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# Dorsal Rhizotomy Changes the Spontaneous Neuronal Activity of Nuclei in the Medial Thalamus

Š. VACULÍN, M. FRANĚK, R. ROKYTA

*Department of Normal, Pathological and Clinical Physiology, Charles University, Third Faculty of Medicine, Prague, Czech Republic*

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## Summary

The aim of this study was to examine the influence of unilateral dorsal root section at the cervicothoracic level of the spinal cord on the spontaneous neuronal activity of medial thalamic nuclei in the rat. Single unit extracellular recordings from thalamic nuclei, nc. parafascicularis and nc. centralis lateralis, were obtained with glass micropipettes. The abnormal bursting activity of these nuclei following deafferentation was registered, although a correlation between the occurrence of this activity and the degree of autotomy behavior was not found. Such bursts were never observed in the studied thalamic nuclei of control rats.

**Key words**

Deafferentation • Medial thalamus • Single neuronal unit activity

## Introduction

Unilateral dorsal root section in the rat is used as a model of central pain (Basbaum 1974), which often develops after brachial plexus avulsion in man (Nashold and Ovelment-Lewitt 1991). After a few days, typical automutilating behavior occurs in such operated rats. This is considered to have a close relation to the pain originating in central structures because there are no more inputs available from the periphery after deafferentation. This behavior consists of licking, scratching and biting the deafferented extremity. Changes after dorsal root section have been described at several levels: the spinal cord, lateral thalamus and cerebral cortex (Albe-Fessard and Rampin 1991). At the lateral thalamic and cortical levels, two types of abnormal activity were found: short bursts of spikes in phase with a wave exhibiting permanent activity and periodically occurring trains of waves with spikes. In spite of the fact that the medial thalamus is considered to form the basis of a "medial pain system" (Vogt 1993), there is no evidence of the electrophysiological changes in the medial thalamus. The medial pain system is involved in processing the motivational-affective features of noxious stimuli and which is of particular importance in the chronic pain syndrome. The medial thalamus consists of two groups of nuclei: rostral and caudal. Nucleus centrum medianum (CM), nc. centralis lateralis (CL) and nc. parafascicularis (pF) are of major importance in this connection. Because of the small size of the CM nucleus and that its function is mostly exerted by the pF in rodents, we investigated the pF and CL nuclei.



Fax +420 2 249 20 590
E-mail: physres@biomed.cas.cz http://www.lf2.cuni.cz/physiolres/physiolres.htm

## Methods

Twenty-five male Wistar rats (16 deafferented and 9 control rats) weighing between 340 and 420 g were used for this study. We employed the same anesthesia for both the deafferentation and the actual recordings. The rats were anesthetized by intramuscular injection of a combination of ketamine (Narkamon 5 %, 100 mg/kg) and xylazine (Rometar 2 %, 16 mg/kg). The rectal temperature of the animals was maintained between 37-38 °C. Section of the dorsal roots C5-Th1 proximal to the spinal ganglion was performed on the left side. After the operation, the animals were kept separately in individual cages and were continuously observed. Immediately after the onset of the autotomy behavior extracellular single unit activity was recorded. According to the Swanson atlas, the stereotaxic coordinates were: AP –4.2 mm, LL 1.5 mm and DV 3.6-6.0 mm to the bregma. Micropipettes were filled with a solution of 0.5 M potassium chloride and Pontamin Sky Blue dye and their resistance was 5-10 MΩ. In control animals, only extracellular single activity was recorded. The data were digitized at a sampling rate of 2000, 3000 or 4000 Hz. The program developed in our laboratory using Microsoft Excel disclosed the differences between spontaneous neuronal activity in control and deafferented rats graphically (the histogram of interspikes intervals). Due to the qualitative difference of the results, no other statistical procedure was employed. At the end of each experiment, the recording sites were marked by an iontophoretically deposited dye, the animals were given an overdose of ketamine and then transcardially perfused with 4 % paraformaldehyde. The brain was removed and incubated in 20 % glucose before freezing and sectioning at 50 μm. The sections were stained with a cresyl violet dye and histologically examined (Nissl method).

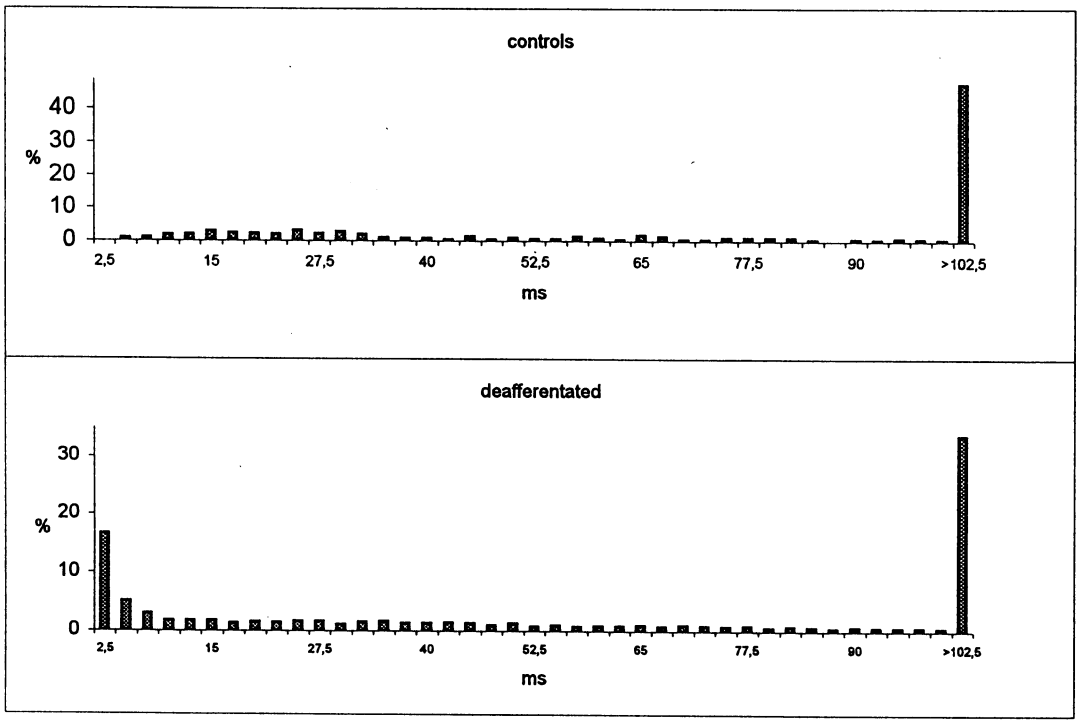


**Fig. 1.** *The histograms of interspikes intervals show the differences between spontaneous neuronal activity of deafferented and control rats.*

## Results

Abnormal behavior occurred in six animals (37.5 %) with deafferentation. In three rats this behavior consisted of licking the extremity (depilation) and in three rats we observed scratching and nibbling. Ten rats (62.5 %) did not exhibit any symptoms of abnormal behavior. Data were obtained from 78 neurons (pF and CL) in deafferented animals and from 33 neurons in control rats. In deafferented rats, 56 neurons were situated contralaterally and 22 ipsilaterally, in the controls it was 25 and 8 neurons, respectively. Two types

of neurons were found in the deafferented rats according to the shape and frequency of spikes: 1) individual spikes and waves or 2) bursts of spikes and waves. Characteristic bursting activity (Fig. 2) was noted in 36 contralateral (64.3 %) and 14 ipsilateral thalamic neurons (63.6 %) of deafferented rats. This activity was composed of a succession of bursts of spikes and waves separated from the next burst by a period of silence or bursts appeared irregularly amongst „normal" spontaneous activity. The bursts comprised 2-6 spikes and waves; their intraburst frequency attained 400 Hz. On the other hand, no correlation was found between the degree of automutilation and the occurrence of the bursts. In the medial thalamic nuclei of all rats exhibiting automutilation bursting activity was always found, but not *vice versa.* Recordings containing bursts were obtained from some but not all neurons of deafferented rats. Bursting activity was never seen in the medial thalamic nuclei of control rats (Fig. 1). All spikes found in the recordings of control animals were similar and consisted of classical biphasic spikes (Fig. 2).

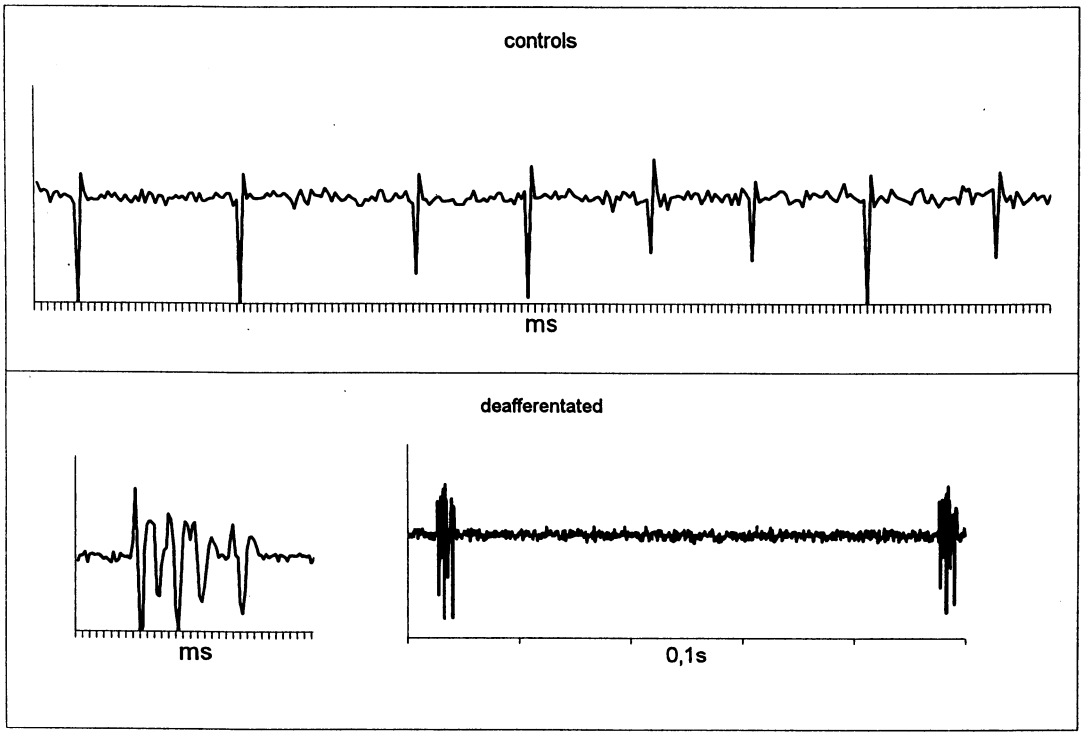


**Fig. 2.** *The graphs of extracellulary recorded neuronal unit activity in deafferented and control rats. Typical unit discharge (above) of pF and CL nuclei in control rats and typical bursting activity of the same nuclei in deafferented rats.*

## Discussion

There are conflicting views about the correlation between autotomy and neuropathic pain in animal models (Rodin and Kruger 1984, Coderre *et al.* 1986). However, it is known that noxious stimuli applied in rodents such as extensive heat (O'Calaghan and Holzman 1975) or chemical irritants (Dubuisson and Dennis 1977) evoke a response during which the animal turns toward the painful part of the body (paw) and licks it. On the other hand, chronic (local) anesthesia of the sciatic nerve does not cause autotomy (Blumenkopf and Lipman 1991). The precise mechanisms underlying autotomy are not known (Kauppila 1998). Both central and peripheral mechanisms are thought to play a role in the induction of autotomy (Wiesenfeld-Hallin *et al.* 1987).

The evidence of altered spontaneous activity in medial thalamic nuclei following dorsal rhizotomy has been presented in this study. Our data are in good agreement with previous findings at spinal cord, lateral thalamus and cerebral cortex levels. Bursting activity following dorsal root sections has been described in neurons in the spinal cord of rats (Lombard and Larabi 1983, Albe-Fessard and Rampin 1991) and cats (Loeser

and Ward 1967), in the lateral thalamus of rats (Lombard *et al.* 1979) and in the cerebral cortex of rats (Albe-Fessard and Rampin 1991). It seems that the abnormal activity progressively moves through the nervous system (Coderre *et al.* 1986). On the other hand, the influence of cortical feedback on thalamic receptive field organization could play an important role (Ergenzinger *et al.* 1998).

It is generally assumed that changes in the function, chemistry and structures of neurons (neural plasticity) develop after deafferentation (Woolf and Mannion 1999). For example, the concentration of substance P, the vasoactive intestinal peptide and somatostatin (Tasker and Dostrovsky 1989), mu-opioid and neurokinin-1 receptors (Goff *et al.* 1998) are altered at the spinal cord level. At the thalamic and cortical levels, the expansion of neighboring receptive fields, unmasking of latent pathways and recruitment of previously ineffective synapses are considered (Knecht *et al.* 1996).

Our study shows that the unilateral dorsal root section influences the shape and frequency of spontaneous neuronal discharges at the micro-electrophysiological level. The spike and wave activity as the only type of unit discharges seems to be characteristic of this pathological condition. Bursting activity was noted in approximately 64 % of the investigated neurons in deafferented animals, while this was not true in any of the investigated neurons of control rats. The bursting discharges are well known in the research of epilepsy and there is no reason to conclude that the underlying molecular mechanisms would be different in these two cases. This conclusion is in good agreement with the fact that antiepileptic drugs can be effective in relieving neuropathic pain (Canavero and Bonicalzi 1996). The appearance of bursts themselves in the medial thalamic nuclei is still not enough for explaining the development of the autotomy behavior. Bursting activity was recorded in animals exhibiting automutilation after deafferentation as well as in deafferented rats without automutilation. In automutilating animals the occurrence of bursts was not present in all recorded neurons and in three deafferented animals without any automutilation only bursting activity of the investigated neurons was found. These results suggest that changes in the firing of neurons of the medial thalamic nuclei do not parallel the autotomy behavior, but they may represent one of the required conditions. It can thus be summarized that the development of the pain syndrome is closely related to the persistent abnormal activity of central neurons and that there is still a gap of information along the pathway between dorsal root section and the sensation of pain in the deafferented extremity.

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## References

ALBE-FESSARD D, RAMPIN O: Neurophysiological studies in rats deafferented by dorsal root sections. In: *Deafferentation Pain Syndromes: Pathophysiology and Treatment.* BS NASHOLD Jr, J OVELMENT-LEWITT (eds), Raven Press, New York, 1991, pp 125-139.

BASBAUM AI: Effect of central lesions on disorders produced by multiple rhizotomy in rats. *Exp Neurol* **42:** 490-501, 1974.

BLUMENKOPF B, LIPMAN JJ: Studies in autotomy: its pathophysiology and usefulness as a model of chronic pain. *Pain* **45:** 203-209, 1991

CANAVERO S, BONICALZI V: Lamotrigine control of central pain. *Pain* **68:** 179-181, 1996.

CODDERE TJ, GRIMES RW, MELZACK R: Deafferentation and chronic pain in animals: an evaluation of evidence suggesting autotomy is related to pain. *Pain* **26:** 61-84, 1986.

DUBUISSON D, DENNIS SG: The formalin test: a quantitative study of the analgesic effects of morphine, meperidine, and brain stem stimulation in rats and cats. *Pain* **4:** 161-174, 1977.

ERGENZINGER ER, GLASIER MM, HAHM JO, PONS TP: Cortically induced thalamic plasticity in the primate somatosensory system. *Nat Neurosci* **1:** 226-229, 1998.

GOFF JR, BURKEY A.R, GOFF DJ, JASMIN L: Reorganization of the spinal dorsal horn in models of chronic pain: correlation with behaviour. *Neuroscience* **82:** 559-574, 1998.

KAUPPILA T: Correlation between autotomy-behaviour and current theories of neuropathic pain. *Neurosci Biobehav Rev* **23:** 111-129, 1998.

KNECHT S, HENNINGSEN H, ELBERT T, FLOR H, HÖHLING C, PANTEV C, TAUB E: Reorganisation and perceptual changes after amputation. *Brain* **119:** 1213-1219, 1996.

LOESER JD, WARD A Jr: Some effects of deafferentation on neurons of the cat spinal cord. *Arch Neurol* **17:** 629-635, 1967.

LOMBARD M-C, LARABI Y: Electrophysiological study of cervical dorsal horn cells in partially deafferented rats. In: *Advances in Pain Research and Therapy*. JJ BONICA et al. (eds), Raven Press, New York, 1983, pp 147-154.

LOMBARD M-C, NASHOLD BS, PELLISSIER T: Thalamic recordings in rats with hyperalgesia. In: *Advances in Pain Research and Therapy*. JJ BONICA et al. (eds), Raven Press, New York, 1979, pp 767-772.

NASHOLD BS, OVELMENT-LEWITT J: *Deafferentation Pain Syndromes: Pathology and Treatment*. Raven Press, New York, 1991.

O'CALLAGHAN JP, HOLTZMAN SG: Quantification of analgesic activity of narcotic antagonists by a modified hot-plate procedure. *J Pharmacol Exp Ther* **192:** 497-505, 1975.

RODIN BE, KRUGER L: Deafferentation in animals as a model for study of pain: an alternative hypothesis. *Brain Res* **319**: 213-28, 1984.

TASKER RR, DOSTROVSKY JO: Deafferentation and central pain. In: *Textbook of Pain*. PD WALL, R MELZACK (eds), Churchill Livingstone, Edinburgh, 1989, pp 154-180.

VACULÍN Š, FRANĚK M, ROKYTA R: The changes of the spontaneous activity of medial thalamic neurons in the rat after the deafferentation. *Physiol Res* **48** (Suppl 1): S132, 1999.

VOGT BA: Structural organisation of cingulate cortex: areas, neurones, and somatodendritic transmitter receptors. In: *Neurobiology of Cingulate Cortex and Limbic Thalamus: A Comprehensive Treatise*. BA VOGT, M ABRIEL (eds), Birkhauser, Boston, MA, 1993, pp 19–70.

WIESENFELD-HALLIN Z, NENNESMO I, KRISTENSSON K: Autotomy in rats after nerve section compared with nerve degeneration following intraneural of *Ricinus communis* agglutinin I. *Pain* **30:** 93-102, 1987.

WOOLF CJ, MANNION RJ: Neuropathic pain: aetiology, symptoms, mechanisms, and management. *Lancet* **353:** 1959-1964, 1999.

**Reprint requests**

Š. Vaculín, Department of Normal, Pathological and Clinical Physiology, Third Faculty of Medicine, Charles University, Ke Karlovu 4, 120 00 Prague 2, Czech Republic. e-mail: svaculin@lf3.cuni.cz