

Dietary n-3 polyunsaturated fatty acids alter the voltage-dependence of Na⁺ currents in rat cardiac myocytes*WR Leifert^{1,2}, A Jahangiri^{1,2}, DA Saint¹, EJ McMurchie²*¹Department of Physiology, University of Adelaide, Adelaide, SA, 5005²CSIRO Health Sciences and Nutrition, Kintore Avenue, Adelaide, SA, 5000

Recent studies have demonstrated a role for the n-3 polyunsaturated fatty acids (PUFAs), as found in fish and fish oils, in preventing cardiac arrhythmias in experimental animals, neonatal and adult cardiomyocytes (1). The electrophysiological mechanism underlying the antiarrhythmic effects of n-3 PUFAs may involve an increase in the threshold for the generation of action potentials (2) suggesting it may be mediated by an effect on inward sodium currents. This study investigated the acute effects of n-3 PUFAs or dietary supplement (for 3 weeks) of fish oil (containing n-3 PUFAs) or saturated fat on whole-cell Na⁺ currents recorded in isolated adult rat ventricular cardiomyocytes using patch-clamp techniques.

The acute effects of the n-3 PUFAs docosahexaenoic acid (DHA, 22:6 n-3), eicosapentaenoic acid (EPA, 20:5 n-3) and α -linolenic acid (ALNA, 18:3 n-3) dose-dependently blocked the whole-cell sodium currents evoked by a voltage step to -30 mV from a holding potential of -90 mV with EC₅₀ values of $6.0 \pm 1.2 \mu\text{M}$, $16.2 \pm 1.3 \mu\text{M}$ and $26.6 \pm 1.3 \mu\text{M}$, respectively. DHA, EPA and ALNA at 25 μM shifted the voltage dependence of activation of the sodium current to more positive potentials by $9.2 \pm 2.0 \text{ mV}$, $10.1 \pm 1.1 \text{ mV}$ and $8.3 \pm 0.9 \text{ mV}$, respectively, and shifted the voltage dependence of inactivation to more negative potentials by $22.3 \pm 0.9 \text{ mV}$, $17.1 \pm 3.7 \text{ mV}$ and $20.5 \pm 1.0 \text{ mV}$, respectively. In addition, the membrane fluidising agent benzyl alcohol (10 mM) shifted the voltage dependence of activation to more positive potentials by $7.8 \pm 2.5 \text{ mV}$ and shifted the voltage dependence of inactivation to more negative potentials (by $-24.6 \pm 3.6 \text{ mV}$). Linoleic acid (18:2 n-6), oleic acid (18:1 n-9) and stearic acid (18:0) were either ineffective or much less potent at blocking the sodium current or changing the voltage dependence of the sodium current compared with the n-3 fatty acids tested. DHA, EPA, ALNA and benzyl alcohol significantly increased sarcolemmal membrane fluidity as measured by fluorescence anisotropy (r_{ss} values of 0.199 ± 0.004 , 0.204 ± 0.006 and 0.213 ± 0.005 and 0.214 ± 0.009 , respectively, compared with 0.239 ± 0.002 for control), whereas stearic, oleic and linoleic acids did not alter fluidity (r_{ss} not significantly different from control).

Dietary supplementation with fish oil significantly increased the proportion of total n-3 polyunsaturated fatty acids in ventricular membrane phospholipids compared with saturated fat supplementation ($18.8 \pm 0.6 \%$ vs $8.1 \pm 1.0 \%$, respectively, $P < 0.001$). The voltage dependence of inactivation of Na⁺ currents was significantly altered ($-73.5 \pm 1.2 \text{ mV}$, $n=5$ vs $-76.7 \pm 0.7 \text{ mV}$, $n=5$, $P < 0.05$, for saturated fat and fish oil treated groups, respectively). The voltage dependence of activation of Na⁺ was not significantly affected by the dietary fish oil treatment.

The results demonstrate that the antiarrhythmic effects of acute and dietary n-3 polyunsaturated fatty acids may partly involve changes in the voltage-dependence of inactivation of Na⁺ currents in rat cardiomyocytes.

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