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Effects of spinal and peripheral nerve lesions on the intersegmental synchronization of the spontaneous activity of dorsal horn neurons in the cat lumbosacral spinal cord☆

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Abstract

In the anesthetized and paralyzed cat, spontaneous negative cord dorsum potentials (nCDPs) appeared synchronously in the L3 to S1 segments, both ipsi- and contralaterally. The acute section of both the intact sural and the superficial peroneal nerve increased the variability of the spontaneous nCDPs without affecting their intersegmental coupling. On the other hand, the synchronization between the spontaneous nCDPs recorded in segments L5–L6 was strongly reduced following an interposed lesion of the left (ipsilateral) dorsolateral spinal quadrant and it was almost completely abolished by an additional lesion of the contralateral dorsolateral quadrant at the same level. Our observations support the existence of a system of spontaneously active dorsal horn neurons that is bilaterally distributed along the lumbosacral segments and affects, in a synchronized and organized manner, impulse transmission along many reflex pathways, including those mediating presynaptic inhibition.

Keywords: Cord dorsum potential; Dorsal horn neuron; Spinal cord

In previous studies [13,14] we provided evidence suggesting that the spontaneous negative cord dorsum potentials (nCDPs) that are recorded in the lumbosacral segments of the anesthetized cat are generated by the synchronous activation of a longitudinally distributed ensemble of the dorsal horn neurons which responds mono- or oligosynaptically to electrical stimulation of low-threshold cutaneous afferents and modulates transmission in several spinal reflex pathways, including those mediating primary afferent depolarization (PAD).

We then observed that the transection of cutaneous and muscle nerves in the ipsilateral hindlimb, or of the ipsilateral dorsal columns between the L5 and L6, or the L6 and L7 segments, had very small effects on the intersegmental synchronization of the spontaneous nCDPs. In contrast, sectioning the ipsilateral dorsal horn and the dorsolateral funiculus at these segmental levels strongly decoupled the spontaneous nCDPs generated rostrally and caudally to the lesion. However, it was not clear if the contralateral spontaneous nCDPs were also synchronized with the ipsilateral nCDPs, and the extent to which this synchronization would be affected by nerve and spinal lesions.

We now report observations in which spontaneous potentials were recorded from the dorsal surface of the lumbosacral cat spinal cord along several lumbosacral segments in both sides. To have more detailed information of the intersegmental coupling of the spontaneous nCDPs, instead of using as a reference those potentials exceeding a preset amplitude, as in our previous studies [13,14], we developed a computer program that allows selection of spontaneous nCDPs with specific shapes and amplitudes by means of a predetermined template. The potentials selected using this template were taken as reference (reference nCDPs) to examine the features of the spontaneous nCDPs occurring in synchrony in other segments (associated nCDPs).

Guidelines contained in NIH publication 85-23 (revised in 1985) on the principles of laboratory animal care were followed throughout. The experimental procedures were similar to those followed previously [13,14]. Briefly, observations were carried out in five adult cats initially

☆ This paper is dedicated to Professor Manfred Zimmermann on the occasion of his 70th birthday and as recognition of his contributions to sensory physiology.

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anesthetized with sodium pentobarbitone (35 mg/kg weight, i.p.), supplemented during the dissection and recording periods with additional doses of 10 mg/kg, i.v. as necessary to maintain an adequate level of anesthesia. The lumbosacral and low thoracic spinal segments were exposed. The ipsilateral sural (SU) and superficial peroneal (SP) nerves were dissected and left intact. After the surgical procedures, the animals were paralyzed with pancuronium bromide (0.1 mg/kg) and artificially ventilated. The tidal volume was adjusted to maintain 4% of CO_2 concentration in the expired air. To prevent desiccation of the exposed tissues, pools were made with the skin flaps, filled with paraffin oil and maintained between 36 and 37 °C by means of radiant heat. At the end of the experiment the animals were euthanized with a lethal dose of pentobarbitone.

Fig. 1A illustrates the spontaneous nCDPs that were recorded simultaneously from four segments in the left side (L7, L6, L5 and L4 ipsi) and from two segments in the contralateral side (L6 and L5 contra). All these potentials appear synchronized with the reference nCDPs (L6 ipsi, see arrow). It may be seen that, although the reference nCDPs had a relatively low variability (because of the selection procedure), the associated nCDPs recorded both from the ipsilateral segment L5 and from the contralateral segments L5 and L6 had a larger variability. This suggests that the coupling between the different sets of neurons is not as tight as initially assumed (see [13]), and that it may involve several interposed interneurons.

Each panel in Fig. 1 shows the 'coupling strength', calculated by dividing the peak amplitude of the mean spontaneous nCDPs recorded in that segment by the amplitude of the reference potential recorded in L6. It may be seen that the coupling strength of the associated spontaneous nCDPs recorded in the same side as the reference nCDPs decreased with increasing distances, both rostrally and caudally (see also [13]). Similar results were obtained in the other four experiments.

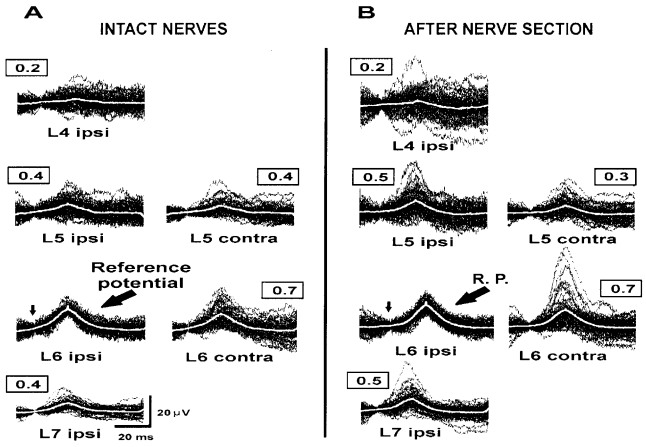

Fig. 1. The acute section of the intact sural and superficial peroneal nerves increases the variability of the ipsi- and contralateral spontaneous nCDPs without affecting their intersegmental coupling. Arrows show the reference L6 ipsi-nCDPs (R.P.) used to select the associated nCDPs generated in the other segments, as indicated. Note that the nCDPs recorded in the contralateral L5 and L6 segments are also coupled to the reference potential. The numbers in each set of records show the coupling strength as defined in the text. After sectioning the SU and SP nerves the coupling strength between the ipsilateral and contralateral nCDPs remained basically unchanged. However, there was a large increase in the variability of the associated nCDPs. For illustration purposes, in both figures the baseline of the individual nCDPs was adjusted to zero at the time indicated by the small arrow on the L6 ipsi-reference nCDPs. The averages were obtained without baseline adjustments and are superposed on the individual records.

Quite interestingly, the associated spontaneous nCDPs recorded from the right (contralateral) side in segment L6 were strongly coupled to the reference nCDPs. Since the electrodes used to record the ipsi- and contralateral nCDPs in the L6 segment were relatively close to each other (3–5 mm), it could be argued that the activity recorded in the right side included potentials generated not only in the same side but also in the left side. Although this factor cannot be completely excluded, the larger variability of the contralateral L6 potentials than that of the L6 reference nCDPs suggests that the main contribution arises locally (see below).

Sectioning the SU and SP nerves increased further the variability of the associated nCDPs, practically without affecting their intersegmental distribution or the coupling strength between these potentials and the reference nCDPs (Fig. 1B). It thus seems that sensory inputs increase the overall excitability of the dorsal horn neurons so that they respond more readily and with lesser variations to intersegmental inputs. When this sensory driving is missing their responses became more variable.

Fig. 2A shows the effects produced in the same experiment by sectioning the left (ipsilateral) dorsal horn and intermediate zone between the L5 and L6 segments (see

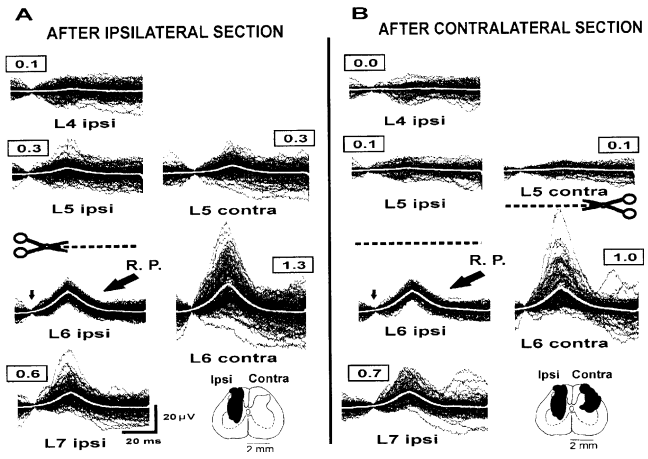

Fig. 2. Effects of spinal lesions on the intersegmental coupling of ipsi- and contralateral spontaneous nCDPs. Same format and experiment as in Fig. 1. Data obtained after the left SU and SP nerves were sectioned. (A) After a spinal lesion between segments L5 and L6 in the left (ipsilateral) side. (B) After an additional contralateral spinal lesion, also between segments L5 and L6 (see histology). The L6 ipsi-reference nCDPs were selected using the same template as for the data displayed in Fig. 1 (see large arrows in both panels). Further explanations in text.

histology). The reference nCDPs in L6 were selected using the same template as before. The mean amplitude of the potentials recorded in the L5 ipsilateral segment, as well the coupling strength were reduced after the section (coupling strength changed from 0.5 to 0.3). It is to be noticed that the amplitude as well as the coupling strength of the potentials recorded from the contralateral L6 segment were instead increased (coupling strength changed from 0.7 to 1.3).

The additional section of the contralateral dorsal horn and dorsolateral fasiculus (DLF) reduced considerably the amplitude of the associated ipsi- and contralateral potentials recorded in the L5 segments as well as their coupling strength (from 0.3 to 0.1 for L5 ipsi- and contra; Fig. 2B). Similar results were observed in the other four experiments.

Altogether the present observations show that the spontaneous nCDPs appear in synchrony on both sides of the spinal cord and that they are largest in the L6 and L5 spinal segments. Sectioning the cutaneous nerves increases the variability of the associated nCDPs, but not their intersegmental distribution. As indicated in the diagram of Fig. 3, we have assumed that there is a bilaterally distributed system of dorsal horn neurons that are interconnected via mono- and oligosynaptic pathways through the ipsilateral DLF and/or dorsal horn. The ensemble of ipsilateral neurons could have connections with dorsal horn neurons in the opposite site and receive excitatory inputs from cutaneous afferents as well as from supraspinal structures [3,12].

The synchronization between the ipsilateral nCDPs appears to be mediated mostly by ipsilateral pathways, although there is also a clear contribution of contralateral pathways, probably involving commissural interneurons (see [3]). We have found that the strength of the coupling varied not only with intersegmental separation but also with the overall level of neuronal activity. In this regard the situation is to some extent similar to what has been observed with the crossed phrenic phenomenon, where increased activity of supraspinal structures during asphyxia or anoxia or by injection of alkylxanthines promotes the activation of crossed pathways in the cervical spinal cord [15].

As shown before [14], the dorsal horn interneurons involved in the generation of the spontaneous nCDPs affect impulse transmission in several reflex pathways, including those mediating PAD and presynaptic inhibition of cutaneous and muscle afferents. Since this system of dorsal horn neurons is also active in nonanesthetized unrestrained preparations [7], it is very likely that it contributes to the generation of a tonic PAD of cutaneous afferents [10,11] not only ipsilaterally but also contralaterally, and may thus affect transmission of low-threshold cutaneous inputs to segmental and supraspinal structures.

This raises the question on the extent to which the modulation of PAD of cutaneous fibers that is introduced by this bilaterally distributed system of dorsal horn neurons accounts for the modality specificity of the PAD elicited in single cutaneous afferents demonstrated time ago by Jänig et al. [5,6]. One possibility is that the sets of dorsal horn

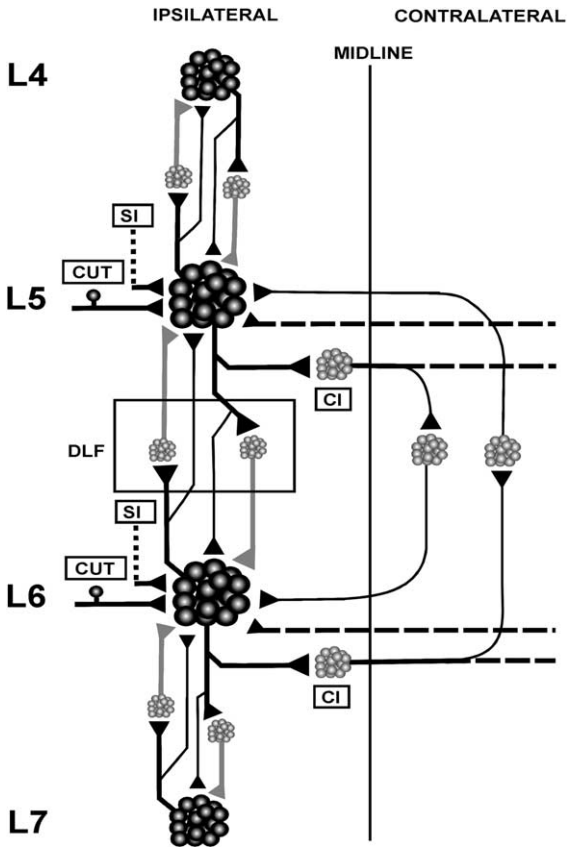

Fig. 3. Generation of synchronous spontaneous nCDPs in the lumbosacral spinal segments. The set of neurons that generate spontaneous nCDPs is represented as a neuronal ensemble bilaterally distributed in four spinal segments. For simplification the diagram shows only the ipsilateral set of neurons, but it is assumed that the same arrangements are present in the other side. These neurons receive monosynaptic connections from low-threshold cutaneous (CUT) afferents and polysynaptic connections from segmental and supraspinal inputs (SI). Neurons in each segment are interconnected with other neurons in neighboring segments, ipsilaterally by mono- and polysynaptic connections via the dorsolateral fasciculus (DLF) and dorsal horn, and contralaterally via commissural interneurons (CI). Synchronization would result from the activation of a minimum number of neurons anywhere in the ensemble. This diagram does not include inhibitory interneurons that could play an important role in the termination of the synchronized bursts of activity.

neurons involved in the generation of the spontaneous nCDPs are organized in small subsets, each one affecting the PAD of cutaneous afferents with the same sensory modality. Another possibility is that anesthesia suppresses inhibitory descending influences which under normal conditions limit the interconnectivity of the dorsal horn neurons affecting PAD and lead to more circumscribed actions, although it must be pointed out that the observations of Jänig et al. [5,6] were also performed in anesthetized preparations.

We are now approaching this question by recording the changes in the spontaneous activity of functionally characterized dorsal horn neurons simultaneously in several spinal segments during the generation of spontaneous nCDPs with specific intersegmental patterns (see [1,8]). Other pending

questions are the extent to which these sets of dorsal horn neurons are involved in the regulation of the synaptic effectiveness of nociceptive afferents [2,16–18], and in the modulation of PAD of cutaneous fibers during fictive and real locomotion [4,9]. Disclosure of the origin and interactions between the different interneuronal ensembles that are involved in the generation of the spontaneous nDCPs is of potential clinical interest because it could be used to examine functional alterations in specific sets of interneurons and their influence on spinal reflex pathways in humans.

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