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Cold-induced pain linked to the garlic and mustard receptor

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Some people experience cold not only as feeling cold, but actually as a painful sensation. This applies even to fairly mild temperatures – anything below 20°C. A group of researchers from Lund University in Sweden have now identified the mechanism in the body that creates this connection between cold and pain. It turns out that it is the same receptor that reacts to the pungent substances in mustard and garlic.

Professor of Pharmacology Peter Zygmunt and Professor of Clinical Pharmacology Edward Högestätt have long conducted research on pain and the connection between pain and irritant substances in mustard, garlic and chilli. In large quantities, these strong spices can cause burning or irritant sensations in the mouth and throat, and can also cause rashes and swelling. When the eyes are exposed, these spices produce strong pain and lacrimation, a property that has been exploited in pepper spray and tear gas. The reason is that the substances affect nerves that are part of the pain system and that are activated by inflammation.

Ten years ago, the Lund research group identified the receptor for mustard and garlic, i.e. the way in which the pungent substances in the spices irritate the nerve cells. Since then, the question of whether this receptor also responds to cold has been a matter of debate. However, the researchers have now demonstrated that this is the case.

"We have worked with Professors of Biochemistry Urban Johanson and Per Kjellbom here in Lund to extract the human receptor protein and insert it into an artificial cell membrane. There we could see that it

reacted to cold," explained Peter Zygmunt.

The findings increase our knowledge of the human body's temperature senses. However, they could also help all those who suffer from cold allodynia, i.e. who are over-sensitive to cold and experience pain when exposed to cold.

"These problems are very common in patients with chronic pain or diseases that affect the nervous system, such as diabetic neropathy. Patients undergoing chemotherapy can also become over-sensitive to cold as a side-effect of their medication. The discomfort and pain experienced by patients can start at relatively mild temperatures, within the temperature span to which the mustard and garlic receptor reacts," said Edward Högestätt.

Receptors for mustard and garlic are found in many locations in the body, including in the skin, bladder and gut. A number of pharmaceutical companies are now attempting to develop drugs to block the receptors in order to reduce problems such as itching, incontinence and pain. The Lund researchers believe that blocking the receptors ought also to relieve pain caused by cold.

Moreover, it is known that the mustard and garlic receptor reacts to chemical substances that irritate the airways. Possible new drugs for people who are affected by perfume, solvents, cigarette smoke, car exhausts and suchlike should therefore also benefit those who are over-sensitive to cold in the airways.

The discovery of the link between the mustard and garlic receptor and cold means that a further part of human temperature sensing has been charted.

"We already know that the chilli receptor not only reacts to chilli, but

also to temperatures over 42°C, such as when you burn yourself on a fire. The menthol receptor reacts to temperatures under 28°C, which are perceived as pleasantly cooling. And now we know that the mustard and garlic receptor reacts to temperatures under 20°C," said Peter Zygmunt.

More information: "Human TRPA1 is intrinsically cold- and chemosensitive with and without its N-terminal ankyrin repeat domain", *PNAS*, Lavanya Moparthia, Sabeen Surverya, Mohamed Kreirb,c, Charlotte Simonsend, Per Kjellboma, Edward D. Högestättd, Urban Johansona, and Peter M. Zygmuntd. Edited by Lutz Birnbaumer, National Institute of Environmental Health Sciences, Research Triangle Park, NC, and approved October 14, 2014 (received for review July 7, 2014) DOI: 10.1073/pnas.1412689111

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