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SPG11 is associated with BMI changes and hypothalamic damage.

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Abstract

SPG11 mutations are the most relevant cause of autosomal recessive Hereditary Spastic Paraplegia(HSP). Patients present with marked weight gain, which contrasts from caquexia generally observed in other neurodegenerative disorders. We have chosen to evaluate the hypothalamus as it is an important CNS metabolic control center. We used MRI, and manually segmented the hypothalamus in patients(n=20) and healthy controls(n=20). Also, we collected BMI data and compared SPG11 patients(n=20) against patients with Friedreich Ataxia (n=20), another neurodegenerative disease model. We found significantly higher BMI in the SPG11 group(p=0.034). Also, the SPG11 group had hypothalamic atrophy when compared to controls(p=0.030).This reinforces our hypothesis that loss of Spatacsin function might be related to abnormal metabolic control in SPG11.

Key words:

SPG11, BMI, neuroimaging.

Introduction

SPG11 mutations are the most relevant cause of autosomal recessive Hereditary Spastic Paraplegia(HSP). Patients with HSP present with marked weight gain, which contrasts from the caquexia generally observed in other related neurodegenerative disorders. As the hypothalamus is an important metabolic control center, our hypothesis is that *SPG11* mutations might affect hypothalamic neurons related to metabolic regulation. We aimed to assess BMI changes in patients with SPG11, comparing against another neurodegenerative disease model, Friedreich´s Ataxia (FA). Also, we investigated whether hypothalamic atrophy would be present in these patients.

Results and Discussion

We have selected a group of 20 patients with confirmed *SPG11* mutations, 20 controls and 20 patients with FA who performed 3T MRI of the brain including the volumetric (3D) sequence of the cranium. Manual segmentation of the hypothalamus followed these respective limits: (a) inferiorly, mammillary bodies (b) laterally, hypothalamic sulcus (c) medially, 3rd ventricle (d) anteriorly, anterior commissure.The images were also segmented using "MRICloud" (MRICloud.org),to obtain total intracranial volume(ETIV). We assessed between-differences regarding BMI and hypothalamic volume using ANOVA; total ETIV, age and sex were covariates of interest in this model. The correlations involving clinical parameters (disease duration and SPRS) were investigated using Pearson correlations. P-values < 0.05 were considered significant.

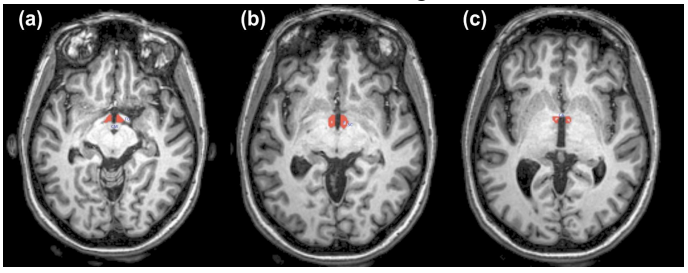

Image 1. Demonstrates hypothalamic segmentation.

Mean age of SPG11 patients was 29 years and there were 9 men. Mean age of SPG11 patients was 29 years and there were 9 men. Mean SPRS score and disease duration were 28 and 13,5 years, respectively. On the SPG11 group, 25% were overweight(OW) and 25% were obese(OB) . SPG11 and FA groups were matched in terms of age, gender and wheel-chair dependency (p>0.05). Despite that, we found significantly higher BMI in the former group(p=0.034). Also, SPG11 group had hypothalamic atrophy when compared to controls(p=0.030). Volumetric changes were not associated with BMI, age, disease duration or SPRS amongst subjects with SPG11.

Chart 1. Demographic data of SPG11 and FA groups.

	SPG11	FA
Nº of men	9	9
Age	Mean=29 / SD= 8	Mean=29 / SD=9
Disease Duration	Mean= 13 / SD= 8	Mean=15 / SD=8
SPRS	Mean=28 / SD=11	-
OW/OB	OW=5 / OB=5	OW=4 / OB= 1
BMI	Mean=25,63 / SD=5,72	Mean=22,35 / SD=3,49

Conclusions

The hypothalamic atrophy combined with higher BMI in the SPG11 group suggests that Spatacsin may play a role in metabolic control dysfunction in SPG11 patients.

Acknowledgement

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