INVOLVEMENT OF THE BASAL GANGLIA AND LIMBIC SYSTEM IN RESTLESS LEGS SYNDROME: MORPHOLOGICAL AND VOLUMETRIC MRI STUDY

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OBJECTIVES

A dysfunction of the dopaminergic inhibitory hypothalamic-spinal pathways has been proposed to have a role in restless legs syndrome (RLS). Several studies of voxel-based morphometry, PET and fMRI have shown an involvement of hypothalamus, thalamus, hippocampus, cerebellum, substantia nigra, frontal and hippocampal gyri. The aim of this study was to investigate subcortical gray matter (SGM) structures by MRI morpho-volumetric techniques in RLS patients vs. controls.

METHODS

We enrolled 45 patients (40 untreated) with RLS (mean age 53.6¬ 14.17 y) [Tab. 1] and 33 sex-matched healthy controls (mean age 50.5 12.96 y). T1-weighted MR images were acquired on a 1.5 Tesla scanner in both groups. The FSL-FIRST software was used for segmentation and shape analysis of the following structures:
thalamus, caudatum, putamen, pallidus, brainstem, hippocampus, amygdala [Fig. 1]. The comparison between the volumes of SGM, measured in normal control subjects and in patients with RLS, was operated by means of the Student's t-test [Tab. 2].

RESULTS

We found a decrease in volume of the left amygdala and pallidus in RLS. The shape analysis showed morphological changes especially in the amygdalae, but also in the hippocampi, right caudatum, left pallidus and left putamen.

CONCLUSIONS

Our study shows a mild but diffuse involvement of SGM structures in RLS; these changes seem to affect more evidently their shape rather than their volume. Our findings indicate a possible role of the basal ganglia and the limbic system in RLS and might support the hypothesis of a prominent involvement of the dopaminergic mesolimbic pathway. The involvement of the limbic system may also explain cognitive and mood changes sometimes found in RLS.

Fig. 1. Shape analysis of the subcortical structures.

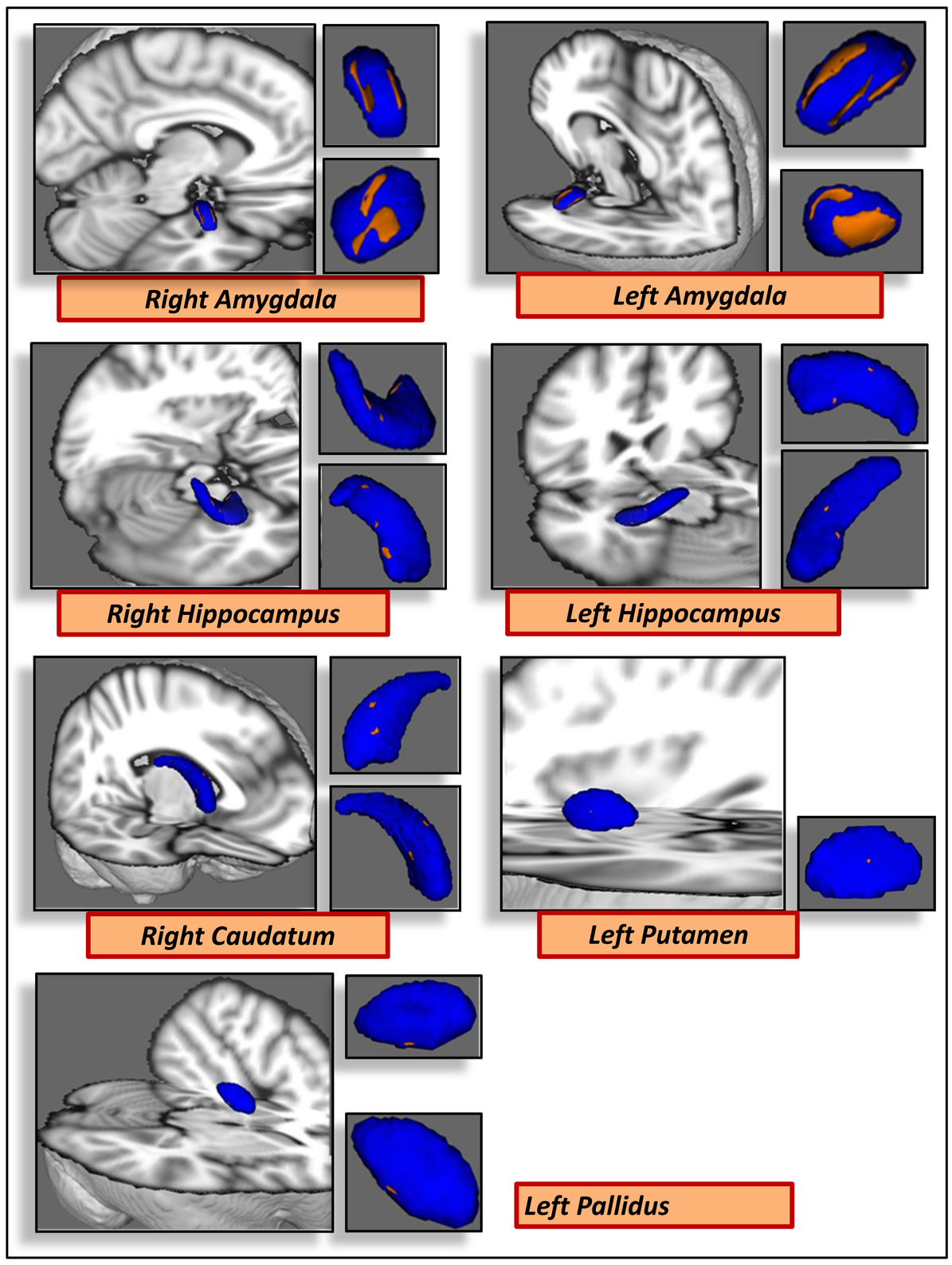

Table 1. Clinical and laboratory parameters in RLS patients (11 M, 34 F).

	Mean	S.D.
Age, years	53.6	14.17
IRLS Severity Scale	25.3	4.22
Epworth Sleepiness Scale	9.1	4.01
Insomnia Severity Index	13.6	4.50
Blood exams		
Glucose (fasting), mg⁄dl	89.1	21.00
Cholesterol (total), mg⁄dl	209.0	27.50
Cholesterol (HDL), mg⁄dl	51.9	10.69
Iron, µg/dl	89.6	27.80
Ferritin, µg/l	80.3	72.37

Table 2. Comparison between volume (in mm^3) of subcortical structures in normal controls and RLS patients.

	Controls (n=33)		RLS (n=45)			
	Mean	S.D.	Mean	S.D.	t-test	p<
Age, years	50.5	12.96	53.6	14.17	-0.989	NS
Left						
Thalamus	9036.4	1056.35	9047.6	816.98	-0.053	NS
Caudate	2418.1	580.19	2436.2	661.85	-0.126	NS
Putamen	6124.9	908.90	6339.9	637.73	-1.228	NS
Pallidus	**1900.1**	**301.01**	**1693.1**	**457.93**	**2.262**	**0.027**
Hippocampus	3613.6	437.44	3706.2	388.45	-0.985	NS
Amigdala	**1488.8**	**419.09**	**1305.0**	**311.22**	**2.224**	**0.029**
Right						
Thalamus	8669.3	901.23	8621.5	836.32	0.241	NS
Caudate	2486.5	448.49	2481.4	524.90	0.045	NS
Putamen	6076.1	804.61	6200.0	614.67	-0.771	NS
Pallidus	1799.9	409.00	1773.3	463.33	0.262	NS
Hippocampus	3778.8	513.31	3941.9	464.11	-1.466	NS
Amigdala	1246.2	289.76	1190.3	246.02	0.919	NS
Brainstem/IV ventricle	18412.4	2478.41	18360.7	2321.79	0.094	NS

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