

**P059** Crossing the barrier: net flux of 27-hydroxycholesterol into the human brain.

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Side-chain oxidized oxysterols have a unique ability to traverse lipophilic membranes.

We tested the hypothesis that there is a net flux of 27-hydroxycholesterol from the circulation into the brain using plasma samples collected from the internal jugular vein and an artery of healthy male volunteers. Two independent studies were performed, one in which total levels of 27-hydroxycholesterol (free steroid and lipoidal esters) and one in which the free fraction of 27-hydroxycholesterol were measured. In the majority of subjects, the level of 27-hydroxycholesterol was higher in the artery than in the vein. The distribution of 27-hydroxycholesterol in human brain autopsy materials was found to be consistent with an extracerebral origin with a concentration gradient from the white to the grey matter – opposite to 24S-hydroxycholesterol, which is exclusively formed in brain. Since the blood-brain barrier is impermeable to cholesterol and 27-hydroxycholesterol is a potent regulator of several cholesterol-sensitive genes, the flux of 27-hydroxycholesterol into the brain may be an important link between intra- and extracerebral cholesterol homeostasis. This flux may also be part of the explanation for the hitherto unexplained link between hypercholesterolaemia and Alzheimer's disease.