain of others is transformed into the nuanced empathy we can have for other people's emotions, and pinpoint the locations in which differences across individuals could account for the striking differences in empathy we can observe around us.

Christian Keysers says, "As a neuroscientist, our dream is to understand how neurons make us who we are. What these patients do, by allowing us to record from these electrodes, is to make that dream come true: we could see in real time, how the pain of someone else is mirrored in the neurons of an observer. After decades of working on empathy, we could see empathy unfold in the human insula."

Efe Soyman says, "Other people's suffering can be inferred from a variety of indicators: a painful expression, the intensity of the event that inflicts pain in them, etc. With this incredibly valuable data we collected from the patients, we see how the

human insula might tune into whichever is available among these various cues when we experience the pain of other people."

More information: Efe Soyman et al, Intracranial human recordings reveal association between neural activity and perceived intensity for the pain of others in the insula, *eLife* (2022). DOI: 10.7554/eLife.75197

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