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Communication

A new paradigm of electrical stimulation to enhance sensory neural function

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ABSTRACT

The ability to improve peripheral neural transmission would have significant therapeutic potential in medicine. A technology of this kind could be used to restore and/or enhance sensory function in individuals with depressed sensory function, such as older adults or patients with peripheral neuropathies. The goal of this study was to investigate if a new paradigm of subsensory electrical noise stimulation enhances somatosensory function. Vibration (50 Hz) was applied with a Neurothesiometer to the plantar aspect of the foot in the presence or absence of subsensory electrical noise (1/f type). The noise was applied at a proximal site, on a defined region of the tibial nerve path above the ankle. Vibration perception thresholds (VPT) of younger adults were measured in control and experimental conditions, in the absence or presence of noise respectively. An improvement of ~16% in VPT was found in the presence of noise. These are the first data to demonstrate that modulation of axonal transmission with externally applied electrical noise improves perception of tactile stimuli in humans.

1. Introduction

Noise is ubiquitous in the nervous system [1], and while somewhat counterintuitive, has been shown to have many beneficial effects in neural function via stochastic resonance [2–4], coherence resonance [5–7], and noise-induced synchronization [5,8]. Of these, stochastic resonance is the only mechanism that has been artificially replicated in vivo and has received much attention as a potential intervention to improve human sensory perception [9–14]. With this method, noise has been added directly to mechanoreceptors through either mechanical or electrical means in an effort to boost perception at these end organ sites. By doing so, researchers have observed considerable gains in the performance of somatosensory related tasks, such as balance, and in various patient cohorts [9,11,14–16]. However, one potential limitation is that the additive noise must be applied at the sensory receptor site, as stochastic resonance is restricted by definition to enhancing the detection of weak signals applied at the sensory end organ. Managing the level of noise applied to each sensory organ is a difficult task, as an optimal level of noise for each end organ would need to be identified and applied. Added to this is the difficulty of maintaining this optimized level during movement, e.g. during gait. It is unknown if artificial noise acting at sites other than the sensory end organ can improve somatosensory function through other mechanisms.

Summation is a powerful force in the representation of somatosensory information. Sherrington and Eccles were first to discover that synaptic inputs, while individually insufficient, may summate to generate postsynaptic action potentials [17]. A study of the primate secondary somatosensory cortex found that synchrony between neurons increased when attention was focused and led to an increase in the combined synaptic effect of a subset of neurons [18]. In summary, synchronized action potentials summate to evoke greater postsynaptic potentials leading to an

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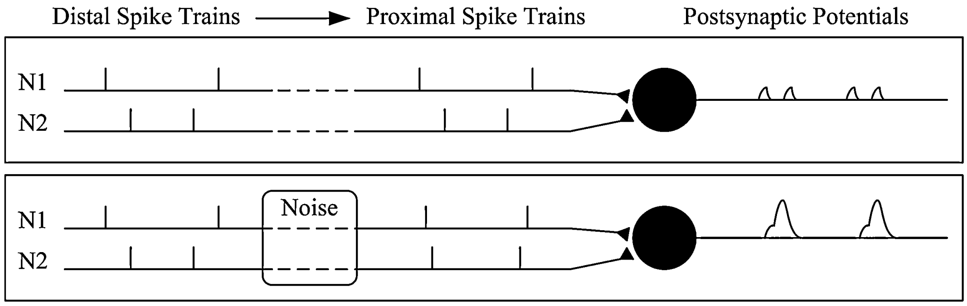

Fig. 1. How noise may modify a sensory stimulus. In the natural case (top) distally generated spike trains are faithfully transmitted proximally along each neuron. In this case action potentials arrive asynchronously at a synapse; the evoked excitatory postsynaptic potentials are small and produce few or no postsynaptic action potentials resulting in a weak neural representation of the stimulus. In the intervention case (bottom), noise added to the neural pathway acts to cause increased synchronization of the synaptic inputs and produce larger excitatory postsynaptic potentials, leading to an enhanced representation of the external stimulus.
Source: Adapted from [19].

enhanced representation of a perceived stimulus [19]. Thus, if any intervention could induce synchronization anywhere in the sensory neural pathway, it may result in a perceived amplification of sensory stimuli.

Action potentials are sensitive to noise, sufficiently to cause variability in both their initiation and propagation [1]. It is also known that subthreshold oscillations of the extracellular field of pyramidal neurons causes shifts in spike-phase distribution and can result in phase locking of spikes to the applied field [20,21]. We hypothesized that application of an external electrical noise stimulus to the sensory neural pathway could modulate the extracellular field potential and induce an effect similar to that seen in pyramidal neurons. Should the group dynamics of parallel neurons be modified and coupled to some degree, previously asynchronous sensory action potentials may become more synchronous, summating to produce postsynaptic potentials (Fig. 1), and now propagate to the neocortex thus increasing sensitivity to sensory inputs.

To test this hypothesis we applied subsensory electrical noise at a site on the tibial nerve pathway above the ankle (i.e. applied to first order neurons) of younger adults while applying a vibration stimulus to a distal site on the plantar aspect of the foot. 1/f type noise was chosen for application in this study as this type of noise is known to occur naturally in neural membranes [22,23] and as such it is less likely that the body would become habituated to this type of signal. As previously mentioned, other authors have used 1/f type noise successfully where noise was added directly to the sensory end organ [9,11,14–16] but not in the manner applied in this current study.

2. Methods

This study was approved by the National University of Ireland Galway Research Ethics Committee.

2.1. Subjects

Ten healthy volunteers (5 female, age 25.4 ± 4.1 years) were recruited from the local student population and colleagues. Written, informed consent was obtained before participation in the study.

2.2. Equipment

2.2.1. Electrical noise

1/f type noise was generated in Labview (National Instruments, Texas, USA) according to the equations described by Pavlik [24]; noise amplitude could also be controlled via this Labview GUI. This noise signal was output as an analogue signal via a National Instruments USB-6009 DAQ. The signal was then converted to a current-controlled signal via a custom circuit.

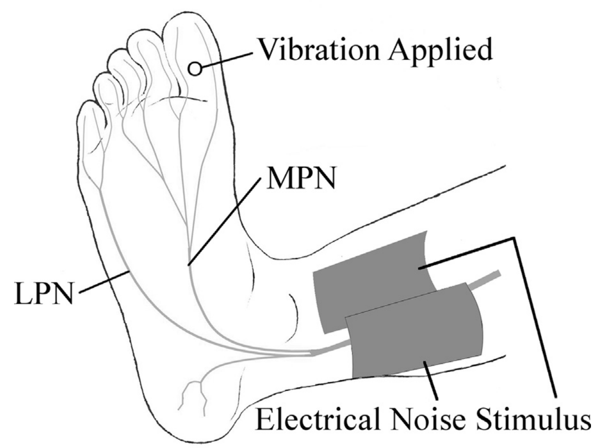

Fig. 2. Experimental setup for subject testing. Trajectories of medial plantar nerve (MPN) and lateral plantar nerve (LPN) are shown as well as the electrode sites for electrical noise stimulation and the site at which vibration was applied.

Axelgaard UltraStim (10 cm × 5 cm) electrodes were used throughout the study (Axelgaard Manufacturing Co. Ltd., CA, USA). Electrodes were placed proximally to the medial and lateral malleoli such that the tibial nerve was stimulated (Fig. 2).

Bipolar electrical noise stimulation was applied with zero mean and in 15 μA s.d. increments up to the maximum 60 μA; this was done to determine if the subject could perceive the electrical noise.

2.2.2. Vibration perception

Results were based on the vibration perception threshold (VPT) at the plantar side of the hallux (big toe, Fig. 2) as measured using a Neurothesiometer and recorded in volts (Horwell, Nottingham, UK). The voltage (vibration intensity) is slowly increased from zero until the subject first perceives the sensation of vibration. This voltage is recorded as the vibration perception threshold (VPT). The vibration frequency was 50 Hz, preferentially activating Pacinian corpuscles [25].

2.3. Experimental procedure

Subjects lay supine for the duration of the test. Two identical control conditions (no noise) and four electrical stimulation conditions with zero mean noise and varied standard deviation (15 μA, 30 μA, 45 μA and 60 μA) were applied. The presentation order of these six conditions was randomized.