DIETARY LIPIDS, AGEING AND BRAIN PATHOLOGIES

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Palmitic and stearic acid methyl esters as potential vasodilators and neurotransmitters

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Cerebral blood vessels are innervated by perivascular nerves from the sympathetic and parasympathetic out-flows of the autonomic nervous system. These nerves play a central role in vascular tone regulation by releasing neurotransmitters either presynaptically on the same or neighboring nerves or postsynaptically on vascular smooth muscle resulting in vasodilation/vasoconstriction. Cerebral arteries receive sympathetic (norepinephrine, NE is the major sympathetic neurotransmitter in the brain) nerve fibers originating from the superior cervical ganglion (SCG) innervating major brain arteries such as pial, basilar, circle of Willis arteries, and is home to palmitic acid methyl ester (PAME) and stearic acid methyl ester (SAME), a recently discovered vasodilator [PAME can induce endothelium-independent vasodilation and is more potent than nitric oxide (NO) donors] and neuroprotective agent (PAME and SAME). PAME and SAME are released from the electrically stimulated SCG in the presence of arginine analogs such as L-arginine and nitric oxide synthase inhibitor (N□-Nitro-L-Arginine). Administration of PAME can enhance post-ischemic cortical cerebral blood flow (in vivo), while SAME can induce neuroprotection.

PAME, but not palmitic acid (PA), can cause potent vasodilation suggesting that methylation of PA is crucial for vasodilation further perpetuated by arginine analogs. Protein arginine methyltransferases (PRMTs) may be responsible for the methylation of PA to form PAME. Arginine methylation (via PRMTs) is a prevalent posttranslational modification that can to be involved in many disease processes such as cell cycle regulation and cancer. However, PRMTs have not been well-documented in the functional role of methylation of PA released from the sympathetic nervous system modulating brain cerebral blood flow and metabolism. Therefore, our long-term goal is to enhance the understanding of cerebral blood flow regulation and ameliorate neurological deficits by defining the possible mechanism(s) of these fatty acid methyl esters.