# Influence of lowered $[Na^+]_o$ on single and trains of action potentials in soleus muscle fibres of the mouse

*S.P. Cairns[1] and J.M. Renaud[2], [1]Division of Sport and Recreation, Faculty of Health, Auckland University of Technology, Private Bag 92006, Auckland 1020, New Zealand and [2]Department of Cellular and Molecular Medicine, University of Ottawa, Ottawa, Canada.*

A reduction of extracellular $[Na^+]$, ($[Na^+]_o$), diminishes peak force and exacerbates fatigue during continuous tetanic stimulation of isolated skeletal muscle (Bezanilla *et al.*, 1972; Bouclin *et al.*, 1995; Cairns & Dulhunty, 1995). The mechanism for this effect is not fully understood. The aim of this study was to determine whether changes to the action potential could explain the reduced force at lowered $[Na^+]_o$ in mammalian skeletal muscle.

Isometric contractions and action potentials were elicited by supramaximal electric field stimulation via wire electrodes (10 V, 0.3 ms pulses) in isolated soleus muscles from mice. Muscles were bathed in control Krebs solution containing 147 mM $Na^+$, and then at lowered $[Na^+]_o$ (100, 60, 40 or 30 mM; NaCl was replaced by N-methyl-D-glucamine) at 25°C. Intracellular recordings of action potentials were made using conventional glass microelectrodes. Trains of action potentials (50 or 125 Hz, for 2 s) were recorded in deep fibres after stretching the muscle, in order to prevent movement artifacts.

**Single action potentials**: Lowered $[Na^+]_o$ had no effect on the resting membrane potential but caused action potentials to become progressively smaller and broader. The overshoot fell from +32 mV at 147 mM $Na^+$, to -20 mV at 30 mM $Na^+$. All fibres were excitable at 147-60 mM $Na^+$, but 19% and 40% of the fibres were inexcitable at 40 and 30 mM $Na^+$, respectively.

**Trains of action potentials**: At 147 mM $Na^+$, the 2-s trains of stimuli triggered action potentials on every occasion (100 or 250 action potentials), in association with a decrease in resting potential (between action potentials) and overshoot during the trains. At 40 mM $Na^+$, complete trains of small action potentials were produced at 50 Hz, as observed in frog muscle fibres (2). However, at 125 Hz there was considerable skipping leading to a complete failure to generate action potentials, usually within 500 ms.

**Action potentials and force**: The peak twitch force - overshoot relationship (determined by combining twitch and single action potential responses) showed that force was well maintained until the overshoot disappeared. Trains of action potentials evoked at 125 Hz at 147 mM $Na^+$, often had the peak of the action potential between 0 and -30 mV and this occurred without any fade (decline of peak force within a tetanus). At 40 mM $Na^+$, the peak tetanic force fell to 53% of the control at 50 Hz, and to 19% of the control at 125 Hz; the difference was linked to the failure to generate action potentials during a train.

In summary, the decline of peak tetanic force at lowered $[Na^+]_o$ can be explained by (i) the presence of inexcitable fibres, and (ii) a failure to generate action potentials during trains when evoked at high frequency. There is a considerable safety margin for a decline of the overshoot before peak twitch force is impaired. Our data also suggests that (iii) smaller action potentials during a train may make a moderate contribution to the decline of peak tetanic force.

Bezanilla, F, Caputo, C, Gonzalez-Serratos, H. & Venosa, R.A. (1972) *Journal of Physiology,* 223: 507-523.

Bouclin, R, Charbonneau. E. & Renaud, J.M. (1995) *American Journal of Physiology,* 268: C1528-C1536.

Cairns, S.P. & Dulhunty, A.F. (1995) *Muscle and Nerve,* 18: 890-898.

---

This work was supported by grants from the New Zealand Lottery Grants Board, and the National Science and Engineering Research Council of Canada.