Role of HDL in brain ischemia/stroke

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Ischemic stroke is the leading cause of adult disability. The obstruction of a cerebral vessel due to the formation of a thrombus or to a ruptured atherosclerotic plaque leads to the destabilization of the endothelial layer forming the blood-brain barrier (BBB). We hypothesized that high-density lipoproteins (HDLs) could provide a protective effect on the BBB, due to their endothelio-protective effects. Indeed, HDLs, in addition dot their function to reverse transporting cholesterol, display antioxidant and anti-inflammatory properties. Using two models of ischemic stroke in rat and mice, we have shown that intravenous injection of HDL particles (10 to 40 mg/kg) at the acute phase of stroke limited the cerebral infarct volume up to 70%. This was associated with a reduced mortality and also, in case of a combined treatment with rtPA (the reference fibrinolytic agent), HDLs limited the hemorrhagic transformation by 90%. These protective effects of HDLs may be due to the protection of endothelial cells, as shown in vitro in a cellular model of BBB submitted to oxygen-glucose deprivation and under proteolytic aggression. Finally, the protective effects of HDLs have been shown to be dependent on endothelial SRB1 (scavenger receptor B1). Taken together, our results suggest that HDL therapy may be suitable for limiting the deleterious effects of ischemia-reperfusion in stroke.