CSF Aβ42/β40 ratio correlates with plasmatic LDL levels.

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Introduction

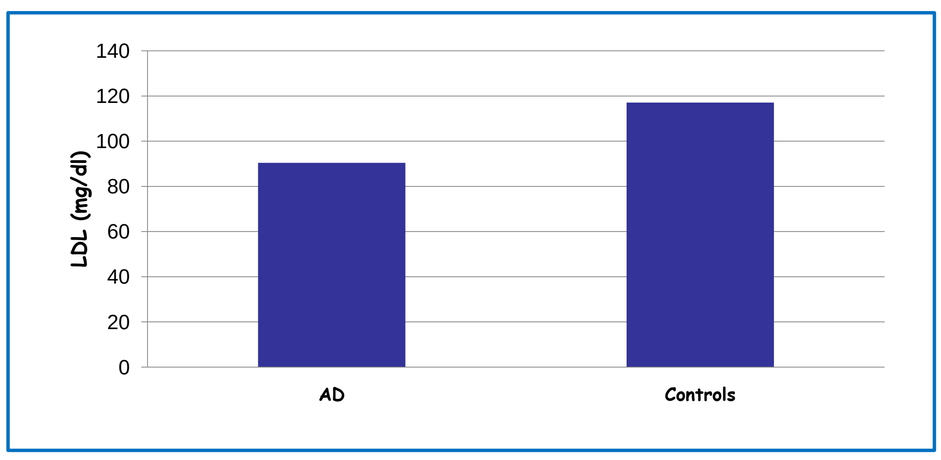
Current wisdom suggests high cholesterol to represent a risk factor for **Alzheimer's disease** (AD). However, literature reports show conflicting pieces of evidence with either positive, neutral or inverse associations between lipid profiles and dementia development [1]. Preclinical studies have documented the role of low-density-lipoprotein receptor on amyloid-β metabolism and brain homeostasis [2, 3]. Advances in AD cerebrospinal fluid (CSF) biomarkers value the added diagnostic relevance of amyloid-β42/β40 ratio, due to its lesser interindividual variability.
The aim of the present study is to investigate whether AD plasmatic **lipid profile** shows peculiar features in comparison to control subjects, and whether it correlates with **CSF biomarker** levels.

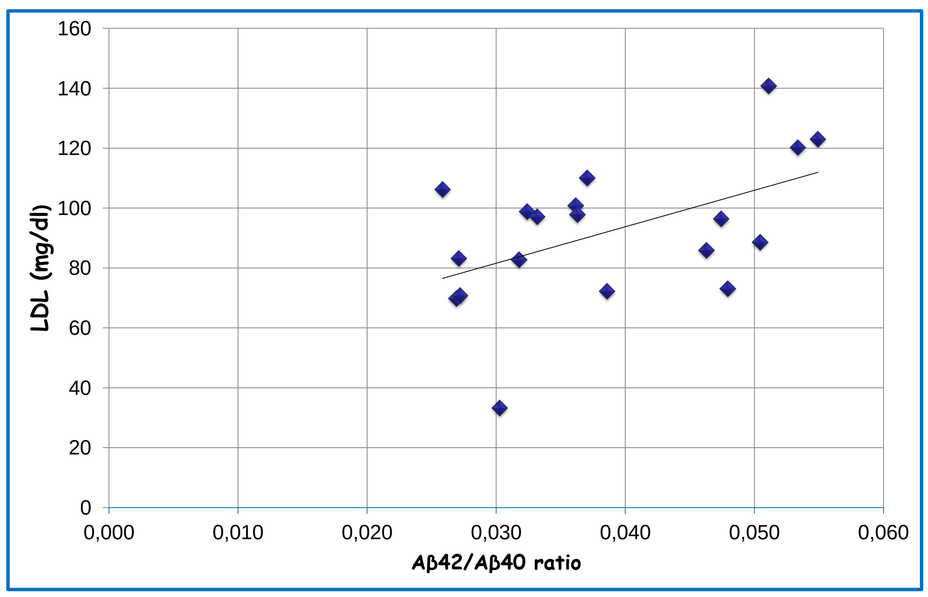
Subjects and methods

We enrolled 19 AD patients basing on the NINCDS-ADRDA criteria and 11 controls subjects. All patients underwent a lumbar puncture with CSF analysis for AD biomarkers (Aβ-42, Aβ-40, T-tau and p-tau) and provided a venous blood sample for standard lipid profile (total and HDL cholesterol, triglycerides; LDL cholesterol was calculated by means of Friedwald formula).
All AD patients showed the typical CSF AD profile with lower CSF Aβ-42 (496 pg/mL, ds= 106 pg/mL) and Aβ-42/Aβ-40 ratio levels (0.038, ds = 0.01) and higher CSF t-tau (680 pg/mL, ds= 215 pg/mL) and p-tau levels (106 pg /mL, ds= 30 pg/mL), whilst all controls showed normal CSF biomarker levels.

Results

We performed a t-test comparing plasmatic lipid indicators: we observed a significant difference in LDL levels between AD (91 mg/dl, ds = 27 mg/dl) and controls (119 mg/dl, ds = 26 mg/dl) (p = 0.018).





Hence we performed a regression analysis in the AD subgroup between CSF biomarkers and plasmatic lipid indicators. The statistical analysis showed a significant linear correlation between **Aβ-42/Aβ-40 ratio and LDL levels** ($r = 0.57$, $p < 0.05$).

Conclusions

Our data suggest an association between **LDL metabolism** and **amyloid pathology**, possibly involving clearance pathways. The present finding has to be framed in the complex and recent advances in brain homeostatic processes, needing further validation and investigation.

References

[1] Michikawa M. Cholesterol paradox: is high total or low HDL cholesterol level a risk for Alzheimer's disease? J Neurosci Res. 2003 Apr 15;72(2):141-6.
[2] Fujiyoshi M, Tachikawa M,, Ohtsuki S et al. Amyloid-β-peptide (1-40) elimination from cerebrospinal fluid involves low-density lipoprotein receptor-related protein 1 at the blood-cerebrospinal fluid barrier. J Neurochem. 2011 Aug;118(3): 407-15.
[3] Zlokovic BV, Deane R, Sagare AP et al. Low-density lipoprotein receptor-related protein-1: a serial clearance homeostatic mechanism controlling Alzheimer's amyloid β--peptide elimination from the brain. J Neurochem. 2010 Dec;115(5):1077-89.