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Invited review

Microneurography as a tool in clinical neurophysiology to investigate peripheral neural traffic in humans

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Abstract

Microneurography is a method using metal microelectrodes to investigate directly identified neural traffic in myelinated as well as unmyelinated efferent and afferent nerves leading to and coming from muscle and skin in human peripheral nerves in situ. The present paper reviews how this technique has been used in clinical neurophysiology to elucidate the neural mechanisms of autonomic regulation, motor control and sensory functions in humans under physiological and pathological conditions.

Microneurography is particularly important to investigate efferent and afferent neural traffic in unmyelinated C fibers. The recording of efferent discharges in postganglionic sympathetic C efferent fibers innervating muscle and skin (muscle sympathetic nerve activity; MSNA and skin sympathetic nerve activity; SSNA) provides direct information about neural control of autonomic effector organs including blood vessels and sweat glands. Sympathetic microneurography has become a potent tool to reveal neural functions and dysfunctions concerning blood pressure control and thermoregulation. This recording has been used not only in wake conditions but also in sleep to investigate changes in sympathetic neural traffic during sleep and sleep-related events such as sleep apnea. The same recording was also successfully carried out by astronauts during spaceflight.

Recordings of afferent discharges from muscle mechanoreceptors have been used to understand the mechanisms of motor control. Muscle spindle afferent information is particularly important for the control of fine precise movements. It may also play important roles to predict behavior outcomes during learning of a motor task.

Recordings of discharges in myelinated afferent fibers from skin mechanoreceptors have provided not only objective information about mechanoreceptive cutaneous sensation but also the roles of these signals in fine motor control. Unmyelinated mechanoreceptive afferent discharges from hairy skin seem to be important to convey cutaneous sensation to the central structures related to emotion. Recordings of afferent discharges in thin myelinated and unmyelinated fibers from nociceptors in muscle and skin have been used to provide information concerning pain. Recordings of afferent discharges of different types of cutaneous C-nociceptors identified by marking method have become an important tool to reveal the neural mechanisms of cutaneous sensations such as an itch.

No direct microneurographic evidence has been so far proved regarding the effects of sympathoexcitation on sensitization of muscle and skin sensory receptors at least in healthy humans.

Keywords: Microneurography; Muscle sympathetic nerve activity; Skin sympathetic nerve activity; Muscle spindle; Skin mechanoreceptor; Muscle nociceptor; Skin nociceptor; Blood pressure; Thermoregulation; Pain; Itch

1. Introduction

Microneurography is a unique method to record neural impulses from human peripheral nerves in situ. Using this method neural traffic can be recorded not only from large myelinated fibers but also from thin unmyelinated fibers.

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The first successful recording of neural impulses from human peripheral nerves was by Hensel and Boman (1960), who used a glass microelectrode to record single unit afferent discharges from an exposed peripheral nerve of healthy humans. Seven years later, two different Swedish groups reported independently much less invasive recording techniques of human neural discharges. Both groups used metal microelectrodes which penetrated percutaneously without anesthesia into the peripheral nerves in healthy human subjects. Knutsson and Widén (1967) used a platinum–iridium microelectrode, while Hagbarth and Vallbo (1967) employed a tungsten microelectrode. The original method of Hagbarth and Vallbo has become widely used all over the world, and is currently called microneurography.

Using this microneurography technique, afferent discharges from muscle and skin, as well as efferent discharges leading to muscle and skin can be recorded from human peripheral nerves to identify the sensory receptors and the effector organs. Thus identified afferent discharges from muscle spindles, tendon organs, muscle nociceptors, skin mechano-, and nociceptors, as well as activity of postganglionic sympathetic efferent nerves innervating muscle and skin can be separately analyzed. Recordings of afferent discharges from muscle spindle are useful to analyze neural mechanisms of motor control. Recordings of afferent discharges from cutaneous mechanoreceptors provide objective signals related to skin mechanoreception such as vibrotactile sensation. Paresthesia was reported to be related to abnormal ectopic discharge generation in sensory fibers (Ochoa and Torebjörk, 1980,). Cutaneous mechanoreceptive afferent discharges contribute to not only sensory functions but also fine motor control. Recordings of afferent discharges from nociceptors in muscle and skin provide valuable objective signals related to pain and other sensation such as an itch. Recordings of sympathetic efferent activity are essential to understand the neural mechanisms of autonomic functions.

Recordings of efferent discharges of α-motor fibers are not practical, because α-motoneuronal efferent activity can be more readily detected by EMG. There have been only a few reports in which skeletomotor activity was microneurographically recorded (Ribot et al., 1986) or conduction velocity of single α-motor fibers was measured using a combination of microneurographic and spike-triggered averaging techniques (Kakuda et al., 1992b). Recording of γ-efferent nerve should be useful to analyze mechanisms of fusimotor control of movements and muscle tonus, but there has been only one report concerning this recording (Ribot et al., 1986), and it was not reconfirmed thereafter by other investigators. The poor reports of γ-efferent recordings may be due to some technical problems of microneurography. By applying the microneurographic technique, not only recordings of neural traffic in peripheral nerves, but intraneural electrical stimulation of afferent and efferent nerve fibers (microstimulation) became possible. Using microstimulation, the functions of skin mechanoreceptors (Vallbo, 1981; Torebjörk et al., 1987), muscle nociceptors (Simone et al., 1994; Marchettini et al., 1996), skin nociceptors (Ochoa et al., 1989), skeletomotor fibers (McNulty et al., 2000), and sympathetic efferent nerves (Kunimoto et al., 1991, 1992a,b) were investigated.

Microneurographic studies have been carried out to elucidate various problems related to neural mechanisms in humans under normal and disease conditions. At the early stage of microneurographic research, this technique was used preferably to investigate afferent discharges in myelinated fibers from muscle and skin. An early review detailing this technique was reported by Vallbo et al. (1979). More recent microneurographic studies have mainly focused on investigation of efferent and afferent discharges in unmyelinated C fibers including sympathetic neural traffic leading to muscle and skin called muscle sympathetic nerve activity (MSNA) and skin sympathetic nerve activity (SSNA) as well as cutaneous nociceptive units. Sympathetic microneurography has become a potent tool of clinical autonomic testing. Spontaneously discharging sympathetic neural traffic in abundant fibers grouped in muscle and skin nerve fascicles can be more easily recorded as identified multifiber activities than as single-unit somatic afferent discharges. Interindividual comparison of neural activity can be done more easily with quantitative analysis in sympathetic neural traffic, particularly in MSNA, than in sensory afferent discharges. Wallin (1981, 1983, 1986) has contributed much to the development of sympathetic microneurography, which has been used not only in ground-based laboratories, but also in space. Autonomic neural functions in space have been evaluated using various indirect methods (Mano, 2005) until 1998, when microneurography was first applied for the first time during spaceflight to clarify how microgravity influences sympathetic neural traffic in humans. For this research, three American and one Japanese astronauts mastered perfectly the technique of microneurography. Two of them aboard Space Shuttle Columbia could measure successfully MSNA from the peroneal nerve of their fellow astronauts. It was revealed that MSNA was rather enhanced during the 12th and 13th days of spaceflight and just after returning to Earth (Cox et al., 2002; Ertl et al., 2002; Fu et al., 2002; Levine et al., 2002). The recordings of unmyelinated C afferent fibers from cutaneous nociceptors were become accelerated by introducing a computer-assisted identification method called marking technique.

In the present review, the usefulness of microneurography as a tool to investigate peripheral neural functions in humans will be described with presentation of topics related to recording.

2. Recording technique of microneurography

Tungsten microelectrodes with an epoxy resin insulated shaft having diameter of about 100–200 μm and a tip diameter of about 1 μm and an impedance around 1–5 MΩ at