TEMPERATURE EFFECTS ON SIMULATED HUMAN NODAL ACTION POTENTIALS AND THEIR DEFINING CURRENT KINETICS

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ABSTRACT

PURPOSE: Nerve conducting properties are sensitive to body temperature. To expand our studies on the nerve conducting properties, the effects of temperature on nodal action potentials and their defining current kinetics are investigated.

MATERIAL AND METHODS: The computations use our temperature dependent multi-layered model of human motor nerve fibre and the temperature is increased in the range of 20-42°C.

RESULTS: In the investigated temperature range, potential amplitudes increase up to 37°C and then decrease. They are slightly changed in the physiological range of 32-37°C. The conduction velocity increases by ~5% in this physiological range, however it increases from 18.18 to 71.5 m/sec (i.e. ~4 times) for the extreme temperatures of 20 and 41°C, respectively. With the temperature increase, the depolarizing afterpotentials decrease reaching the resting potential value (-86.7 mV) at temperature close to 39°C and then they become hyperpolarized. The potential durations progressively decrease with the progressive increase of the temperature. For the temperature range of 20-39°C, action potentials at the nodes of Ranvier are determined mainly by the nodal sodium current (I_{Na}), as the contribution of nodal fast and slow potassium currents (I_{Kf} and I_{Ks}) to the total nodal ionic current (I_i) is negligible. However, the contribution of the nodal I_{Kf} and I_{Ks} to the membrane repolarization is large for the temperatures higher than 39°C.

CONCLUSION: The results obtained are important for the interpretation of temperature dependent nerve conduction measurements in health.

Key words: temperature, action potential parameters, ionic current kinetics, human motor nerve axon, computational neuroscience

INTRODUCTION

The nerve conduction study, which is part of the laboratory studies that include blood tests, muscle or nerve biopsy, genetic testing, etc. is still successfully realized. The main nerves function is to transmit information from one site to another. The effects of temperature on standard measures of nerve conduction are well established. The nerve conduction velocity increases by ~5% per degree C as the temperature increases from 29 to 38°C (3,4,6) whereas the nerve amplitude slightly decreases

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(1,2,5). It is therefore customary to ensure that skin temperature is within defined limits before clinical nerve conduction measurements. Extremes of temperature have long been known to produce permanent neuronal dysfunctions in health and disease. However, they have been much less studied.

The aim of this study is to investigate the changes of nodal action potentials in human motor nerve fibres and to provide a deeper understanding of the mechanisms underlying these changes when the temperature increases from 20 to 42°C.

MATERIAL AND METHODS

The computations use our modified temperature dependent model of motor nerve axons (8). It is derived from our multi-layered model of human motor nerve fibre (7,9), in which the complex myelin sheath structure of 150 interconnected parallel lamellae is simulated by alternating 150 lipid and 150 aqueous layers. All calculations are carried out for fibres with: an axon diameter of 12.5 µm; an external fibre diameter of 17.3 µm; nodal diameter of 5 µm; nodal area of 24 µm²; myelin thickness of 2.4 µm; periodicity of myelin lamellae of 16 nm and periaxonal space thickness of 20 nm. The temperature dependent nodal action potentials and their defining current kinetics are investigated in the range of 20-40°C. The action potential stimulation is simulated by adding a short (0.1 ms) rectangular depolarizing current pulse to the center of the first node. This case of point application of current intra-axonally at the node closely approximates the effects of point application of current extra-axonally at the node and realizes a point fibre polarization.

RESULTS

Comparison of the nodal action potentials at temperatures given in the panel figures is presented for human motor nerve fibres (Fig. 1). The potentials at the given temperatures are at each node from the 7th to the 14th, except in the last panel figure (20-42°C) where they are compared at node 10 only. The potentials are of constant amplitudes at the successive nodes for all investigated temperatures. Potential amplitudes increase up to 37°C and then decrease, with the temperature increase from 20 to 42°C. They are 22.5, 29.8, 35.0, 36.5, 37.5, 38.1, 38.2, 34.0 and 27.3 mV at the temperature 20, 25, 30, 32, 34, 36,

37, 40, and 42°C, respectively. With the temperature increase, the depolarizing afterpotentials decrease reaching the resting potential value (-86.7 mV) at temperature close to 39°C and then the afterpotentials become hyperpolarized. The potential amplitudes are slightly changed in the physiological range of 30-37°C. Conduction velocities, calculated from the times of the potential maxima at the nodes are 18.18, 27.8, 39.7, 45.4, 51.3, 58.0, 61.25, 70.5 and 70.0 m/s at the temperature 20, 25, 30, 32, 34, 36, 37, 40, and 42°C, respectively. The potential duration progressively decreases with the progressive increase of the temperature.

The nodal action potentials are determined by their current kinetics (Fig. 2 and Fig. 3). The currents presented are at node 10 only. To provide a better illustration: (i) the nodal ionic currents (I_{Na} , I_{Kf} , I_{Ks} , I_i) are presented in Fig. 2 and Fig. 3a; (ii) the nodal transaxonal current (I_a , dotted line) and the nodal external membrane current (I_m) are presented in Fig. 2 and Fig. 3b and (iii), all these currents are presented in Fig. 2 and Fig. 3c. The current kinetic changes in the physiological range of 32-37°C (Fig. 3) are not so sensitive to these temperatures compared to those at the extreme temperatures of 20 and 40°C (Fig. 2), where the current changes are large. The expected large inward current at the node of Ranvier resulting from the activation of a large number of nodal sodium Na^+ channels can be seen in all investigated temperature cases. The nodal I_{Na} current (Fig. 2 and Fig. 3a,c) is activated rapidly by the membrane depolarization, and then it is inactivated. The contribution of nodal K^+ (fast and slow) channels to the membrane repolarization is less apparent in the physiological range of 32-37°C, while in the range of 20-30°C it is virtually absent. However, the contribution of nodal K^+ channels to the membrane repolarization is large for temperatures higher than 39°C (Fig. 2a,c). Consequently, for the temperature range of 20-39°C, the nodal action potentials are determined mainly by the nodal sodium current (I_{Na}), as the contribution of nodal fast and slow potassium currents (I_{Kf} and I_{Ks}) to the total nodal ionic current (I_i) is negligible. The contribution of nodal I_{Kf} and I_{Ks} to the membrane repolarization is large for temperatures higher than 39°C. Compared to the case at 30°C, amplitudes of the nodal ionic currents (I_{Na} , I_{Kf} , I_{Ks} , I_i) are the largest at 40°C (Fig. 2).

Fig. 1. Comparison between the nodal action potentials of human motor nerve fibres at temperatures given in the panel figures. The potentials in response to the applied 0.1 ms current stimuli are presented at each node from the 7th to the 14th except in the last panel figure (20-42°C) where the potentials are compared at node 10 only

Fig. 2. Current kinetics defining the nodal action potentials of human motor nerve fibres at temperatures given in the panel figures. Currents: (a) I_{Na} (sodium), I_{Kf}, I_{Ks} (fast, slow) potassium, I_i (total ionic); (b) I_a (transaxonal, dotted lines), I_m (external membrane); (c) currents from (a) and (b) are given together. Note that the x-scales of the panel figures are different in the first column and the last two columns

Fig. 3. Current kinetics defining the nodal action potential of human motor nerve fibres at temperatures given in the panel figures. Currents: (a) INa (sodium), IKf, IKs (fast, slow) potassium, Ii (total ionic); (b) Ia (transaxonal, dotted lines), Im (external membrane); (c) currents from (a) and (b) are given together

At the node, the transmembrane potential (V_m) is composed of the transaxonal potential (V_a), and the 'transmyelin' nodal gap potential. The latter is zero, as the resistive nodal gap is not taken into account in the used model. However, the nodal transmembrane (external membrane) current (I_m , in Fig. 2 and Fig. 3b), for all investigated cases, is less than the current across the nodal axolemma (I_a). This is because the longitudinal current flows through the paranodal seal resistance (R_{pn}) to the periaxonal space.

DISCUSSION

The present study investigates and compares the effects of temperature on the conducting properties of human motor nerve axons. The principle finding is that the nodal action potential parameters are sensitive to temperature over the physiological range and are high sensitive to extreme body temperatures. The conduction velocities and action potential parameters (amplitude, duration, afterpotential) for the physiological case are in agreement with the clinical data (1-6). The high sensitivity of nodal action potentials to extreme temperatures is first quantitatively presented in this study. The same is valid for the presented here temperature dependent current kinetics defining the human nodal action potential abnormalities.

CONCLUSION

The results obtained are important for the interpretation of temperature dependent nerve conduction measurements in health.

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