

People with DFNA2 hearing loss show increased touch sensitivity

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People with a certain form of inherited hearing loss have increased sensitivity to low frequency vibration, according to a study by Professor Thomas Jentsch of the Leibniz-Institut für Molekulare Pharmakologie (FMP)/Max Delbrück Center for Molecular Medicine (MDC) Berlin-Buch and Professor Gary Lewin (MDC), conducted in cooperation with clinicians from Madrid, Spain and Nijmegen, the Netherlands. The research findings, which were published in *Nature Neuroscience*, reveal previously unknown relationships between hearing loss and touch sensitivity: In order to be able to 'feel', specialized cells in the skin must be tuned like instruments in an orchestra.

The members of the Spanish and Dutch families who participated in the study were quite amazed when the researchers from Berlin unpacked their testing equipment. Many of the family members suffer from hereditary DFNA2 [hearing loss](#), but the researchers were less interested in their hearing ability than in their sense of touch. The hearing impairment is caused by a mutation which disrupts the function of many hair cells in the inner ear. This mutation, the researchers suspected, might also affect the sense of touch.

Tiny, delicate hairs in our inner ear vibrate to the pressure of the sound waves. The vibrations cause an influx of positively charged potassium ions into the hair cells. This electric current produces a nerve signal that is transmitted to the brain – we hear. The potassium ions flow through a channel in the cell membrane and again out of the hair cells. This potassium channel, a protein molecule called KCNQ4, is destroyed by

the mutation in hearing-impaired people. The sensory cells gradually die off due to overload. "But we have found that KCNQ4 is present not only in the ear, but also in some sensory cells of the skin," Thomas Jentsch explained. "This gave us the idea that the mutation might also affect the sense of touch. And this is exactly what we were able to show in our research, which we conducted in a close collaboration with the lab of Gary Lewin, a colleague from the MDC who is specialized in touch sensation."

Whether we caress our child, search in our bag for a certain object or hold a pen in our hand – each touch conveys a variety of precise and important information about our environment. We distinguish between a rough and smooth surface by the vibrations that occur in the skin when the surface is stroked. For the different touch stimuli there are sensory cells in the skin with different structures – through the deformation of the delicate structures, electric nerve signals are generated. Exactly how this happens is still a mystery – of the five senses of Aristoteles, the sense of touch is the least understood.

Clearly there are parallels to hearing, as the findings of Matthias Heidenreich and Stefan Lechner from the research groups of Thomas Jentsch and Gary Lewin show. As a first step, the researchers in the Jentsch lab created a mouse model for deafness by generating a mouse line that carries the same mutation in the potassium channel as a patient with this form of genetic hearing loss. The touch receptors in the skin where the KCNQ4 potassium channel is found did not die off due to the defective channel like they did in the ear, but instead showed an altered electric response to the mechanical stimuli in the mutated mouse. They reacted much more sensitively to [vibration](#) stimuli in the low frequency range. The outlet valve for potassium ions normally functions here as a filter to dampen the excitability of the cells preferentially at low frequencies. This normally tunes these mechanoreceptors to moderately high frequencies in normal people. In mice lacking functional KCNQ4

channels, these receptors can no longer distinguish between low and high frequencies.

The deaf patients with mutations in the potassium channel who were examined by Stefan Lechner and Matthias Heidenreich showed exactly the same effect. They could even perceive very slow vibrations that their healthy siblings could not perceive. Due to mutations in the KCNQ4 channel gene, the fine tuning of the mechanoreceptors for normal touch sensation was altered.

The sensation of touch varies greatly from person to person – some people are much more sensitive to touch than others. DFNA2 patients are extremely sensitive to vibrations, according to Gary Lewin and Thomas Jentsch. "The skin has several different types of mechanoreceptors, which respond to different qualities of stimuli, especially to different frequency ranges. The interaction of different receptor classes is important for the touch sensation. Although the receptors we studied became more sensitive due to the loss of the potassium channel, this may be outweighed by the disadvantage of the wrong 'tuning to other frequencies'. With KCNQ4 we have for the first time identified a human gene that changes the traits of the touch sensation."

More information: KCNQ4 K⁺ channels tune mechanoreceptors for normal touch sensation in mouse and man. [dx.doi.org/10.1038/nn.2985](https://doi.org/10.1038/nn.2985)

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