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

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Marcella Palumbo

Born in Matera (MT), and now working at the University of Parma (PR).

Keywords: HDL function; Cholesterol homeostasis; Neurodegenerative diseases.

My future research plans: To further my research into evaluating HDL functions and cholesterol homeostasis in neurodegenerative diseases.

What do I want to be when I grow up?

When I grow up, I want to be a cholesterol whisperer! The kind of scientist who can convince HDL particles to reveal their deepest secrets — especially about how they keep our brains healthy and balanced.

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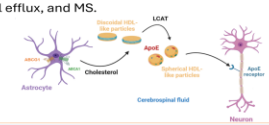
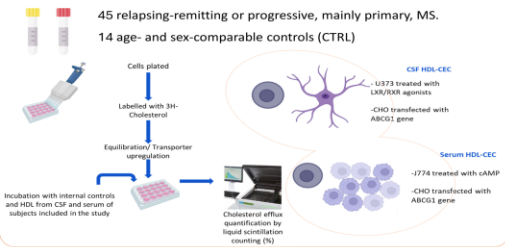
Background and objective

Multiple sclerosis (MS) is an inflammatory and immune-mediated neurodegenerative disease in which cholesterol plays a key role. Dysregulation of cholesterol efflux in the central nervous system has been associated with neurodegenerative disorders. However, whether dysfunctions also occur in MS has not yet clarified. For this reasons, this study aimed to investigate the relationship between cholesterol metabolism, focusing on CSF and serum HDL function, namely the capacity to promote cholesterol efflux, and MS.



Patients, materials and methods



Results

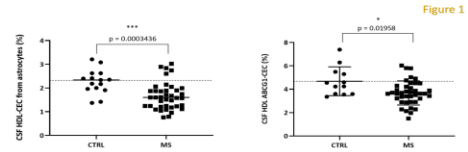
Clinical demographics data

Table 1

Patients' characteristics	CTRL N = 14	MS N = 45	P value
Age - years	46 ± 15.12	40 ± 13	0,1452
Male - n (%)	7 (50)	17 (37.8)	0,4162
Clinical data			
EDSS – (0 - 10)	-	2.3 (1.50 – 2,875)	-
RM9 (>9 lesions) – n (%)	-	21 (53.3)	-
OCB positive – n (%)	-	34 (75.56)	-
Lipid profile—mg/dL			
Total Cholesterol	206.9 ± 38.76	187.1 ± 42.48	0,1868
HDL Cholesterol	50.78 ± 9.4	61.29 ± 14.02	**0,0386**
LDL Cholesterol	135 ± 36.98	120.8 ± 34.22	0,2308
Triglyceride	168 (107.0 – 246.2)	69 (53- 96.5)	**<0,0001**

The two groups were comparable for age and sex. The Disability Status (EDSS) and the Oligoclonal bands positivity (OCB+) were assessed only in the MS group. No differences were reported for total and LDL cholesterol levels, while significantly higher HDL and lower triglyceride levels were found in MS (p=0.0386 and <0.0001 respectively) **(Table 1)**.

Figure 1



CSF HDLs promoted a significantly lower cholesterol efflux from astrocytes in MS subjects compared to controls (-32%, p=0.0003), and lower efflux specifically through the transporters ABCG1 (-18%, p=0.0196)(**Figure 1A and B**). No significant differences were observed between the groups for the serum HDL-cholesterol efflux capacity ABCA1- and ABCG1-mediated (**Figure 2A and B**).

Figure 2

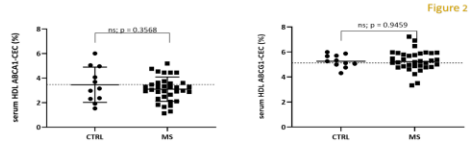
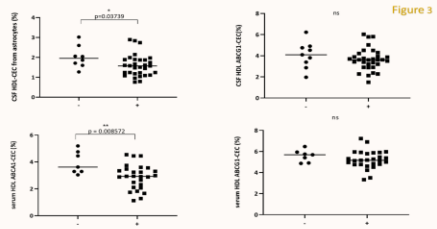


Figure 3



Stratifying the MS population based on the positivity of the prognostic parameter OCB, an indicator of disease severity, CSF HDL-cholesterol efflux capacity from astrocytes (-21%, p=0.0374) and serum HDL-cholesterol efflux capacity ABCA1-mediated (-27%, p=0.0086) were significantly lower in subjects OCB+ (**Figure 3A and C**).

Conclusions

MS is associated with a dysfunction in CSF HDL capacity to promote cholesterol efflux, the first step of cerebral cholesterol transport, suggesting cerebral HDL as a potential pharmacological target. In addition, the observation that also serum HDL-CEC ABCA1-mediated is lower in MS subjects OCB+ may put the premises to study serum HDL-CEC as a potential less invasive biomarker of the disease.

For questions and curiosities, please contact
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