The Progression of Long-Chain Fatty Acids from Herbivore to Carnivore and the Evolution of the Nervous System

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In herbivorous mammals the long-chain products of the C_{18} vegetable polyenoic fatty acids are mainly incorporated into cell structural constituents such as the phospholipids (Gale, Crawford & Woodford, 1969). In large herbivores the principal C_{22} polyenoic fatty acid has been found to be a docosapentaenoate (Crawford, Gale & Woodford, 1969). This finding appears to hold for large herbivores from both tropical (e.g. buffalo and eland) and northern latitudes (e.g. moose, red deer and black-tailed deer). In small mammals, such as the mouse, rat and guinea pig, fed on herbivorous diets the principal C_{22} acid is the docosahexaenoate; phospholipids from human tissues also contain more docosahexaenoate than pentaenoate.

A number of factors could be responsible for the fact that large herbivores produce such small proportions of the polyenoic acid with six double bonds, of which diet and growth rate are of particular interest. The herbivore eats linoleic ($C_{18:2,n-6}$) acid and linolenic ($C_{18:3,n-3}$) acid whereas carnivorous animals also include the long-chain derivatives from other animal tissues. We have compared the liver phospholipids of herbivores (eland) and carnivores (spotted hyena) from the same ecosystem. The phosphatidylethanolamine in the eland contained a balance of $C_{22:5}$ acid/$C_{22:6}$ acid of 7.6:6.4% whereas in the hyena the balance was 4.0:15%. The sphingomyelin fraction in the eland liver contained 1.6% of the fatty acids as nervonic acid ($C_{24:1}$) whereas the hyena fraction contained 5.6%. In additional studies of buffalo and hartebeeste the proportion of docosahexaenoate was less than in the eland; the same difference of an increase in the proportions of long-chain acids and the degree of unsaturation was also found in the leopard.

Large carnivores grow more slowly than do herbivores of similar adult body weights. Although carnivorous animals eat a different diet compared with herbivores, their tissue protein composition seems similar (Crawford, Gale, Somers & Hansen, 1970), but their structural fats are clearly different. More than 50% of the dry weight of brain grey matter is fat. The brain/body-size ratio is consistently greater and the development of the peripheral nervous and vascular system is more extensive in the carnivorous animals. Comparative studies show that brain also contains significantly lower proportions of parent vegetable polyenoic acids and higher proportions of their long-chain derivatives than is found in normal liver or muscle in the same animal. We also see greater proportions of the long-chain fatty acids and higher degrees of unsaturation in the carnivores. It may be that their different dietary structure and slower growth made possible the continued evolution and development of the nervous and vascular system. It is noteworthy that the phosphatidylethanolamine from human grey matter contains between 20 and 30% of the fatty acids as the docosahexaenoate.

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Lipolysis and the Regulation of Fatty Acid Metabolism in the Liver

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There has been renewed interest in the possibility that lipolysis of liver glycerides may contribute significantly to ketogenesis and possibly stimulate gluconeogenesis (Bewsher & Ashmore, 1966; Williamson, Herczeg, Coles & Danish, 1966). A triglyceride lipase is considered to be activated by 3′:5′-cyclic-AMP, the concentration of which in turn may be increased by glucagon and decreased by insulin.

A basic difference in lipolysis between livers of fed and starved animals should be reflected in the concentrations of tissue long-chain free fatty acids. A new and specific radioassay for long-chain free fatty acids in tissues has been developed. Male rats were anaesthetized with sodium pentobarbital and a portion of the liver was taken with tongs cooled in liquid N_2. Lipids were extracted with chloroform–methanol (2:1, v/v). After isolation of the fatty acids by t.l.c., they were methylated by using a mixture of boron trifluoride in [*Me*-^{3}H]methanol. Finally, the [^{3}H]methyl esters of the fatty acids were extracted with hexane and their radioactivities measured. The concentration of long-chain free fatty acids was 0.69 ± 0.04 (mean $\pm$ S.E.M.) and 0.32 ± 0.02 μmol/g in the livers of starved and fed rats respectively.

Rat livers were perfused as described by Mayes & Felts (1966). After equilibration, a flash injection of [1-^{14}C]oleate was given into the hepatic portal vein and blood was collected from the hepatic vein. The liver appeared to reach an isotopic steady state after 20 min, when ^{14}C-labelled ketone bodies and ^{14}C-labelled very-low-density lipoproteins were secreted at a steady rate. Incorporation of ^{14}C into