# When touch turns to pain

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Researchers in Tübingen and Trieste (Italy) have made a major contribution to understanding the sense of touch and pain. A team led by Dr Jing Hu (Werner Reichardt Centre for Integrative Neuroscience – CIN, Tübingen) discovered that two substances contained within nerve cell membranes have a crucial impact on our perception of touch. They were able to show how the interaction of these two substances can be interrupted in such a way that touch stimuli are not transmitted and constant pain is alleviated.

How we feel what we feel: this question has occupied neuroscientists for a long time. We know less about the sense of touch than any other of our five senses – even though the skin covers our entire bodies. But more importantly, millions of patients suffering pain could expect more efficacious help if we knew more about the origins of our tactile sense.

Pushing, pulling, piercing, chafing – these words can describe perceptions of touch; but in exaggerated form, they can also become sources of pain. A mechanical contact produces an electrical impulse in the cellular membranes of neurons that conduct touch stimuli to the brain, known as mechanoreceptors. However until relatively recently, scientists were unable to explain just how this happens and which biochemical and biophysical mechanisms are at work. Since the 1980s we have at least known that ion channels play a major role: when the nerve cell is deformed, this stimulates certain proteins that run right through the cell membrane like a channel. The deformation opens this protein channel for a specific kind of ion, which enters the cell and produces an electrical impulse.

Dr. Hu and her team were now able to show that this is not all: the cell membrane surrounding the ion channels is just as important. If it is soft, it yields easily to pressure, which does not create an impulse. But if it is more rigid, the ion channels in the area respond strongly to the deformation.

The behavior of these cell membranes is controlled by two substances. That molecule of ill repute, cholesterol, has been well-known for a long time. But Hu and her colleagues now showed that – at least in mice – a stomatin-like protein-3, or STOML3, plays a decisive role too. Only the interaction of cholesterol and STOML3 effects a stiffening of the cell membrane under soft pressure. This makes the activation of surrounding ion channels possible. If one of the pieces of this puzzle is not present, or if their reaction is disrupted, there is no stimulus.

Through behavioral studies in mice, the scientists showed that this mechanism could apply similarly in human pain patients. If new drugs are developed following this line of inquiry, even patients suffering from allodynia might stand to benefit in the future: this condition turns even the slightest of touches into intense pain.

**More information:** Yanmei Qi et al. "Membrane stiffening by STOML3 facilitates mechanosensation in sensory neurons," *Nature Communications* (2015). DOI: 10.1038/ncomms9512

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