



Clinical Note

Pain affect without pain sensation in a patient with a postcentral lesion

M. Ploner, H.-J. Freund, A. Schnitzler*

Department of Neurology, University of Duesseldorf, Moorenstrasse 5, 40225 Duesseldorf, Germany

Received 13 October 1998; received in revised form 29 December 1998; accepted 1 January 1999

Abstract

We report findings from clinical examination and cutaneous laser stimulation in a 57-year-old male, who suffered from a right-sided postcentral stroke. In this patient, we were able to demonstrate (i) a dissociation of discriminative and affective components of pain perception and, for the first time in humans, (ii) the dependence of sensory-discriminative pain component and first pain sensation on the integrity of the lateral pain system. © 1999 International Association for the Study of Pain. Published by Elsevier Science B.V.

Keywords: Pain perception; Somatosensory cortex

1. Introduction

Cerebral structures involved in pain processing are commonly divided into a lateral and a medial pain system (Albe-Fessard et al., 1985). These two systems diverge at the thalamic level. The main constituents of the lateral pain system are the lateral thalamic nuclei and the primary (SI) and secondary (SII) somatosensory cortices (Kenshalo and Willis, 1991). The medial pain system essentially consists of the medial thalamic nuclei and the anterior cingulate cortex (Vogt et al., 1993).

These anatomically segregated systems are supposed to subservise functionally different components of pain perception. Experimental and lesion data in humans indicate a close association between motivational-affective aspects of pain and the medial pain system (Vogt et al., 1993; Craig et al., 1996; Rainville et al., 1997). However, an association between the sensory-discriminative component of pain perception and the lateral pain system, as deduced from neurophysiological experiments in monkeys (Kenshalo and Willis, 1991), has not yet unequivocally been proven in humans.

A further characteristic of pain perception is the appearance of two subsequent and qualitatively distinct sensations

following single painful stimuli. Peripherally, the neural basis of this phenomenon is a dual pathway for pain with A δ -fibers mediating pricking first pain and C-fibers mediating dull second pain (Bishop and Landau, 1958). Centrally, a representation of first pain in the lateral pain system has been suggested (Hassler, 1976), but no direct evidence for this has been presented so far.

Here, we report findings from clinical examination, cutaneous laser stimulation and magnetic resonance imaging (MRI) of a patient with a selective ischemic lesion of the right SI and SII cortices. This patient offered the unique possibility to study possible dissociations between sensory-discriminative and motivational-affective components of pain perception and between first and second pain. Our results demonstrate, for the first time in humans, a loss of pain sensation with preserved pain affect, and provide clear evidence for the crucial role of the lateral pain system in the sensory-discriminative pain component and in first pain sensation.

2. Case report*2.1. Case history*

A 57-year-old male with no history of previous neurological diseases suffered from a cardioembolic stroke in the

* Corresponding author. Tel.: +49-211-811-7893; fax: +49-211-811-9033; e-mail: schnitz@neurologie.uni-duesseldorf.de

territory of the right middle cerebral artery. While initial left hemiparesis resolved within the first few hours left-sided sensory deficits persisted. MRI performed 3 days after stroke showed a lesion confined to the right postcentral gyrus and the parietal operculum extending from 12 mm to 54 mm above the anterior commissure-posterior commissure-line, thus comprising the hand area of SI and SII (Fig. 1). No other lesions were visible on the scans studied. Preserved median nerve somatosensory evoked short-latency potentials and diminished long latency potentials suggested integrity of peripheral somatosensory pathways and partial lesion of SI.

2.2. Clinical examination

Evaluation of the patient's deficits 5 and 12 days after stroke was based on extensive clinical examination including light touch, static tactile thresholds with von Frey-hair stimuli, two-point and sharp-dull discrimination, sense of movement, graphaesthesia, stereognosis, thermaesthesia (test tubes filled with hot and cold water), pallesthesia and motor testing.

While sensory examination of the patient's right side was within normal limits, left-sided examination revealed hypaesthesia of foot, leg and face and anaesthesia of hand and arm, in all the above mentioned tests except for nearly normal pallesthesia (Table 1). In particular, thermal stimuli did not evoke any sensation. Motor testing showed only

marginal left-sided pronation when maintenance of arms against gravity was examined without any further motor deficit. These deficits remained stable and unchanged across the two examinations.

2.3. Cutaneous laser stimulation

Controlled, selective thermanociceptive stimuli were applied by means of cutaneous laser stimulation (Bromm and Treede, 1991) using a Tm:YAG-Laser (Baasel Lasertechnik) with a wavelength of 2000 nm, a pulse duration of 1 ms and a spot diameter of 6 mm. Twelve days after stroke, pain thresholds on the dorsum of feet and hands were determined with increasing and decreasing stimulus intensities at 50 mJ steps (actual output intensity can vary up to 5% from demanded intensity). The threshold was defined as intensity that elicited painful sensations in at least three of five applications. Reaction times to 20 painful laser stimuli (stimulus intensity 450 mJ) applied to the dorsum of each hand were measured in two subsequent runs. Stimulation site was slightly changed between successive stimuli, interstimulus intervals varied randomly between 10 and 14 s. The patient was instructed to lift the index finger contralateral to stimulation as soon as any sensation was perceived. Finger lift was detected by a photoelectric barrier. Due to the failure to correctly place the index finger of the proprioceptively impaired left hand into the photoelectric barrier motor reactions of the sensory impaired left hand could not be recorded

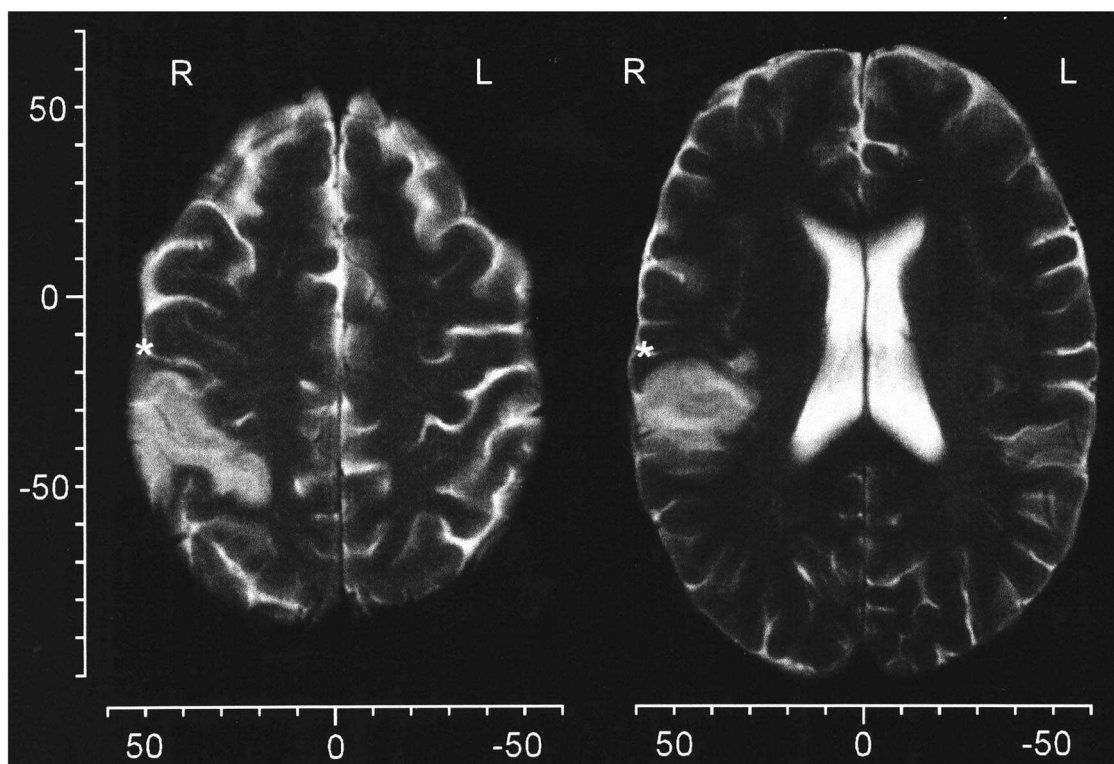


Fig. 1. Transaxial MRI-slices at 42 mm (left) and 18 mm (right) parallel above the anterior commissure-posterior commissure-line. Scales give coordinates in mm according to the Talairach frame of reference (Talairach and Tournoux, 1988). Markers (*) indicate the central sulcus.

Table 1

Sensory testing	Right hand	Left hand
von Frey-hair stimuli (mN)	2.83	>6.65
Two-point-discrimination (mm)	12	–
Sharp-dull-discrimination ^a	5/5	0/5
Sense of mcp joint movement ^a	5/5	0/5
Graphaesthesia ^a	5/5	0/5
Stereognosia ^a	5/5	0/5
Pallaesthesia (tuning fork)	100%	75%
Pain threshold (mJ)	200	– ^b

^aNumber of correct trials.

^bAt 350 mJ and more the patient described a ‘clearly unpleasant’ feeling. mcp, metacarpophalangeal; –, no sensation.

and thus reaction times could not be determined for six stimuli to the normal right hand. In two prior control runs mean reaction times to binaural acoustic stimuli had been 300 ms (SD = 67 ms) for right index finger lift and 246 ms (SD = 64 ms) for left index finger lift, so that prolonged reaction times due to accompanying left-sided motor deficits could reliably be excluded.

Pain thresholds were 200 mJ for right hand and both feet. Evoked pain sensations were characterized as ‘pinprick-like’ and were well localized within 2–3 cm. For left hand, up to an intensity of 600 mJ, no pain sensation could be elicited. However, at intensities of 350 mJ and more, the patient spontaneously described a ‘clearly unpleasant’ intensity dependent feeling emerging from an ill-localized and extended area ‘somewhere between fingertips and shoulder’, that he wanted to avoid. The fully cooperative and eloquent patient was completely unable to further describe quality, localization and intensity of the perceived stimulus. Suggestions from a given word list containing ‘warm’, ‘hot’, ‘cold’, ‘touch’, ‘burning’, ‘pinprick-like’, ‘slight pain’, ‘moderate pain’ and ‘intense pain’ were denied nor did the patient report any kind of paraesthesias (all descriptions translated from German). Reaction times to laser stimuli on the right hand showed a bimodal distribution with medians at 400 ms and 1000 ms. By contrast, stimulation of the left hand yielded exclusive long-latency responses with a median at 1426 ms (Fig. 2).

3. Discussion

In the patient reported here, clinical examination and cutaneous laser stimulation revealed prolonged reaction times to painful laser stimuli, an elevated pain threshold, loss of sensory-discriminative pain component and preserved motivational-affective dimension of pain. This clear perceptual dissociation was paralleled by an anatomical dissociation between affected lateral pain system and spared medial pain system. This pattern of impairment shows the essential role of SI and/or SII for the sensory-discriminative aspects of pain perception in humans. By

contrast, detection of and reaction to painful stimuli as well as pain affect do obviously not require integrity of SI and SII. Nevertheless, damage to SI and SII produced hypalgesia in our patient, suggesting interaction between medial and lateral pain system in normal pain experience.

Most previous lesion studies in humans agreed on the crucial importance of the postcentral gyrus and/or the parietal operculum in pain perception (Sweet, 1982; Boivie et al., 1989; Greenspan and Winfield, 1992). Although these studies are clinically well documented, the partial lack of information about lesion extent, presence of additional lesions and manifold, and ambiguous clinical presentations interfered with a consistent concept of these structures in human pain perception. Moreover, clinical examination of pain perception was carried out with non-selective pain-evoking stimuli. Thus, activation of pain afferents was always contaminated by activation of tactile pathways. Cutaneous laser stimulation, as applied in our study, overcomes this limitation by selective activation of thermanociceptive afferents (Bromm and Treede, 1991). Thus, our findings refer to cutaneous but not necessarily to deep nociception.

More recent evidence for an involvement of SI and SII in pain processing comes from functional imaging studies. Most of them showed pain associated increases of cerebral blood flow in contralateral SI and SII (Talbot et al., 1991; Coghill et al., 1994; Casey et al., 1996; Craig et al., 1996; Andersson et al., 1997; Derbyshire et al., 1997; Rainville et al., 1997). According to the Talairach-coordinates (Talairach and Tournoux, 1988), activation foci were located in regions corresponding to our patient’s lesion. But again,

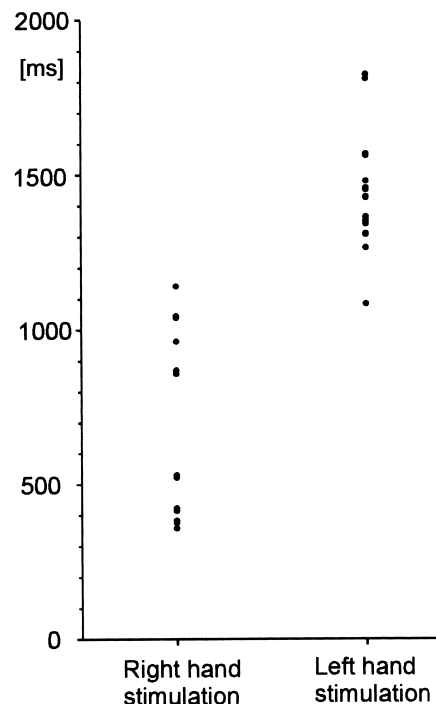


Fig. 2. Reaction times to cutaneous laser stimulation of the normal right ($N = 14$) and the affected left ($N = 20$) hand.

only in a few of these studies were selective painful stimuli applied (Andersson et al., 1997; Derbyshire et al., 1997). Additionally, while it has been possible to vary pain affect experimentally without changing physical stimulus parameters (Craig et al., 1996; Rainville et al., 1997), an inverse experiment has not yet been carried out. Thus, selective evaluation of the sensory-discriminative pain component and the subserving cerebral structures is lacking.

Our observation of an association between SI and sensory-discriminative pain component is supported by experimental animal data (Kenshalo and Willis, 1991): nociceptive neurons in SI of monkeys encode stimulus intensity and are somatotopically organized, features that are predestinating for discriminative functions. By contrast, nociceptive neurons in SII seem to reflect learning of, or attention to, pain-evoking stimuli rather than direct involvement in sensory-discriminative aspects of pain perception.

While bimodal distribution of reaction times to laser stimulation of the unaffected right hand is in accordance with previous results in healthy subjects (Campbell and LaMotte, 1983), reaction times to left-sided painful stimuli showed a loss of short-latency responses that are believed to be related to activation of A δ -fibers and first pain sensation (Campbell and LaMotte, 1983). Thus, loss of short-latency reactions in our patient supports generation of first pain sensation in the lateral pain system (Hassler, 1976). Interestingly, both the patient's description of the perceived stimulus and the prolonged reaction times to laser stimulation of the affected left hand are not fully consistent with properties of second pain (Bishop and Landau, 1958; Campbell and LaMotte, 1983). In agreement with results of human psychophysical (Koltzenburg et al., 1993) and imaging (Andersson et al., 1997) studies using selective C-fiber stimulation, this suggests a contribution of the lateral pain system to second pain sensation.

In conclusion, we were able to demonstrate, for the first time in humans, the representation of sensory-discriminative pain component and first pain sensation in the lateral pain system. In contrast, pain affect and the ability to detect painful stimuli do not, in principle, require integrity of these structures.

Acknowledgements

This study was supported by the Huneke-Stiftung and the Deutsche Forschungsgemeinschaft (SFB 194). Thanks to Dr. C.J. Ploner (Charité Berlin) for helpful comments on the manuscript.

References

- Albe-Fessard, D., Berkley, K.J., Kruger, L., Ralston, H.J. and Willis, W.D., Diencephalic mechanisms of pain sensation, *Brain Res.*, 356 (1985) 217–296.
- Andersson, J.L., Lilja, A., Hartvig, P., Langstrom, B., Gordh, T., Handwerker, H. and Torebjork, E., Somatotopic organization along the central sulcus, for pain localization in humans, as revealed by positron emission tomography, *Exp. Brain Res.*, 117 (1997) 192–199.
- Bishop, G.H. and Landau, W.M., Evidence for a double peripheral pathway for pain, *Science*, 128 (1958) 712–713.
- Boivie, J., Leijon, G. and Johansson, I., Central post-stroke pain—a study of the mechanisms through analyses of the sensory abnormalities, *Pain*, 37 (1989) 173–185.
- Bromm, B. and Treede, R.D., Laser-evoked cerebral potentials in the assessment of cutaneous pain sensitivity in normal subjects and patients, *Rev. Neurol. (Paris)*, 147 (1991) 625–643.
- Campbell, J.N. and LaMotte, R.H., Latency to detection of first pain, *Brain Res.*, 266 (1983) 203–208.
- Casey, K.L., Minoshima, S., Morrow, T.J. and Koeppe, R.A., Comparison of human cerebral activation pattern during cutaneous warmth, heat pain, and deep cold pain, *J. Neurophysiol.*, 76 (1996) 571–581.
- Coghill, R.C., Talbot, J.D., Evans, A.C., Meyer, E., Gjedde, A., Bushnell, M.C. and Duncan, G.H., Distributed processing of pain and vibration by the human brain, *J. Neurosci.*, 14 (1994) 4095–4108.
- Craig, A.D., Reiman, E.M., Evans, A. and Bushnell, M.C., Functional imaging of an illusion of pain, *Nature*, 384 (1996) 258–260.
- Derbyshire, S.W., Jones, A.K., Gyulai, F., Clark, S., Townsend, D. and Firestone, L.L., Pain processing during three levels of noxious stimulation produces differential patterns of central activity, *Pain*, 73 (1997) 431–445.
- Greenspan, J.D. and Winfield, J.A., Reversible pain and tactile deficits associated with a cerebral tumor compressing the posterior insula and parietal operculum, *Pain*, 50 (1992) 29–39.
- Hassler, R., Interaction between the systems involved in fast pain perception and in slow, persistent pain, *Langenbecks Arch. Chir.*, 342 (1976) 47–61.
- Kenshalo, D.R. and Willis, W.D., The role of the cerebral cortex in pain sensation. In: A. Peters and E.G. Jones (Eds.), *Cerebral Cortex*, Vol. 9, Plenum Press, New York, 1991, pp. 153–212.
- Koltzenburg, M., Handwerker, H.O. and Torebjork, H.E., The ability of humans to localise noxious stimuli, *Neurosci. Lett.*, 150 (1993) 219–222.
- Rainville, P., Duncan, G.H., Price, D.D., Carrier, B. and Bushnell, M.C., Pain affect encoded in human anterior cingulate but not somatosensory cortex, *Science*, 277 (1997) 968–971.
- Sweet, W.H., Cerebral localization of pain. In: R.A. Thompson and J.R. Greer (Eds.), *New Perspectives in Cerebral Localization*, Raven Press, New York, 1982, pp. 205–242.
- Talairach, J. and Tournoux, P., *Co-planar Stereotaxic Atlas of the Human Brain*, Thieme, Stuttgart, 1988.
- Talbot, J.D., Marrett, S., Evans, A.C., Meyer, E., Bushnell, M.C. and Duncan, G.H., Multiple representations of pain in human cerebral cortex, *Science*, 251 (1991) 1355–1358.
- Vogt, B.A., Sikes, R.W. and Vogt, L.J., Anterior cingulate cortex and the medial pain system. In: B.A. Vogt and M. Gabriel (Eds.), *Neurobiology of Cingulate Cortex and Limbic Thalamus: a Comprehensive Handbook*, Birkhauser, Boston, MA, 1993, pp. 313–344.