Cerebrospinal fluid and plasma HDL (dys)function in Multiple Sclerosis

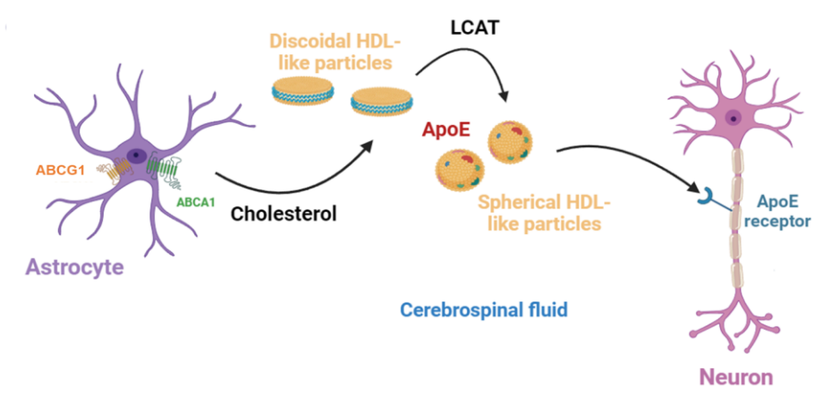
marcella.palumbo@unipr.it

Marcella Palumbo(1), Martina Ugolotti (1), Matteo Minetti (2), Erica Curti (3), Franco Bernini (1), Franco Granella (2), Maria Pia Adorni (2), Francesca Zimetti (1)

[1] Department of Food and Drug, University of Parma, Parma.[2] Unit of Neurosciences, Department of Medicine and Surgery, University of Parma, Parma. [3] Neurology Unit, Department of General and Specialized Medicine, Parma University Hospital, Parma.

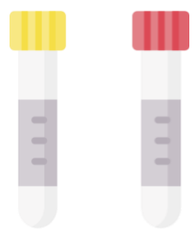
Background and objective

Multiple sclerosis (MS) is an inflammatory and immune-mediated neurodegenerative disease in which cholesterol plays a key role. Dysregulation of cholesterol transport mediated by cerebral HDL in the central nervous system (CNS) has been associated with neurodegenerative disorders. However, the precise involvement of these HDL-like lipoproteins in multiple sclerosis (MS) is still not clear.



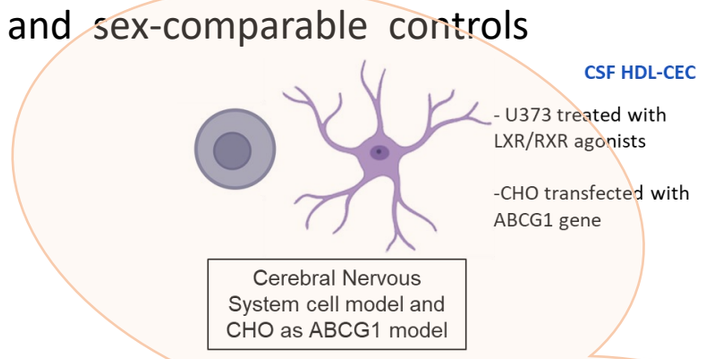
This study aimed to investigate the relationship between cholesterol metabolism and MS, focusing on cerebral and serum HDL function to promote cerebral and peripheral cellular cholesterol efflux (HDL-CEC).

Patients, materials and methods



HDL from CSF and Serum of:
25 relapsing-remitting or progressive, mainly primary, MS.

12 age- and sex-comparable controls (CTRL)



- Cholesterol efflux was measured with a standardised radioisotopic technique on central and peripheral cell models:

Results

Table 1

Patients' characteristics	CTRL N = 12	MS N = 25	P value
Age - years	43 ± 14.76	38 ± 12.26	0.2787
Male - n (%)	5 (38.46)	9 (36)	>0,9999
Clinical data			
EDSS – (0 - 10)	-	2.00 (1.50 – 3.00)	-
OCB positive – n (%)	-	20 (80)	-
Lipid profile—mg/dL			
Total Cholesterol	208.1 ± 39.68	184.7 ± 45.14	0.1644
HDL Cholesterol	53.44 ± 9.59	61.33 ± 14.67	0.1462
LDL Cholesterol	143.89 ± 31.72	116.57 ± 34.17	**0.0469**
Triglyceride	138.5 (107.0 - 203.8)	72.5 (54.6- 101.8)	**0.0010**
Disease Modifying therapy (DMT) – n (%)			
Treated – n (%)	0 (100)	21 (84)	**<0,0001**

Clinical demographics data

- The two groups were comparable for age and sex.
- The Disability Status (EDSS) and the Oligoclonal bands (OCB) positivity were assessed only in the MS group, confirming MS diagnosis.
- No differences were reported for total and HDL cholesterol, while a lower level of LDL and triglycerides in MS group was found **(Table 1)**.

MS CSF and Serum HDL Cholesterol efflux capacity (CSF/serum HDL-CEC)

- In CSF HDL-CEC from astrocytes was significantly lower in MS subjects compared to controls (p=0.002631). Specifically, ABCG1-CEC was reduced in MS patients compared to controls (p=0.02192) **(Figure 1)**.
- No significant differences were observed for the serum HDL-CEC ABCA1- and ABCG1-mediated between groups **(Figure 2)**.

Figure 1

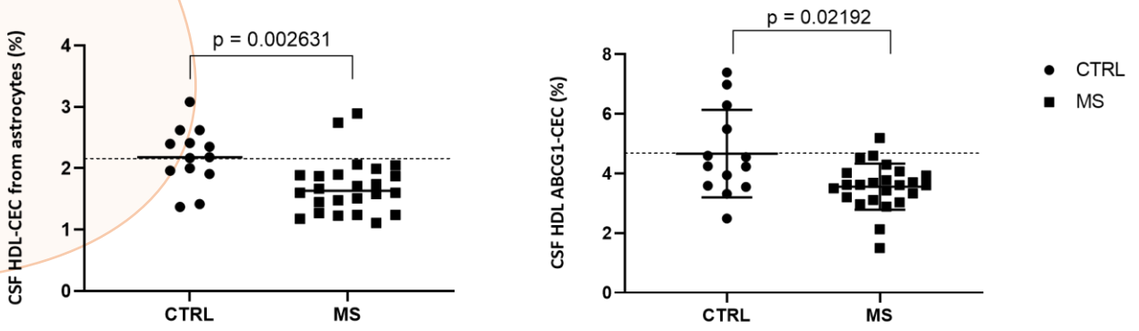
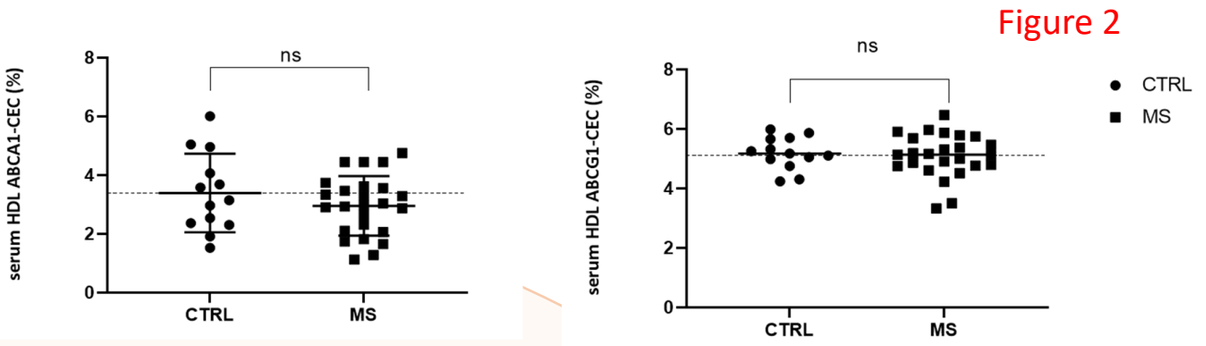


Figure 2



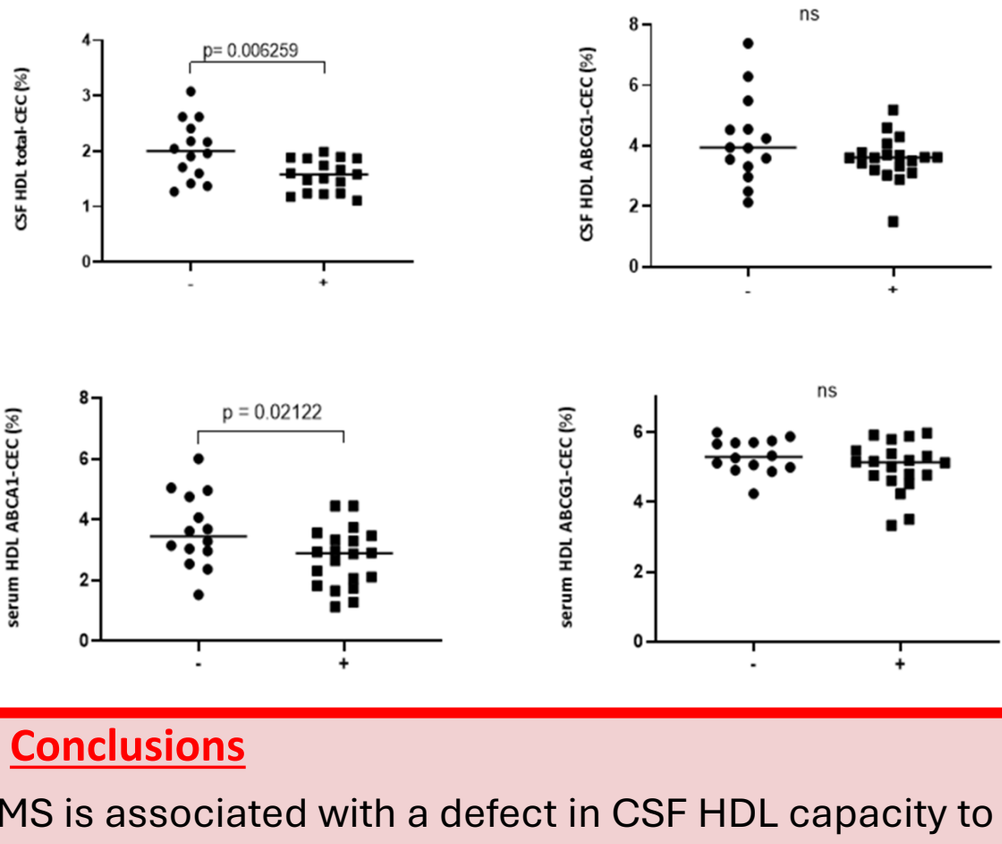


Figure 3

- OCB negativity ≤1
- + OCB positivity ≥2

(-) = CTRL 10/14; MS 4/14
(+) = MS 20/21

CSF/serum HDL-CEC after stratification for OCB positivity (all subjects)

- Stratification of the population based on the presence of OCB, revealed that CSF HDL-CEC from astrocytes (p=0.009179) and serum HDL-CEC ABCA1-mediated (p=0.02467) were significantly lower in subjects OCB+ **(Figure 3)**.

Conclusions

MS is associated with a defect in CSF HDL capacity to promote the first step of cerebral cholesterol transport, suggesting that cerebral HDL and its function may be considered a potential pharmacological target.
In addition, the observation that CSF and serum HDL-CEC is lower in MS subjects OCB+ suggests that HDL (dys)function may be correlated with the presence of OCB. The reason of this link deserves further investigations.

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