A novel therapeutic strategy for experimental stroke using docosahexaenoic acid complexed to human albumin

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Introduction: Docosahexaenoic acid (DHA; 22:6, n-3) complexed to human albumin (DHA-Alb) is highly neuroprotective after temporary middle cerebral artery occlusion (MCAo) in rats. This study evaluated whether treatment with DHA-Albisneuroprotective in permanent MCAo in young and aged rats and whether protection persists with chronic survival.

Methods: In series 1, male young Sprague-Dawley (SD) rats underwent permanent MCAo and were treated with DHA (5mg/kg), Alb (0.63 or 1.25g/kg), DHA-Alb (5mg/kg+0.63g/kg or 5mg/kg+1.25g/kg) or saline i.v. at 3 h after onset of stroke. Behavior was evaluated on days 1, 2 and 3 after MCAo. Ex vivo imaging of the brains and histopathology were conducted on day 3. In series 2, male aged (18-months old) SD rats received 2 h MCAo and were treated with DHA, Alb, DHA-Alb (5mg/kg+0.63g/kg) or saline at 3 h after stroke. Behavior was evaluated on days 1, 2, 3 and 7 after MCAo. Ex vivo imaging of the brains and immunohistochemistry were conducted on day 7. In series 3, SD rats received 2 h MCAo and were treated with DHA, Alb, DHA-Alb (5mg/kg+1.25g/kg) or saline at 3h after stroke. Behavior and neurogenesis were evaluated during 3 weeks after MCAo.

Results: In series 1: Rats treated with low and moderate doses of DHA-Alb showed improved neurological scores compared to Alb-treated rats on days 2 and 3. Total, cortical and subcortical lesion volumes computed from T2WI images were reduced by a moderate dose of DHA-Alb by 25%, 22%, 34%, respectively, compared to the corresponding Alb group. In series 2: DHA-Alb treatment improved the neurological score (by 33%-45%), as well as total and cortical lesion volumes computed from T2WI images (by 62% and 69%). In addition, DHA-Alb decreased ED-1-activated microglia/microphages and increased NeuN and GFAP-positive cell count compared to the Alb group. In series 3, DHA-Alb improved behavior and enhanced neurogenesis 3 weeks after stroke.

Conclusions: DHA-Alb protected the brain from permanent MCAo in young and aged rats and promoted enduring ischemic neuroprotection. This treatment might provide the basis for future therapeutics for patients suffering from ischemic stroke.