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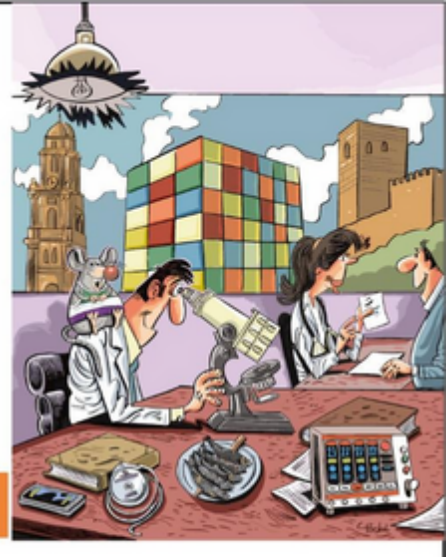

Structural Brain Alterations in Pediatric Migraine: A Pilot Voxel-Based Morphometry Study

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Background & Rationale

Chronic pain affects 20–30% of children and adolescents in Spain, with 5% experiencing severe disability. Migraines and medication overuse headaches are common causes, affecting 10% of children. The problem is widespread and worsening, imposing significant economic and quality-of-life burdens. Despite its impact, **pediatric migraine remains under-researched and inadequately treated** due to limited understanding, lack of effective therapies, and absence of objective biomarkers for symptom tracking and personalized treatment.

In this study, we aimed to generate preliminary data as a foundation for **identifying key brain substrates of pediatric migraine using magnetic resonance (MR) imaging**. To achieve this, we analyzed anatomical MR images to detect structural alterations in our pediatric pilot database. **Voxel-based morphometry (VBM)** was employed to assess differences in local brain tissue concentrations between pediatric migraine patients and healthy controls (HC). Additionally, we explored potential **volumetry changes in gray matter (GM)** as well as potential **increased brain age** related to pain.

Materials & Methods

Dataset: MR data from nine pediatric patients (10.44±7.73 years old; range 4-14; 6 females), including six with persistent headaches and three diagnosed with migraines, and ten healthy controls (8.70±5.72 years old; range 2-16; 4 females) with no history of pain, disease, or radiological abnormalities, were retrospectively analyzed.

Statistical Analysis: Statistical analyses were conducted using the CAT12/SPM12 module to assess anatomical differences between groups via VBM on T1-weighted MR images. Age and total intracranial volume (TIV) were included as covariates, with cluster correction applied. A p-value < 0.05 was considered statistically significant.

Exploratory Analysis

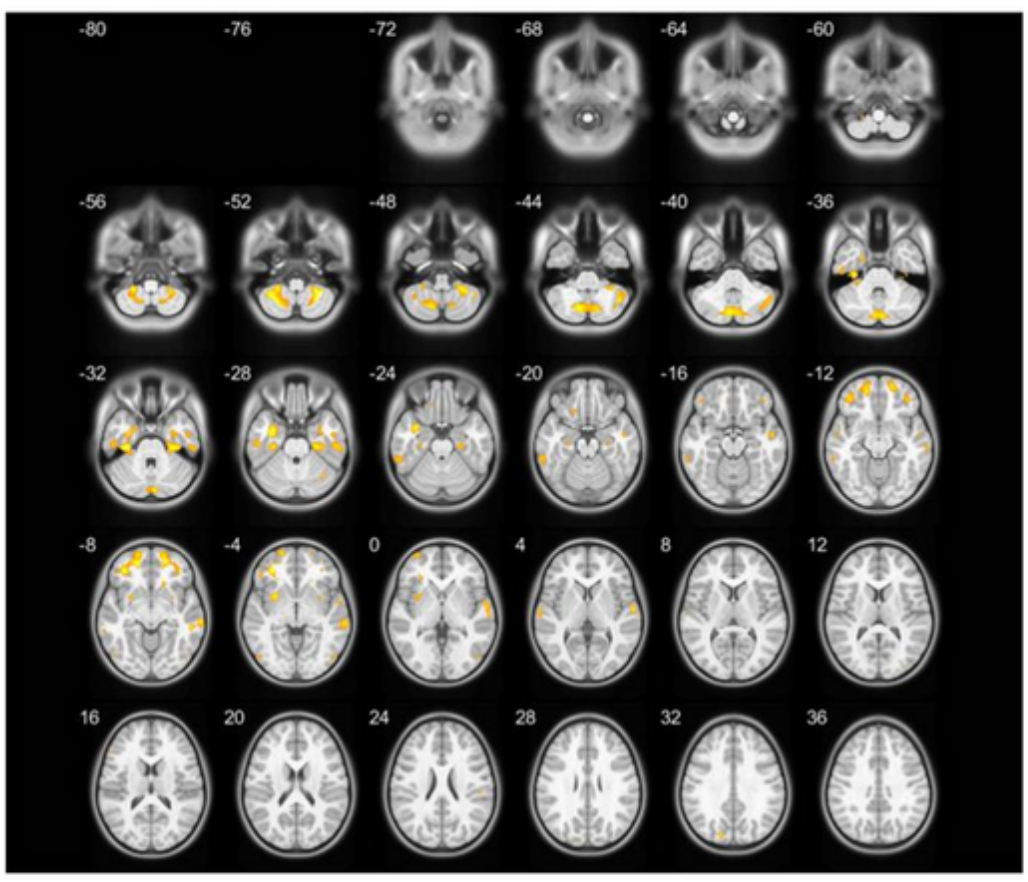
Volumetry Changes in GM: GM volumetry was performed using FreeSurfer, which automatically segmented GM from anatomical T1-weighted images. The percentage of GM (%GM) was then calculated by normalizing GM volume to the total intracranial volume (TIV).

Predicted Age Difference (PAD): PAD was computed using the brain age estimation tool BabyPy, which calculates the difference between predicted brain age and chronological age based on MR data. PAD reflects the extent to which the brain appears older or younger than the individual's actual age.

These analyses were also conducted to assess differences between persistent headaches and migraine, in addition to comparisons HC.

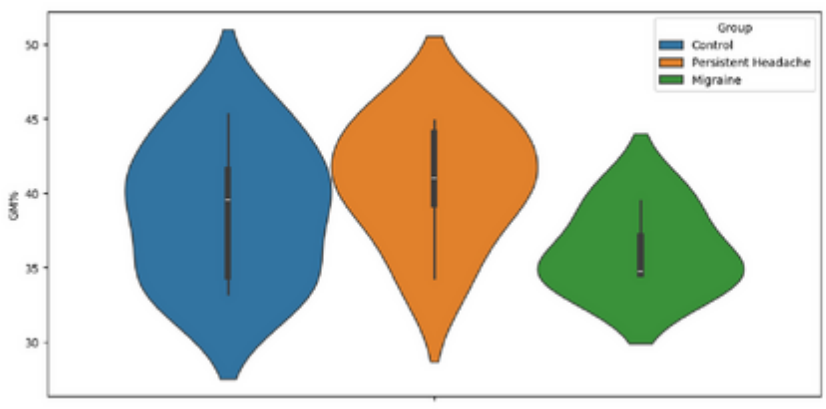
Results

Whole-brain VBM analysis revealed **significant structural alterations** in the superior frontal gyrus, middle frontal gyrus, superior temporal gyrus, hippocampus, and the posterior lobe of the cerebellum. These findings suggest that patients may already **exhibit notable atrophy** in these regions compared to HCs. Moreover, these areas are closely linked to key functions commonly associated with **pain processing and chronic pain**, including sensory perception, emotional regulation, cognitive control, and memory.

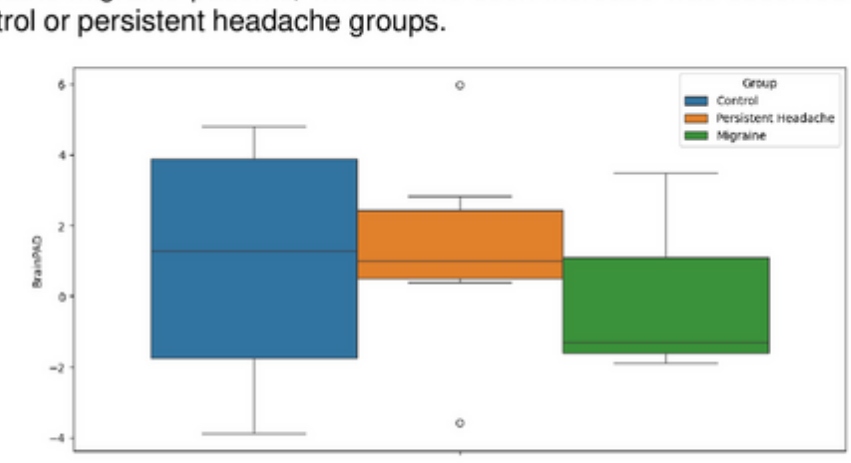


Exploratory Results

Volumetric analyses revealed a **trend toward differences in %GM** between pediatric migraine patients and both healthy controls and those with persistent headaches, while %GM appeared similar between controls and persistent headache groups.



Similarly, PAD analyses indicated a **trend toward increased brain age** in pediatric migraine patients, whereas no such increase was observed in the control or persistent headache groups.



Discussion & Conclusion

This pilot study reveals significant **structural alterations** in brain regions involved in pain processing, cognition, and emotion in pediatric migraine patients. We also found trends to **volumetry changes in %GM** as well as a trend toward **increased brain age** in pediatric migraine patients. While preliminary, our findings highlight the need for further research to develop biomarkers and improve personalized treatment strategies.

References

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