Heptanoate is neuroprotective in vitro but triheptanoin post-treatment did not protect against middle cerebral artery occlusion in rats

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 Triheptanoin, the medium-chain triglyceride of heptanoate, has been shown to be anticonvulsant and neuroprotective in several neurological disorders. In the gastrointestinal tract, triheptanoin is cleaved to heptanoate, which is then taken up by the blood and most tissues, including liver, heart and brain. Here we evaluated the neuroprotective effects of heptanoate and its effects on mitochondrial oxygen consumption in vitro. We also investigated the neuroprotective effects of triheptanoin compared to long-chain triglycerides when administered after stroke onset in rats. Heptanoate pre-treatment protected cultured neurons against cell death induced by oxygen glucose deprivation and N-methyl-D-aspartate. Incubation of cultured astrocytes with heptanoate for 2 h increased mitochondrial proton leak and also enhanced basal respiration and ATP turnover, suggesting that heptanoate protects against oxidative stress and is used as fuel. However, continuous 72 h infusion of