Membrane lipid composition and its effect on Na^+,K^+-ATPase molecular activity: insights from mammals, birds and ectotherms

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The basal metabolic rate (BMR) of animals varies dramatically, being several-fold higher in endotherms compared to ectotherms, and much greater, on a mass-specific basis, in smaller vertebrates compared to larger vertebrates. Despite this large variation in metabolic rate between species, a significant and relatively constant proportion of metabolism is associated with membrane-linked energy consuming processes (e.g. Na^+ cycling), regardless of the absolute level of BMR. The majority of these membrane-associated processes are mediated by membrane-bound proteins, and here we have measured the molecular activity (turnover rate) of the Na^+,K^+-ATPase enzyme, a ubiquitous membrane protein that is a significant contributor to BMR, in a range of tissues* from species (five mammals, eight birds and three ectotherms) that vary greatly in their metabolic intensity. Additionally, we have analysed membrane acyl composition in the same tissues to determine the role of the lipid milieu surrounding membrane proteins, in regulating their activity.

Na^+,K^+-ATPase molecular activity varied approximately 20-fold across the different species (1,600 - 29,000 ATP.min^{-1}), and was generally greater in animals with a higher BMR (i.e. small vertebrates > large vertebrates and endotherms > ectotherms). These variations in molecular activity were associated with differences in membrane lipid composition, with membranes from more metabolically active species having a higher unsaturation index (i.e. number of double bonds per 100 fatty acid chains). The trends in membrane unsaturation were primarily due to significant and substantial variations in the concentration of the highly polyunsaturated omega-3 fatty acid, docosohexaenoic acid (22:6(n-3)), which ranged between 0.5% and 40% of the total fatty acids across the different species. When linear correlations were calculated between Na^+,K^+-ATPase molecular activity and the relative percentage of individual fatty acids in the membrane, 22:6(n-3) displayed the strongest correlation for any fatty acid in the combined data sets for both the endothermic species ($R=0.69$, $N=39$, $P<0.0001$) and the ectothermic species ($R=0.78$, $N=12$, $P=0.003$). Our results suggest that membrane lipid composition, and particularly 22:6(n-3) content, may play a role in determining the pace (or rate) of metabolism, *via* an effect on the molecular activity of membrane-bound proteins.

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* Tissues were obtained from euthanased animals.