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Dorsal horn neurons were characterized according to their input from cutaneous myelinated and unmyelinated fibres. Units receiving input from both classes of primary afferents were found to respond to stimulation of low threshold mechanoreceptors and of nociceptors. The nociceptor-induced discharges of these neurons were tonically depressed by descending control systems and also by stimulation of collateral fast-conducting afferent nerve fibres. Both types of inhibition were found to be independent of each other. [The *SCI* ® and the *SSCI* ® indicate that this paper has been cited in more than 265 publications.]

The Quest for Spinal Pain Neurons

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In the early 1970s, the physiology of pain had gained renewed interest triggered mainly by the controversy over the physiological mechanisms presumed by R. Melzack and P.D. Wall's gate control hypothesis.[1] There was a general feeling among the researchers in this field that a more precise analysis of the transmission of nociceptive input in the spinal dorsal horn would be crucial for a better understanding of pain mechanisms. It also was clear that controlled natural stimulation of sensory nerve endings, and not merely electrical stimulation of peripheral nerve trunks, was required to provide the relevant input for such an analysis.

Thus, when the youngest of us (Handwerker) came from Zürich to Heidelberg to join M. Zimmermann in the 2d Department of Physiology, we decided to start with an attempt toward a better characterization of the cutaneous nociceptors forming the input to the central nervous system using well-controlled forms of noxious stimulation.[2] With that study at the level of primary afferent fibres, we continued a line of research that had been initiated by A. Iggo more than a decade before.[3]

Shortly afterward, we had the opportunity to work together when Iggo came for a few months to Heidelberg as a guest professor. We decided to extend the analysis of nociceptive information processing to the secondary neurons in the spinal dorsal horn and posed the question, "Which of the neurons receiving mono- and polysynaptic input from primary afferents are relevant for pain?" Of course, we were intrigued by the nociceptor-specific cells in lamina I of the dorsal horn, which had been described two years before by P.N. Christensen and E.R. Perl.[4] However, when we searched for them with well-controlled electrical stimulation of A and C fibres, and with natural stimulation of cutaneous mechanoreceptors and nociceptors, we found that neurons receiving both types of input were much easier to encounter. Of course, the time of the guest professorship was limited, and thus we decided to concentrate on that group of neurons that we labelled "class 2." We found that these neurons were quite efficient in coding the information from cutaneous nociceptive C fibres evoked by controlled radiant heat stimulation of the skin. This provided an argument in favor of their possible relevance for the processing of pain and the mediation of nocifensive reflexes.

Apparently these class 2 neurons had some features in common with Melzack and Wall's[1] hypothetical "T cells," and hence we studied the modulation of their nociceptive responses by stimulation of myelinated afferents. In addition, we used a cold block of the spinal cord to switch off the descending modulation from the brain. Both activation of myelinated afferents and descending influences resulted in the depression of the responses of class 2 cells to noxious input, and apparently these two modulating systems acted independently of each other.

For the three of us, it was great fun to work together in the laboratory in the Haus Landfried, a former tobacco factory, where the 2d Department of Physiology was temporarily located at the time. The laboratories were grouped around a large social room in which we often sat discussing our experiments over a cup of coffee or tea. A big advantage of this old house was that it was located at some distance from the rest of the university buildings, where, at that time, the aftermath of the German student revolution still provided a somewhat disturbed environment for scientific work.

Most data were collected during a frenetic few weeks. But after the departure of Iggo, it took some time to bring the paper together. Control experiments were performed and several drafts of the manuscript crossed the channel in both directions. Probably the paper gained from this slow maturation. When agreement on the final draft had been obtained, the new journal *Pain* was announced, and we decided to submit the paper there and not to one of the established journals. Indeed, it appeared in volume 1 of *Pain*, which proves that sometimes papers in new journals may be quite successful.

Analysis of the transmission in the dorsal horn has continued till today.[5,6] In particular, the descending inhibitory systems have turned out to provide a powerful control of the brain on the incoming nociceptive information.[5,6] Meanwhile, the activation of spinal inhibitory systems became one of the guiding concepts in the development of new analgesic therapies.

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2. **Beck P W, Handwerker H O & Zimmermann M.** Neuronal outflow from the cat's foot during noxious radiant heat stimulation. *Brain Res.* 67:373-86, 1974. (Cited 215 times.)
3. **Iggo A.** Cutaneous heat and cold receptors with slowly conducting (C) afferent fibres. *Quart. J. Exp. Physiol.* 44:362-70, 1959. (Cited 145 times.)
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6. **Yaksh T L,** ed. *Spinal afferent processing.* New York: Plenum Press, 1986.

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