

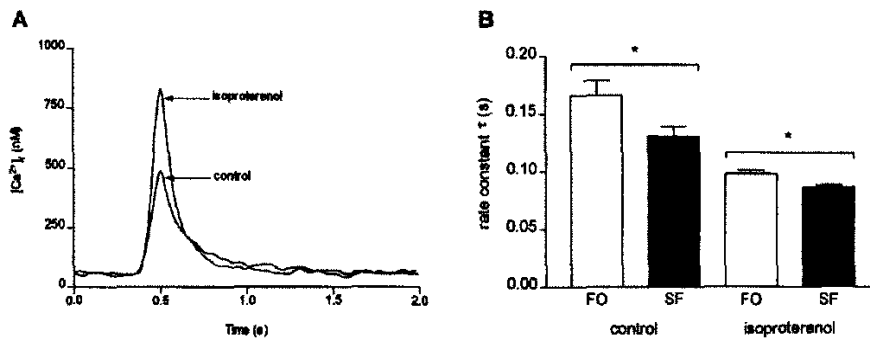
### Dietary fish oil prevents arrhythmic contractility and increases $\text{Ca}^{2+}$ transient decay time in adult rat cardiac myocytes

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The n-3 polyunsaturated fatty acids have been reported to exhibit cardioprotective effects in human clinical studies, experimental animal models and in isolated cell studies (1,2). Since  $\text{Ca}^{2+}$  overload and aberrant  $\text{Ca}^{2+}$  handling is associated with cardiac arrhythmias, we studied the effects of dietary incorporation of n-3 polyunsaturated fatty acids (PUFAs) into cardiac membrane phospholipids on arrhythmic contractility and cardiac myocyte  $\text{Ca}^{2+}$  handling (using Fura-2) in electrically-stimulated, adult rat ventricular cardiomyocytes. Dietary lipid supplementation (10 %) with fish oil (FO) for 3 weeks significantly increased the proportion of total n-3 polyunsaturated fatty acids (in particular, docosahexaenoic acid, 22:6, n-3) in ventricular membrane phospholipids compared with a saturated fat (SF) supplemented diet ( $26.2 \pm 0.9\%$  vs  $6.9 \pm 0.9\%$ , respectively,  $P < 0.001$ ). Cardiomyocytes from the FO dietary group were significantly ( $P < 0.001$ ) less susceptible to isoproterenol-induced arrhythmic contractile activity compared with the SF group. Sarcoplasmic reticulum (SR) store content of  $\text{Ca}^{2+}$  was similar in cells from both dietary groups. The SR  $\text{Ca}^{2+}$  pump inhibitor, 2,5-di-tert-butylhydroquinone (DBHQ) significantly decreased the amplitude of  $\text{Ca}^{2+}$  transients by approximately 62 % in both groups. The rate constant ( $\tau$ ) for the decay in  $\text{Ca}^{2+}$  transients following DBHQ treatment was increased in the FO group ( $0.722 \pm 0.034$  s,  $n=8$ ) compared with SF ( $0.594 \pm 0.031$  s,  $n=8$ ,  $P < 0.05$ ).  $\beta$ -adrenergic stimulation increased end-diastolic and systolic  $[\text{Ca}^{2+}]_i$  and decreased the  $\tau$  for  $\text{Ca}^{2+}$  transient decay in both groups. The  $\text{Ca}^{2+}$  transient decay was significantly increased in the FO group under non-stimulated conditions as well as following stimulation by  $0.5 \mu\text{M}$  isoproterenol.



A, Effect of isoproterenol on electrically stimulated  $\text{Ca}^{2+}$  transients and B, rate constant of decay of  $\text{Ca}^{2+}$  transients. FO; fish oil ( $n=8$ ), SF; saturated fat ( $n=8$ ). Mean  $\pm$  SEM. \* $P < 0.05$  by Student's unpaired t-test.

The antiarrhythmic effect of the FO supplement (n-3 PUFAs) was not associated with changes in SR  $\text{Ca}^{2+}$  content, diastolic or systolic  $[\text{Ca}^{2+}]_i$ . The increase in the time constant of decay of  $\text{Ca}^{2+}$  transients ( $\tau$ ) following dietary supplementation with FO may indicate altered functioning of the sarcolemmal  $\text{Na}^+ - \text{Ca}^{2+}$  exchanger by n-3 PUFA membrane incorporation.

1. Leifert WR, Jahangiri A, McMurchie EJ. J Nutr Biochem 1999;10:252-270.
2. Leifert WR, McMurchie EJ, Saint DA. J Physiol 1999;520.3:671-679.