Preparing for a cool life -- seasonal changes in lipid composition

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We are all encouraged to eat polyunsaturated fatty acids, as these are "good for us". The (relative) levels of particular classes of polyunsaturated fatty acids have been associated with a plethora of human illnesses. The latest findings of Walter Arnold and his group at the University of Veterinary Medicine, Vienna suggest that changes in fatty acid concentration of inner organs might be largely independent from diet composition. The work is published in *PLoS ONE*.

Animal cell membranes are a bilayer of phospholipids (charged fat molecules) made up to various degrees of fatty acids that must be acquired from the diet. The essential polyunsaturated fatty acids have been shown to be important in resistance to a variety of diseases and in coping with changes in body temperature. It is generally believed that mammals are unable to alter the proportions of essential fatty acids in their cell membranes except by changing their diets. Furthermore, mammals are unlikely candidates for extensive temperature-induced alteration, known to occur in fish or reptiles, because they typically maintain high and rather constant body temperatures.

Arnold and colleagues at the Research Institute of Wildlife Ecology, University of Veterinary Medicine, Vienna have investigated changes in the fatty-acid composition of cell membranes in an exceptional model, wild-living alpine marmots. As typical hibernators, alpine marmots lower their body temperatures to close to the ambient temperature throughout most of the winter. Even during the regular interruptions of hibernation their body temperature remains a few degrees below typical summer

levels. Amazingly, the amount of so-called "n-6" polyunsaturated fatty acids (those with the final double bond at the sixth position) in the membranes was found to increase dramatically before the start of hibernation, apparently to prepare the body, and particularly the heart, for operation at very low temperatures. Consistent with this idea, the transition to a higher content of n-6 fatty acids in membranes takes place extremely rapidly just before the animals enter their hibernation chambers. The changes are reversed, again over a short time, around the termination of hibernation in spring, when the animals return to a life at high body temperatures.

A selective process for membrane remodelling

The fatty acids incorporated in the membranes probably stem from the marmots' white adipose tissue. Surprisingly, however, fatty acids are not simply taken from the fat stores at random but n-6 polyunsaturated fatty acids are transported preferentially, although the mechanism remains a mystery.

These new and unexpected findings show that mammals can make highly significant and rapid seasonal changes to the lipid composition of their cell membranes. But the results go far beyond this. During and immediately after hibernation marmots are unable to eat anything – their food is under a thick layer of snow – so the changes cannot be related to immediate dietary influences. Instead, the work of Arnold's group strongly implies that animals have specific ways of transporting individual (groups of) fatty acids in the body. And because the animals hibernate underground, isolated from any external signals, the changes are probably controlled by an endogenous clock as part of an annual cycle.

It seems unlikely that the mechanisms are specific to animals that hibernate. All mammals – including humans – reduce their body

temperature to some extent during winter, so the results are directly applicable to us. As Arnold says, "the humble marmot could revolutionize our way of thinking about fatty acid metabolism. The idea that changes in the essential fatty acid content of membranes can only be made via the diet is clearly too simple." To illustrate the importance of the subject, Arnold notes further that "the incidence of heart attacks in humans, well known to increase when membranes contain a high n-6 to n-3 ratio, peaks at the end of winter." Could this relate to a conserved seasonal peak of n-6 polyunsaturated fatty acid concentrations in heart muscle?

More information: dx.plos.org/10.1371/journal.pone.0018641

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