Review

Microneurographic recording from unmyelinated nerve fibers in neurological disorders: An update

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HIGHLIGHTS

- Microneurography allows recordings from sympathetic or nociceptive fibers.
- Recently it has been widely used to explore autonomic impairments in neurological disorders.
- Microneurography has also been used to show abnormal nociceptor outflow.

ABSTRACT

Microneurography is a unique neurophysiological technique allowing direct recording of unmyelinated postganglionic sympathetic or afferent nociceptive fibers by tungsten needles inserted into a peripheral nerve fascicle. In recent years, microneurography has been used to ascertain autonomic impairments in central neurological disorders such as sleep disorders, Parkinson's disease, amyotrophic lateral sclerosis, or vasovagal syncope. Abnormal resting muscle sympathetic nerve activity (MSNA) and skin sympathetic nerve activity (SSNA) or the abnormal sympathetic response to arousal have been described in these disorders, thereby clarifying important pathophysiological aspects of the underlying impairment.

In addition, microneurography was also recently used to demonstrate absent or decreased sympathetic outflow in diseases affecting the peripheral nervous system such as Ross syndrome, pure autonomic failure, and small-fiber neuropathy.

Microneurography has also been used to study nociceptor outflow in pain disorders affecting the peripheral nervous system such as small-fiber neuropathy, diabetic neuropathy, erythromelalgia, complex regional pain syndrome, and fibromyalgia. In these disorders, microneurography mainly documented mechano-insensitive C-nociceptor hyperexcitability that might account for the ongoing pain.

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Contents

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1. Introduction

The microneurographic technique for recording action potentials in human peripheral nerves was developed by Hagbarth and Vallbo in the 1960s (Hagbarth and Vallbo, 1968). The new method soon proved able to monitor impulse traffic, in not only myelinated but also unmyelinated postganglionic sympathetic fibers or afferent nociceptive fibers (Vallbo et al., 1979, 2004). This was an important step forward because until then the only way of exploring sympathetic activity in humans was to gather neural drive from sympathetic effector recording such as heart rate (HR), blood flow, and blood pressure (BP), whereas no objective method was available to record peripheral nociceptive transmission.

Microneurographic nerve recording is performed with a tungsten microelectrode inserted through the skin into a nerve fascicle of an underlying nerve placed in close contact with the axon (Wallin, 2006). The active insulated tungsten microelectrode has a shaft diameter of 200 μm with an uninsulated tip of a few micrometers. The reference electrode is a low-impedance needle inserted a few centimeters away from the active electrode. The nerve discharges are fed into a low-noise amplifier operating within the frequency range 200 Hz–8 KHz. Useful extra equipment include sound monitoring to discriminate neural signals from noise, a unit for instantaneous frequency display of single-unit impulses, and a resistance–capacitance circuit with an adjustable time constant to display integrated multiunit neural activity (Vallbo et al., 1979; Mano et al., 2006).

Although microneurography is invasive and technically demanding requiring well-trained recorders, its main advantage is the possibility to record action potentials from unmyelinated axons. Thin tungsten needle electrodes record not only synchronized volleys but also a single-unit discharge of unmyelinated fibers. No transcutaneous compound action potential can be recorded from unmyelinated axons because of their small currents and a pronounced dispersion due to the low conduction velocities varying from 0.5 to 1.5 m/s.

2. Sympathetic outflow recording

The tungsten microelectrode is inserted through the skin into a skin or muscle nerve fascicle of an underlying nerve. Most extremity nerves can be used but the peroneal or tibial (mainly in Japan) nerves at the knee are a common choice. The sympathetic fibers are located in bundles inside Schwann cells. The recording is usually made by multifiber recording, that is, the electrode picks up activity from many sympathetic fibers, depicting it in a mean voltage (integrated) neurogram. Individual sympathetic axons can also be recorded and the action potentials are analyzed in the original neurogram. Multifiber recording is easier and quicker and is mainly used in a clinical setting, whereas single-unit recording is more difficult and time consuming and is reserved for specific or research purposes.

2.1. Resting sympathetic activity and its effector responses

An important early microneurographic finding was the demonstration of marked differences in temporal pattern between skin and muscle sympathetic activities (SSNA and MSNA, respectively). In muscle nerves, the sympathetic bursts occurred in the cardiac rhythm primarily during temporary reductions of BP (Delius et al., 1972a), whereas in skin nerves the bursts had a much more varied appearance, lacked cardiac rhythmicity and showed no relationship to spontaneous BP variations (Hagbarth et al., 1972). Furthermore, responses to maneuvers usually differed between the two types of activities (Delius et al., 1972b). An important reason for differentiation between skin and muscle is that arterial baroreceptors have a strong modulatory influence on muscle but not on SSNA. This is illustrated by the finding that temporary baroreceptor deafferentation, achieved by bilateral local anesthetic blocks of the vagus and glossopharyngeal nerves, led to a marked increase in MSNA, eliminating its cardiac rhythmicity and the inverse relationship with BP variations. As skin sympathetic activity remained largely unchanged, the character of the two types of activity became much more similar (Fagius et al., 1985). Several studies have demonstrated that SSNA is mainly related to thermoregulatory mechanisms, whereas MSNA is involved in cardiovascular activity (Vallbo et al., 1979; Delius et al., 1972a; Hagbarth et al., 1972; Wallin, 2006; Joyner et al., 2010). Microneurographic outflow signals are better interpreted when recorded together with sympathetic effector responses such as BP for MSNA or skin vasomotor response (SVR), induced by skin vasoconstriction (Kolev et al., 1995), and skin sudomotor response (SSR), expressing skin potential changes induced by a sweat gland activation (Marchello et al., 1996), for SSNA.

2.2. Arousal effect on sympathetic activity

Microneurographic recordings have made a significant contribution to clarifying the effect of arousal stimuli on sympathetic activity. Firstly, it was shown that any surprising sensory stimulus regularly evokes a sympathetic discharge in skin (Hagbarth et al., 1972) but not in muscle nerves even if recent reports (Donadio et al., 2002a,b) showed that sensory stimuli giving rise to psychological alertness (arousal) cause a short-lasting inhibition of MSNA in approximately 50% of healthy subjects. In a given individual, the degree of inhibition was found to be reproducible over several months, suggesting that the response behavior is characteristic for the individual (Donadio et al., 2002a,b; Wallin et al., 2013). Importantly, subjects in whom inhibition occurred also had a lower