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Prevalence of Right-to-left Shunt (RLS) and volumetric brain changes in patients with episodic and chronic migraine

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Background

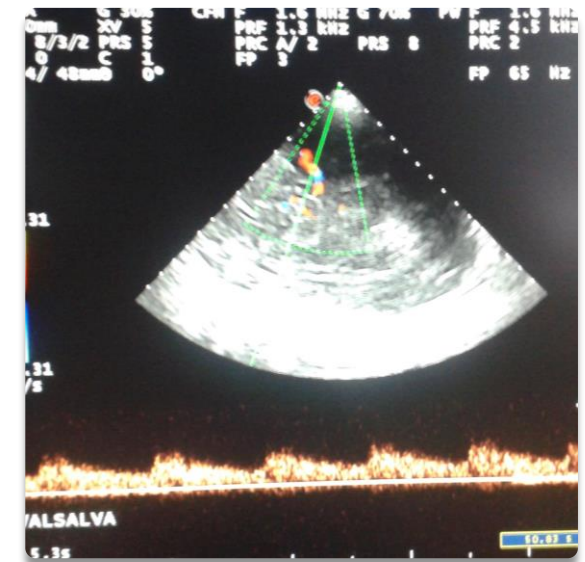
- ▶ Patent Foramen Ovale (PFO) is the most common Right-to-left shunt (RLS) condition (15-35% of the general population)
- ▶ Many studies showed an higher prevalence of PFO in migraineurs than in non-migraneurs, especially in migraine with aura, but the role of PFO in migraine pathogenesis is still controversial
- ▶ A role of WMHs in migraine is clearly suggested by a large number of studies, but at present no firm conclusions can be made about this association.
- ▶ No clear association between RLS and WMHs in migraineurs
- ▶ Several studies showed the existence of grey matter abnormalities in migraine, but the possible significance of these alterations remain unclear

Aims

- ▶ Evaluation of the prevalence and the characteristics of RLS in a sample of migraineurs
- ▶ Analysis of the correlation between PFO and volumetric brain changes in specific cortical and subcortical structures
- ▶ Evaluation of the prevalence and the extension of white matter lesions (WML) and determination if there is a correlation between WML and presence and characteristics of PFO
- ▶ **Is there a role of PFO in determining any structural changes in grey matter in patients with migraine?**

Methods

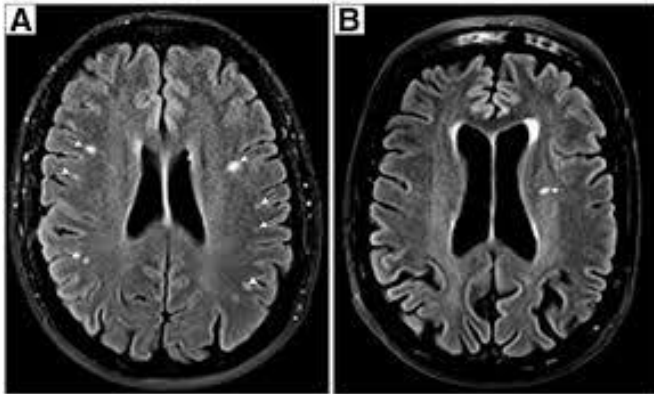
- ▶ Transcranial Doppler sonography with the intravenous injection of agitated saline
 - ▶ Permanent RLS: occurs during rest
 - ▶ Latent RLS: occurs after Valsalva Maneuver
- ▶ 3 Tesla MRI scanner (Discovery MR750w)
- ▶ Analysis of structural T1w volumes with a fast diffeomorphic registration algorithm (Diffeomorphic Anatomical Registration using Exponentiated Lie algebra, DARTEL) and Voxel Based Morphometry (VBM)
- ▶ Visual analysis of T2w, T1w and Flair sequences in order to identify white matter hyperintensities (WMH) using Fazekas scale and Scheltens scale



Characteristics of study population

Characteristics	Right-to-left shunt	No Right-to-left shunt
N of patients (total 27)	13	14
Age (yrs)	45.0±9.9	38.0±8.5
Disease duration (yrs)	25.3±11.2	12.7±6.9
Migraine characteristics		
Episodic migraine (16)	9 (4 permanent)	7
Chronic migraine (11)	4 (all permanent)	7
Aura (N pts 8)	6	2

White matter hyperintensities (WMHs) and infarct-like lesions (ILLs)



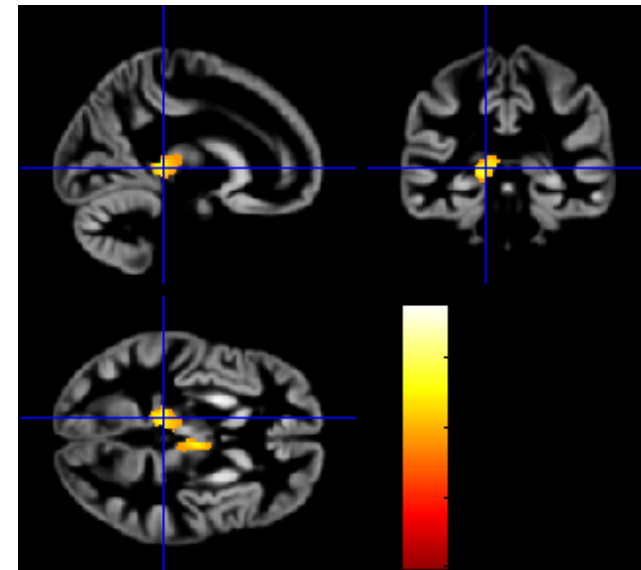
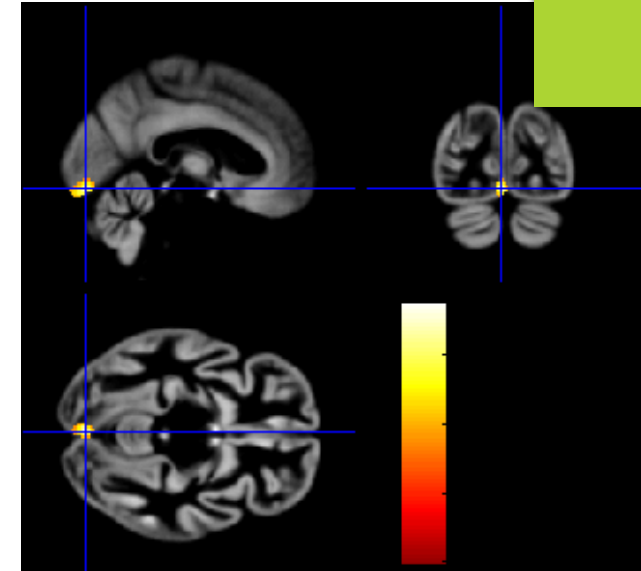
Characteristics	RLS (N. pts 13)	No RLS (N. pts 14)
Score ≥ 1 on Fazekas scale	2 (15.4%)	1 (7.1%)
Score ≥ 1 on Scheltens scale for WMH	4 (30.8%)	3 (21.4%)
Score ≥ 1 on Scheltens scale for PVH	2 (15.4%)	3 (21.4%)
Score ≥ 1 on Scheltens scale for ITF	1 (7.7%)	0
ILLs	1 (7.7%)	1 (7.1%)

WMH: white matter hyperintensities; PVH: periventricular hyperintensities; ITF: infra-tentorial foci of hyperintensities; ILL: infarct-like lesions

- No significant association between white matter alterations and right-to-left shunt

Grey Matter Changes

- Clusters of reduced grey matter volume in the RLS+ patient group detected respectively at the level of the left calcarine gyrs (up image) and of both thalami (down image), superimposed onto the averaged normalized grey matter maps of the 27 patients ($p < 0.05$)



Discussion

- ▶ Our findings suggest that the presence of RLS can be associated with structural changes of grey matter in patients with migraine.
- ▶ The literature showed reproducible findings of altered grey matter volume (GMV) and white matter integrity in the frontal lobe, occipital lobe, and limbic system in migraineurs compared with healthy controls
- ▶ Little is known about the role of RLS on structural brain alterations in migraineurs, especially grey matter alterations
- ▶ Some studies (Yoon et al, 2012; Xie et al. 2017) reported an association between RLS and white matter integrity

Limitations of the study and Future perspectives

► **Limitations:**

- Little size of the study sample
- Lack of a control group
- Differences in mean age and disease duration in the two groups of patients

► **Future perspectives:**

- Expand the number of patients
- Add a control group of healthy patients
- Make the groups homogeneous
- Apply a quantitative analysis method to the evaluation of white matter alterations

Conclusions

- ▶ A better characterization of grey matter alterations, which may be detected through advanced neuroimaging analyses, can lead to:
 - Better understanding of the role of PFO in the pathogenesis of migraine
 - Searching for “vulnerable” brain areas in which structural alterations could be reproducible in future studies
 - Developing more tailored management approaches in patients showing an association between PFO and migraine