Insights from the EXPOSITION Study: Exposome-related microRNA Expression and Clinical Outcomes in People with Multiple Sclerosis

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INTRODUCTION

MicroRNAs (miRNAs) are emerging as promising biomarkers of neuroinflammation and may capture the influence of lifestyle and environmental exposures in people with multiple sclerosis (pwMS). The EXPOSITION study[1] aims to elucidate relationships between internal exposome markers including miRNA profiles and clinical, demographic, and lifestyle factors in pwMS.

OBJECTIVE(S)

To assess the associations between the relative expression of five candidate miRNAs and clinical, demographic, and lifestyle variables, with a particular focus on the exposome and functional and psychological outcomes in pwMS.

METHODS

In this cross-sectional analysis, we included 139 pwMS (median age 45 years [IQR: 35–56], 65% female) from the provinces of Pavia and Milan in the Lombardy region of Italy. Relative expression levels of five candidate miRNAs (mir30, mir146, mir330, mir574, mir664) were quantified and compared across clinical and lifestyle categorical variables groups using the Mann-Whitney U test (for binary variables) or the Kruskal-Wallis test (for variables with more than two categories). Spearman correlation analyses were conducted to assess the relationship between each miRNA and continuous variables, including age, BMI, EDSS, dietary inflammatory index, and quality of life scores.

RESULTS

There were no statistically significant differences in microRNA expression between EDSS disability groups or across most clinical or lifestyle variables. Notably, mir146 expression was significantly higher in participants with a pro-inflammatory dietary pattern compared to those with an anti-inflammatory pattern ($p = 0.0187$), and mir146 was positively correlated with the mental health component of the quality of life MSQoL-29 questionnaire (rho = 0.336, $p = 0.0174$) [Table 1]. In contrast, higher disability status (EDSS >4) was significantly associated with older age (median 51 vs. 44 years, $p = 0.047$), more frequent prior relapses (94% vs. 69%, p

DOI: 10.54103/2282-0930/29291

= 0.040), and lower physical (p = 0.039) and mental (p = 0.034) quality of life. Significant group differences were also observed for MS type (p = 0.008), MS stage (p = 0.034), and occupational status (p = 0.063, trend) between the two EDSS groups. No significant associations were identified between disability status and microRNA expression, diet category, physical activity, or MRI lesion status.

Table 1 Summary of MicroRNA Expression by Exposome and Clinical Variables using preliminary data from EXPOSITION exposome study

	MicroRNA Expression				
	mir30	**mir146**	**mir330**	**mir574**	**mir664**
Dietary Inflammatory Index (DII)[#]: DII < 0 anti-inflammatory vs DII >0 proinflammatory	anti-inflammatory: 0.00395 (0.00314, 0.00504) vs. proinflammatory: 0.00914 (0.00484, 0.0187); p=0.0821	anti-inflammatory: 0.0155 (0.0129, 0.023) vs. proinflammatory: 0.0802 (0.0287, 0.153); p=0.0187	anti-inflammatory: 0.00298 (0.00229, 0.00624) vs. proinflammatory: 0.00752 (0.00308, 0.01); p=0.486	anti-inflammatory: 0.0314 (0.0176, 0.057) vs. proinflammatory: 0.0427 (0.0295, 0.0591); p=0.505	anti-inflammatory: 0.00223 (0.00186, 0.0026) vs. proinflammatory: 0.00328 (0.00253, 0.005); p=0.414
Expanded Disability Status Scale Score (EDSS)[#]: EDSS ≤ 4 vs. EDSS > 4	EDSS ≤ 4: 0.00838 (0.00406, 0.0163) vs. EDSS > 4: 0.00832 (0.00623, 0.00914); p=0.841	EDSS ≤ 4: 0.0778 (0.019, 0.151) vs. EDSS > 4: 0.0218 (0.0161, 0.0549); p=0.181	EDSS ≤ 4: 0.00542 (0.00268, 0.00958) vs. EDSS > 4: 0.00752 (0.00575, 0.00851); p=0.818	EDSS ≤ 4: 0.0423 (0.0289, 0.0618) vs. EDSS > 4: 0.0352 (0.0326, 0.0477); p=0.835	EDSS ≤ 4: 0.0035 (0.00266, 0.00515) vs. EDSS > 4: 0.00224 (0.00185, 0.00264); p=0.286
MSQOL-29 Mental[§]	rho=0.274; p=0.0599	rho=0.336; p=0.0174	rho=0.141; p=0.424	rho=0.137; p=0.327	rho=0.139; p=0.462
Age (in years)[§]	rho=-0.0143; p=0.917	rho=0.0382; p=0.778	rho=0.146; p=0.356	rho=0.0906; p=0.48	rho=-0.0301; p=0.861

MSQOL - Multiple Sclerosis Quality of Life, [#] Median (IQR), [§] Spearman rank correlation

CONCLUSIONS

In this preliminary analysis, higher disability among pwMS was more strongly linked to clinical history, age, and quality of life than to lifestyle factors or circulating miRNA levels. Mir146 may act as a molecular intermediary between dietary inflammation, mental health, and neuroinflammatory processes in MS. These findings highlight the need for replication and longitudinal validation in larger, independent cohorts.

BIBLIOGRAPHY

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DOI: 10.54103/2282-0930/29291