Gut microbiota and physical activity in pediatric onset multiple sclerosis

Da Silva T, Stephens S, Zhu F, Arnold DL, Banwell B, Bar-Or A, Bernstein C, Bonner CH, Graham M, Knox N, O'Mahony J, Marrie RA, Mirza AI, Van Domselaar G, Waubant E, Zhao Y, Tremlett H, Yeh EA on behalf of the Canadian Demyelinating Disease Network.

ABSTRACT

BACKGROUND

Physical activity (PA) is associated with MRI metrics, disability, and relapses in pediatric-onset multiple sclerosis (POMS), but the mechanisms underlying these relationships remain unknown. PA may alter gut microbiota in MS and influence disease activity through modulation of the gut-brain axis. The relationship between PA and the gut microbiome in POMS is unknown.

OBJECTIVES

To examine the relationship between PA level and gut microbiome characteristics - alpha and beta diversity - in POMS, monophasic acquired demyelinating syndromes (mono-ADS), and unaffected controls.

METHODS

Individuals with a diagnosis of POMS or mono-ADS, and unaffected controls enrolled in the Canadian Pediatric Demyelinating Disorders Study were included. All participants provided a stool sample for microbiome analysis with 16S ribosomal RNA sequencing. PA level was assessed using the Godin Leisure-Time Exercise Questionnaire (active vs non-active). Alpha diversity was assessed as species evenness (Shannon index) and richness (Chao1), and beta-diversity was calculated using weighted Unifrac. Associations between clinical characteristics

and microbiota were assessed non-parametric tests (Kruskall-Wallis or Mann-Whitney) using SPSS, and permutational multivariate analysis of variance using R.

RESULTS

Participants included: POMS (n=37, mean 18.7±4.4 years, 78%F), mono-ADS (n=40, 14.8±5.0 years, 52%F) and HC (n=36, 18.0±5.5 years, 61%F). PA level differed significantly across groups (p=0.004), with higher PA levels in mono-ADS vs MS (85% active in mono-ADS, 54% active in MS; p=0.001). Alpha diversity did not differ across groups or PA level (p>0.8 and p>0.9 for both alpha diversity metrics, respectively). Similarly, beta-diversity did not vary across groups or PA level (both p=0.7). In the MS group, alpha-diversity species evenness (Shannon index) was higher in the active vs. non-active group (median [IQR] active: 0.70 [0.66-0.73], inactive: 0.68 [0.65-0.69]; p=0.04; effect size 0.4). This relationship was not present in the non-MS groups (p>0.9).

CONCLUSIONS

The relationship between gut microbiome alpha diversity (evenness) and physical activity differed in POMS versus those with monophasic illnesses and otherwise unaffected controls. Future studies will evaluate the effect of age and sex on these parameters, how the microbiome mediates the effects of physical activity, as well as differences in microbiome composition at the taxon-level across physical activity levels in MS.