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Research Report

Somatic nerve stimulation evokes qualitatively different somatosympathetic responses in the cervical and splanchnic sympathetic nerves in the rat

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ABSTRACT

Input from unmyelinated and myelinated nociceptors drives somatosympathetic responses to painful stimuli. Here we report that somatosympathetic responses recorded simultaneously in the cervical and splanchnic sympathetic nerves of the urethane-anaesthetized rat are qualitatively different. High intensity electrical stimulation of the sciatic nerve (SN) evoked characteristic biphasic responses in splanchnic nerve activity ($N=6$), but only monophasic responses in the cervical nerve ($N=4$). By colliding sympathoexcitatory responses to SN stimulation with precisely triggered baroinhibition evoked by electrical stimulation of the aortic depressor nerve, we found that cervical responses are analogous to the first phase of the splanchnic response, and that the biphasic splanchnic response is due to the arrival of two distinct afferent volleys at the site of sympathetic integration. Extracellular recordings of responses to SN stimulation in barosensitive neurons in the rostral ventrolateral medulla (RVLM; $N=16$) support these findings; responses were typically biphasic, although the relative magnitudes of the two phases were highly variable, and in some cases the longer-latency volley was completely absent. Our results suggest that sympathetic responses to somatic stimuli, mediated by the RVLM, are non-uniform and are dependent on the target of the particular sympathetic output. The identification of RVLM sympathetic premotor neurons with both biphasic and monophasic responses indicates that the difference in the splanchnic and cervical nerve responses is due to specific channeling of activity evoked by myelinated and unmyelinated nociceptors to the medulla. The results are discussed with regard to the differential control of sympathetic nerve activity.

1. Introduction

Cardiorespiratory activity is constantly modified by afferent inputs that encode the internal and external environments; intero- and exteroception respectively. In general, interoceptive input (e.g. blood pressure and oxygen saturation, visceral input, and immune status) is conveyed by the vagal afferent system, whereas exteroceptive input is detected by periph-

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eral mechano- and thermoceptive afferents and relayed in the spinal dorsal horn. Such inputs provide critically relevant drive that enables autonomic control centers to tailor output to the moment-to-moment requirements of the animal. In common with interoceptive drive (except the baroreflex), exteroceptive input constantly modulates autonomic activity at a subconscious level but will, if not adequately compensated, drive higher centers to evoke appropriate behavioral responses.

The afferent limb of the somatosympathetic reflex comprises mechanical, chemical and heat nociceptors that innervate the skin, muscle, joints and bone. It is a hierarchical reflex composed of spino-spinal and spino-bulbo-spinal loops, parts of which also drive bulbo-mesencephalic-bulbo, hypothalamo-spinal and hypothalamo-cortical loops (see Craig, 2003; Janig et al., 1972; Sato and Schmidt, 1973). Bulbospinal sympathetic premotor neurons in the rostral ventrolateral medulla (RVLM) form a critical relay in the supraspinal component of the somatosympathetic reflex. Disruption of RVLM transmission greatly attenuates sympathetic and pressor responses evoked by somatic nerve stimulation (Kiely and Gordon, 1994; Makeham et al., 2005; Miyawaki et al., 2001, 2002; Nagata et al., 1995; Stornetta et al., 1989; Verberne and Guyenet, 1992).

Surprisingly, no previous studies have focused on the expression of somatosympathetic reflexes in multiple sympathetic beds in the rat, the species of choice in the field, despite Janig and colleagues' detailed description of somatosympathetic responses in the cat over 30 years ago (Janig et al., 1972). Any differences in the representation of supraspinally mediated somatosympathetic responses between diverse sympathetic outputs would have important implications regarding the central organization of such reflexes. To paraphrase Morrison (2001), differential responses to activation of reflexes that drive sympathetic premotor neurons are most easily explained by differential inputs to populations of functionally dedicated premotor neurons. The question of how such differential control is orchestrated has developed as a topic of considerable interest in recent years (see Coote, 2007; Janig, 1984; Morrison, 2001).

In order to examine whether responses evoked by sciatic nerve (SN) stimulation were differentially processed by sympathetic premotor neurons that drive sympathetic nerves with different targets, we chose two preganglionic nerves with contrasting targets; the greater splanchnic nerve, which, *inter alia*, provides vasoconstrictor tone to the mesentery and controls catecholamine release from the adrenal gland, and the cervical nerve, which innervates the pineal body, iris, salivary, cochlea and lacrimal glands, in addition to vascular targets in the head and neck. In order to investigate the central organization of the reflex, we used baroinhibitory drive evoked by electrical stimulation of the aortic depressor nerve (ADN), to 'collide' excitatory somatosympathetic responses with inhibitory ADN responses, which predominate the somatosympathetic response (Li et al., 1998). Finally, we recorded from markedly barosensitive neurons in the RVLM in order to determine whether the different properties of the somatosympathetic responses observed in the cervical and splanchnic nerves were represented by sympathetic premotor neurons in this area.

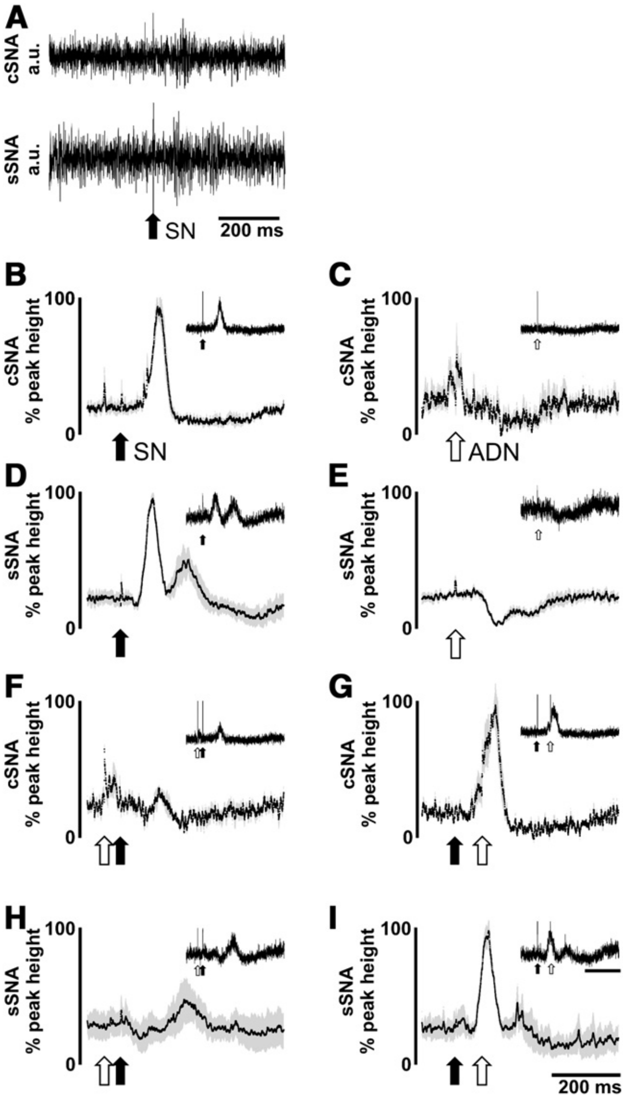

Fig. 1 – Simultaneously recorded cervical and splanchnic sympathetic responses to intermittent stimulation of the sciatic (SN; closed arrows) and aortic depressor nerves (ADN; open arrows). A. Raw data show cervical (cSNA; top) and splanchnic (sSNA; bottom) responses to a single SN stimulus (40 V, 3 ms). B–I: Pooled rectified and smoothed cervical (N = 4) and splanchnic (N = 6) responses to SN and ADN stimulation. Black and grey data denote mean ± SEM respectively. Insets show averaged rectified responses to 100 stimuli (0.5 Hz) recorded in a single experiment. SN stimulation evokes a monophasic excitation of cSNA (B) and a biphasic excitation in sSNA (D). ADN stimulation (15 V, 0.2 ms) has no significant effect on cSNA (C) but inhibits sSNA (E). Collision of ADN-evoked sympathoinhibition with the cSNA response evoked by SN stimulation abolishes it (F) and the first peak of the splanchnic response (H). Adjustment of stimulus timing such that ADN-evoked baroinhibition is collided with the second peak of the splanchnic response to SN stimulation has no effect on the cervical response (G) but attenuates the second phase of the splanchnic response (H). Horizontal scale bars are 200 ms in all figures. Vertical scaling for raw data identical in all figures. a.u.: arbitrary units.