ORAL PRESENTATIONS

Lower cerebral arterial blood flow is associated with greater serum neurofilament light chain levels in multiple sclerosis patients

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Background

Hypoperfusion, vascular pathology, and cardiovascular risk factors are associated with disease severity in multiple sclerosis (MS).[1,2] In particular, the total cerebral arterial blood flow (CABF), measured as a sum of all arterial flow in the neck, was associated with the cognitive performance of MS patients.[3]

Objective

To assess relationships between CABF and serum neurofilament light chain (sNfL), as neuronal damage biomarker with good prognostic value and treatment responsiveness.[4] If the cerebrovascular changes are an independent pathophysiological factor in MS, a relationship should remain significant after controlling for common MS-based disease measures (*i.e.*, T2 lesion volume and brain volume).

Materials and methods

Total CABF was measured in 137 patients (86 clinically isolated syndrome (CIS)/relapsing-remitting (RR) and 51 progressive MS (PMS)) and 48 healthy controls (HCs) using Doppler ultrasound. sNfL was quantitated using a single molecule assay (Simoa). Three point zero T magnetic resonance imaging (MRI) examination allowed quantification of T2 lesion and whole-brain volume (WBV). Multiple linear regression models determined the sNfL associated with CABF after correction for demographic and MRI-derived variables.

Results

After adjustment for age, sex and body mass index (BMI), total CABF remained statistically significant and model comparisons showed that CABF explained additional 2.6% of the sNfL variance (β=-0.167, p=0.044). (Table 1) CABF also remained significant in a step-wise regression model (β=0.18, p=0.034) upon the inclusion of T2 lesion burden and WBV effects. The explained sNfL variance improved from 17.4%, 22.7% with the presence of at least 2 CVD variable and 25.8% with both CVD and CABF predictors. Lastly, the disease-modifying therapy was not kept in the final model as an independent predictor of sNfL. Patients in the lowest CABF quartile (CABF≤761 mL/min) had significantly higher sNfL (34.6 pg/mL versus 23.9 pg/mL, adjusted-p=0.042) when compared to the highest quartile (CABF≥1130 mL/min).

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Table 1. Multivariable regression models exploring the association between serum neurofilament light chain levels and cerebral arterial blood flow in multiple sclerosis patients after including demographic factors and MS-based MRI pathology.

sNfL regression model	Explanatory variable	Beta	R^2	Standardized β	t-statistics	VIF	p-value
Model 1 (n=137)	Sex	-2.81	0.177	-0.060	-0.719	1.04	0.474
	Age	0.505		0.268	3.191	1.06	**0.002**
	BMI	-0.683		-0.196	-2.342	1.05	**0.021**
Model 2	T2-LV	0.001	0.206	0.180	2.142	1.07	**0.034**
Model 3	Total CABF	-0.013	0.232	-0.169	-1.990	1.09	**0.049**

MS: multiple sclerosis; BMI: body mass index; sNfL: serum neurofilament light chain; CABF: cerebral arterial blood flow; T2-LV: T2 lesion volume; VIF: variance inflation factor. In the first model, sex, age, and BMI were entered regardless if they significantly explain the sNfL levels. In a second step-wise model, CABF, WBV, and/or T2-LV were only added if they were identified as significant factors. P-value lower than 0.05 was considered statistically significant and shown in bold. In the regression model, sNfL levels were considered as a dependent variable, whereas age, sex, BMI, total CABF, T2-LV and WBV were added as independent variables (predictors). The demographic variables of age, sex and BMI are always entered in the model. With the step-wise inclusion of independent predictors (CABF, T2-LV and WBV) the model is created only if the predictors are significant.

Conclusions

Lower CABF is associated with increased sNfL in MS patients, highlighting direct and independent relationship between cerebral hypoperfusion and axonal pathology. This relationship remained significant in the CIS/RRMS after adjusting for age, sex, and BMI effects.

References

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