Definition of the metabolic pattern of ANGPTL3 deficient mice on a chow diet and under dysmetabolic conditions

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Aim: ANGPTL3 controls lipid and lipoprotein metabolism through lipoprotein lipase and endothelial lipase inhibition and the prevention of lipoprotein-derived triglycerides hydrolyzation.
Here we present the metabolic profile of ANGPTL3 deficient mice in physiology and during the development of metabolic disorders.
Methods: Angptl3 KO mice (C57BL6/J background) and their littermate controls (wild-type, WT) were fed a chow and a High Fat Diet (HFD, 60%kcal from lipids) for 16 weeks.
During the diet protocol, changes in lipids and lipoprotein profile, under fast, fed, and fast-refeed setting were assessed. The metabolic phenotype was assessed, with a Glucose Tolerance Test (GTT) and an Insulin Tolerance Test (ITT); the lipids absorption profile was assessed with an Oral Lipid Tolerance Test (OLTT).
Results: ANGPTL3 KO mice fed *ad libitum* a chow diet are hypolipidemic (plasma triglycerides levels: 42,42±8,80 mg/dL in ANGPTL3 KO mice compared to 122,02±55,09 mg/dL in WT mice; plasma cholesterol levels: 44,00±9,11 mg/dL in ANGPTL3 KO mice compared to 76,51±15,87 mg/dL in WT mice).
After 16h fasting, ANGPTL3 KO mice on a chow diet are hypolipidemic and display small lipoproteins less rich in cholesterol and triglycerides, as established in humans, and the same holds true for mice fed a HFD diet.
On HFD, ANGPTL3 KO mice gain less body weight, suggesting an improved metabolic profile compared to WT animals.
The hypolipidemia is conserved during all the timepoints of OLTT, both in mice on chow or HFD, suggesting a different lipid management; in spite, no significant differences in the circulating glycaemia has been proved with a GTT after 16h of fasting; likewise, a similar sensitivity to insulin has been outlined with an ITT after 4h of fasting.
Conclusions: This metabolic profiling of ANGPTL3 KO mice on chow diet or HFD highlights that these mice are hypolipidemic and may have beneficial metabolic features compared to controls.

Cholesterol esterification is hampered in alzheimer's disease and cholesteryl esters composition is consequently altered

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Introduction and Aim: Several epidemiological studies indicate a strong inverse association between the risk of developing Alzheimer's disease (AD) and plasma HDL-C levels. The mechanism by which plasma HDL influence the pathogenesis and progression of AD is still unsolved and since cholesterol esterification is a crucial step in HDL metabolism it could be involved. The purpose of this study was to evaluate cholesterol esterification and HDL subclasses in plasma and cerebrospinal fluid (CSF) of Alzheimer's Disease (AD) patients.
Methods: The study enrolled 70 AD patients and 74 cognitively-normal controls comparable for age and sex. Lipids and lipoprotein profile, cholesterol esterification, and cholesterol efflux capacity (CEC) were evaluated in plasma and CSF using assays set for measurement in plasma, which were appropriately modified for CSF.
Results: AD patients have normal plasma lipids, but significantly reduced unesterified cholesterol and unesterified/total cholesterol ratio. Lecithin:cholesterol acyltransferase (LCAT) activity and cholesterol esterification rate (CER), two measures of the efficiency of the esterification process, were reduced by 29% and 16%, respectively, in plasma of AD patients. Plasma HDL subclass distribution in AD patients was comparable to that of controls, but the content of small discoidal preβ-HDL particles was significantly reduced. In agreement with the reduced preβ-HDL particles, cholesterol efflux capacity mediated by the transporters ABCA1 and ABCG1 was reduced in AD patients' plasma. The CSF unesterified to total cholesterol ratio was increased in AD patients, and CSF CER and CEC from astrocytes were significantly reduced in AD patients. In the AD group, a significant positive correlation was observed between plasma unesterified cholesterol and unesterified/total cholesterol ratio with Aβ1-42 CSF content.
Conclusions: Taken together data indicate that cholesterol esterification is hampered in plasma and CSF of AD patients, and that plasma cholesterol esterification biomarkers (unesterified cholesterol and unesterified/total cholesterol ratio) are significantly associated to disease biomarkers (i.e., CSF Aβ1-42).