Abnormal hypothalamus and related brain regions in Prader-Willi Syndrome evaluated in vivo by Diffusion Tensor Imaging (DTI)

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Introduction & Objectives

Prader-Willi syndrome (PWS) is a genetic disorder caused by the lack of expression of the paternally inherited genetic material located in 15q11-q13[1]. It is characterized by neonatal hypotonia, intellectual disabilities, obesity and behavioral disturbance. Patients present with several neuroendocrinological abnormalities, such as growth hormone deficiency, hypogonadotropic hypogonadism, and hyperphagia, as the result of possible involvement of the hypothalamo-hypophyseal system[2].

Diffusion tensor imaging (DTI) provides information about structural properties of white matter. A commonly used DTI measurement is fractional anisotropry (FA), which serves to characterize white matter tracts by mapping the degree of water diffusion anisotropy (i.e., diffusion directionality) related to fiber density, axonal diameter and myelination degree.

To our knowlege there is only one study in PWS patients using DTI and it was not focused in the hypothalamo-hypopshyseal region[3]. So, the objective of the present study was to evaluate the hypothalamus and related brain regions in adult patients with PWS using DTI.

Methods

Twenty patients (11M, 9F, aged 28.3 ± 7.4) with PWS and twenty age- and gender-matched control subjects (11M, 9F, aged 28.1 ± 7.0) were recruited for this study. MRI data was acquired from all participants using a 1.5 Tesla Sigma Excite system (General Electric, Milwaukee, WI, USA). Diffusion-weighted scans were obtained using spin-echo single-shot echo-planar sequences of 25 directions with a B-factor of 1000 s/mm2. Twenty-six slices were acquired with repetition time [TR] 8300 ms; echo time 94 ms; thickness 5 mm, no gap; pulse angle 90°; field of view 26 cm; 128 x 128 acquisition matrix reconstructed into a 256 x 256 matrix. The twenty-six slices were prescribed parallel to AC-PC line.

DTI images were preprocessed and Fractional Anisotropy (FA) maps were calculated using Functional MRI of the Brain (FMRIB) Software Library 5.0 (FSL). Data was re-sliced to a 1mm × 1mm × 1 mm anatomical resolution and normalized to standard MNI space. After, a smoothing (8mm) was applied and voxel-wise two sample t-test was done between groups using SPM8.

Individual FA DTI maps were included in second-level (group) SPM analyses using 2-sample *t*-test. Results were considered significant with clusters of 1.032 ml (1,032 voxels) at a height threshold of $p<0.005$, which satisfied the family-wise error (FWE) rate correction of $P_{FWE}< 0.05$ according to Monte Carlo simulations.

Results

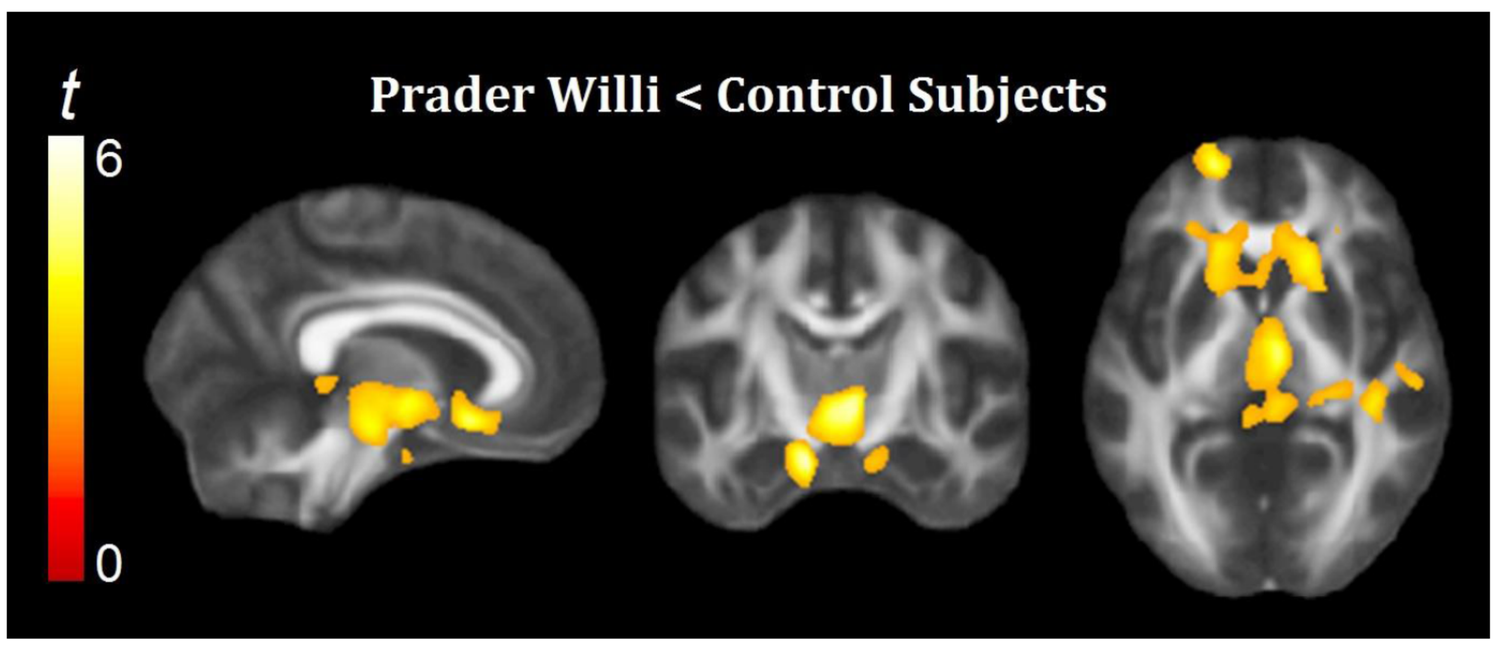

Table 1. Differences between groups.

	Cluster size, ml (voxels)	*x y z*	*T*
R Striatum	799270	20 4 -9	5.00
Striatum	799270	-23 3 -12	4.65
Hypothalamus	799270	4 -11 -3	5.25
Amygdala	799270	-12 -8 -21	5.61
Sub-Genu	799270	-5 17 -12	4.80

x y z, coordinates given in Montreal Neurological Institute (MNI) space. Statistics at $p<0.005$.

Figure 1. Fractional Anisotropy (FA) differences between Prader-Willi patients and control subjects. FA is significantly reduced in the hypothalamus and anatomo-functionally connected structures such as the amygdala, the striatum and the subgenual part of the anterior cingulate cortex.

Conclusions

DTI results confirm the presence of extensive structural anomalies in white matter connecting the hypothalamus with related brain structures that may underlay endocrinological disorders and hyperphagia in these patients.

References

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