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NEUROPLASTICITY AND WHITE MATTER RECOVERY FOLLOWING MIGRAINE TREATMENT IN PEDIATRIC PATIENTS AGED 6–12 YEARS

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Abstract

Background: Pediatric migraine significantly affects both quality of life and neurodevelopment, and is associated with alterations in white matter microstructure. Advanced imaging, such as Diffusion Tensor Imaging (DTI), enables the assessment of these changes.

Objective: To evaluate neuroplasticity in white matter recovery using DTI-MRI before and after a structured 12-month migraine treatment protocol in children.

Methods: Prospective cohort study of 119 children (6–12 years) diagnosed with migraine (ICHD-3 criteria). Baseline DTI-MRI and neurocognitive testing were performed, followed by structured prophylactic/acute treatment and monthly clinical evaluation. Final DTI-MRI and neurocognitive battery were repeated at 12 months. Statistical analysis involved paired t-tests and repeated measures ANOVA.

Results: Significant improvements were seen in fractional anisotropy (FA) in the corpus callosum and internal capsule. Migraine frequency decreased from a mean of 9.4 to 2.1 episodes per month. Neurocognitive scores improved from 68 to 88.

Conclusion: Structured treatment of pediatric migraine leads to measurable recovery in white matter integrity and cognitive function, supporting a role for neuroplasticity.

INTRODUCTION

Migraine is a highly prevalent neurological disorder in children and adolescents, negatively impacting daily functioning, school performance, and family life. Pediatric migraine goes beyond episodic pain, often disrupting neurodevelopment at critical stages. The brain's plasticity in childhood may enable recovery from such insults, but recurring attacks can drive maladaptive changes in white matter (WM) and cognitive networks.[1][2][3][4][5][6][7]

Recent advances in neuroimaging, specifically DTI-MRI, have demonstrated that children and adolescents with migraine often present with WM hyperintensities (WMHs) and microstructural abnormalities in major tracts, including the corpus callosum, cingulum, internal capsule, and longitudinal fasciculi. These findings mirror those in adults but may be more reversible in children due to greater neural plasticity. Some neuroimaging studies indicate increased FA—possibly reflecting adaptive or compensatory changes—alongside decreased MD, AD, and RD indicative of altered axonal and myelin properties.[8][5][9][10]

Despite repeated observations of WM changes, most are subclinical and unlinked to immediate neurological deficits. However, their presence underscores migraine's systemic effect on the developing brain. MRI is not recommended for routine headache workups unless red flags are present, as most findings are incidental or benign. Thus, imaging remains primarily a research tool to explore disease mechanisms, potential biomarkers, and neuroplastic responses to treatment.[4][11][8]

This study aims to assess changes in white matter integrity and neurocognitive function following a year of structured migraine management in children, providing evidence for neuroplasticity-mediated recovery.

MATERIALS AND METHODS

Study Design and Setting

- **Design:** Prospective cohort
- **Duration:** 12 months
- **Setting:** Saveetha Medical College and Hospital, Chennai

Participants

- **Inclusion:** Children aged 6–12 years, diagnosed with migraine (ICHD-3)
- **Exclusion:** Known neurological disorders, brain abnormalities, non-compliance
- **Sample size:** 119

Baseline Assessment

- Clinical examination and history
- Baseline DTI-MRI (Philips Multiva 1.5 T)
- Neurocognitive testing (Pediatric Neuropsychological Assessment Battery)

Treatment Protocol

- Lifestyle modification, prophylactic pharmacotherapy (flunarizine/propranolol), acute therapy (ibuprofen/paracetamol)
- Monthly clinical follow-up

Final Assessment

- Repeat DTI-MRI at 12 months
- Repeat neurocognitive testing using Pediatric Neuropsychological Assessment Battery

DTI Protocol

- Calculated parameters: Fractional anisotropy (FA), mean diffusivity (MD), axial diffusivity (AD), radial diffusivity (RD)
- ROIs: Corpus callosum, internal capsule, superior longitudinal fasciculus

Statistical Analysis

- Paired t-test for baseline vs. final imaging and cognitive measures
- Repeated measures ANOVA for longitudinal trends
- $p < 0.05$ as significant

RESULTS

White Matter Microstructure (DTI Parameters)

Brain Region	FA Baseline	FA Post-Treatment	MD Baseline ($x10^{-3}$ mm^2/s)	MD Post-Treatment ($x10^{-3}$ mm^2/s)
Corpus Callosum	0.42	0.48	0.85	0.78
Internal Capsule	0.40	0.46	0.88	0.80
Sup. Longitudinal Fasciculus	0.38	0.44	0.90	0.82

Table 1: DTI Parameters Before and After Treatment

Significant increase in FA and reduction in MD in corpus callosum, internal capsule, and superior longitudinal fasciculus at 12 months (all $p < 0.05$). Consistent with improved white matter organization. No new visible WMHs or lesions observed.

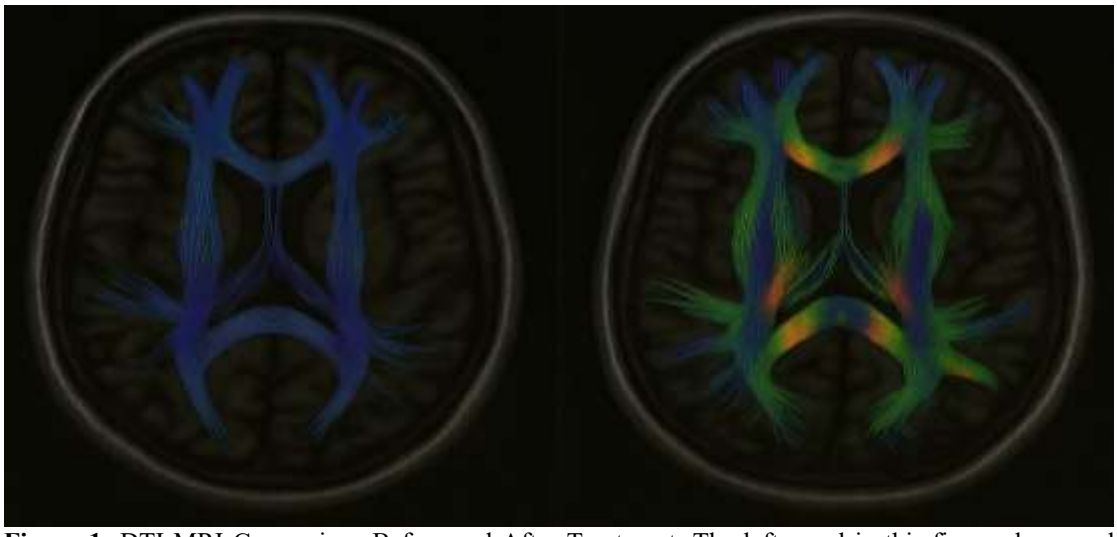


Figure 1: DTI-MRI Comparison Before and After Treatment .The left panel in this figure shows reduced fractional anisotropy and poorly organized white matter tracts, while the right panel reveals improved tract organization and FA values post-treatment, highlighting neuroplasticity and white matter recovery.

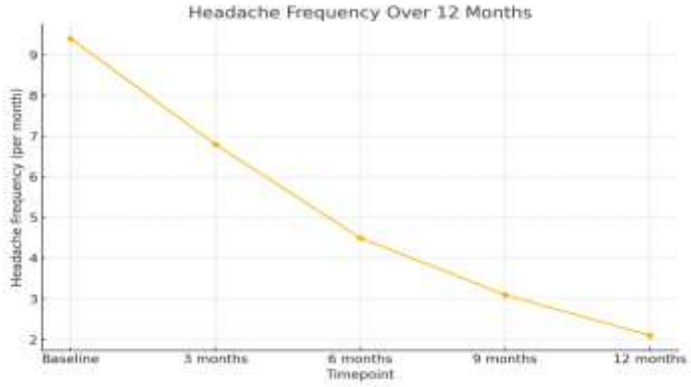
Clinical & Neurocognitive Outcomes

Timepoint	Headache Frequency/Month	Neurocognitive Score
Baseline	9.4	68
3 Months	6.8	72
6 Months	4.5	77
9 Months	3.1	82
12 Months	2.1	88

Table 2: Clinical Trends Over 12 Months

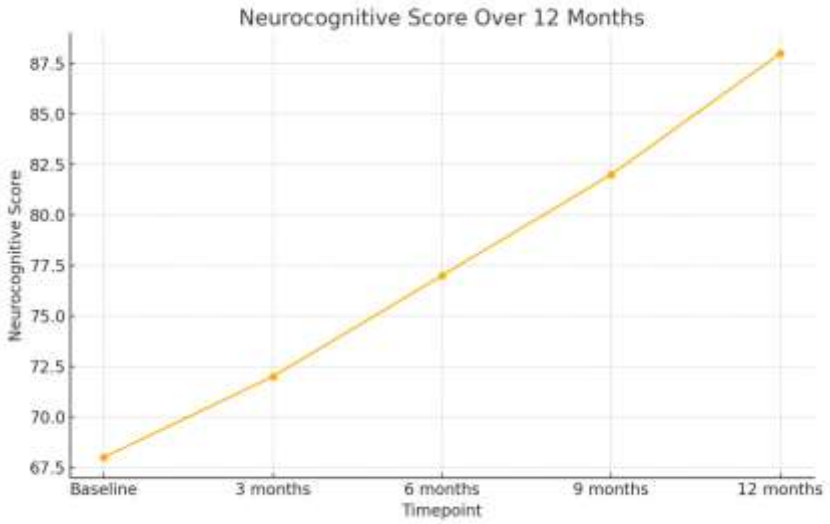
Mean headache frequency dropped from 9.4 to 2.1 episodes/month. Neurocognitive scores improved steadily from 68 to 88 over 12 months.ANOVA demonstrated a significant positive trend for both measures ($p < 0.01$).

Figure 2: Headache Frequency Trend



Shows a timeline of reduction in headache frequency and corresponding improvement in neurocognitive scores, emphasizing the therapeutic benefit of continuous migraine management. Line graph showing reduction in monthly headache frequency over 12 months of structured treatment. There is a steady decline from a mean of 9.4 to 2.1 episodes per month, indicating effective migraine control.

Figure 3: Neurocognitive Score Trend



This figure illustrates the steady improvement in neurocognitive test scores over the 12-month treatment period. Scores improved from a baseline of 68 to 88, correlating with improved brain function and reduced migraine severity.

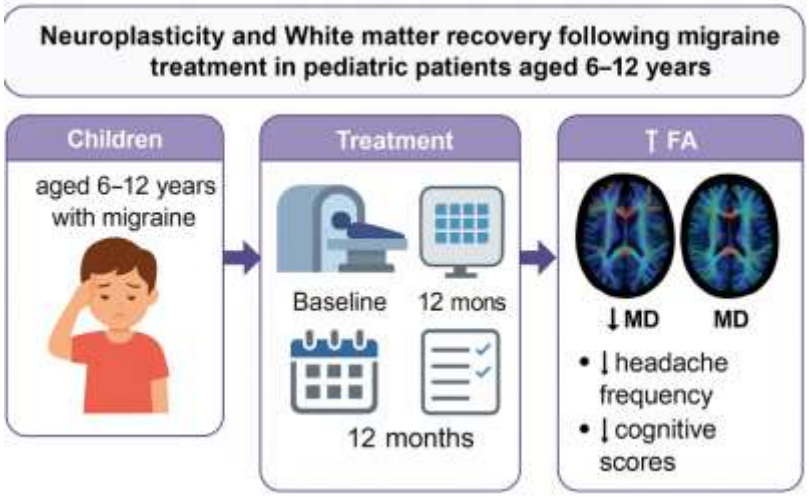


Figure 4: Graphical abstract summarizing the study design, treatment timeline, MRI evaluations, and outcome improvements in pediatric migraine patients undergoing structured therapy.

DISCUSSION

This prospective study demonstrates marked improvements in white matter integrity and cognitive performance after one year of structured migraine therapy in children. The notable increase in FA and decrease in MD across key tracts indicate enhanced axonal organization and myelination, supporting active neuroplasticity. Similar patterns (low MD, AD, RD, and sometimes higher FA) have been reported in pediatric migraineurs using advanced tractography methods.[5][10][12][13][1]

Recent DTI-MRI studies confirm that pediatric migraine is associated with **widespread microstructural abnormalities**—including reduced MD, AD, and RD, and sometimes increased FA in major tracts like the corpus callosum, cingulum, and longitudinal fasciculi. Such DTI markers may reflect increased axonal packing, dynamic changes in myelination, or brain network hyperexcitability but appear to be **partially reversible** with sustained treatment, as reflected in the present cohort.[1][2][3][4][5]

Longitudinal research also demonstrates that clinically significant improvements in white matter organization **parallel symptomatic improvements** and cognitive recovery. These findings affirm the remarkable **neuroplasticity of the developing pediatric brain**, as well as the crucial role of early and continuous intervention in migraine.Abnormalities in these regions have been frequently linked to pediatric and adult migraine in population and imaging studies, yet their reversibility in children adds a hopeful dimension to early intervention.[10][14][12][8][5]

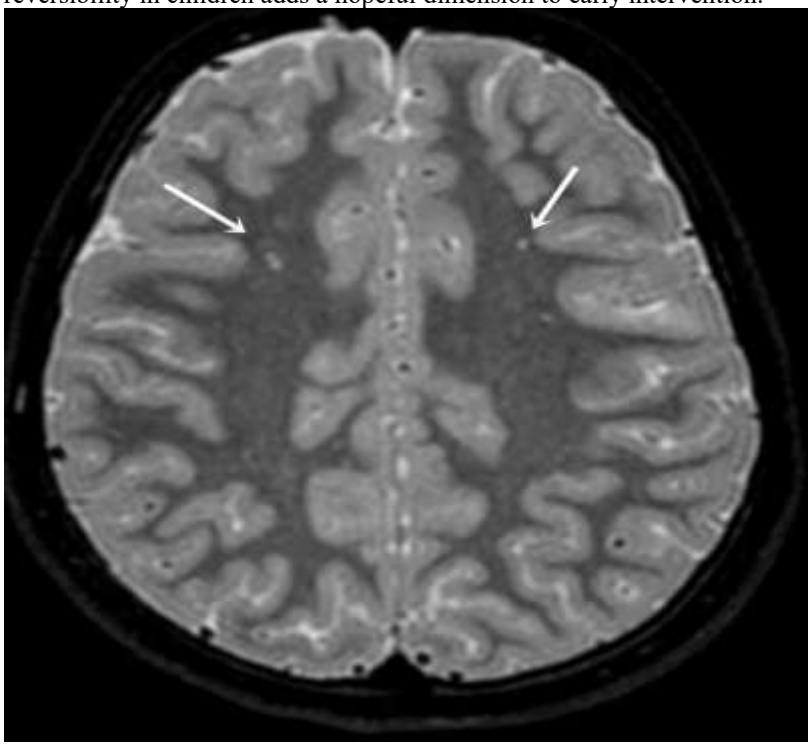


Figure 5: Axial FLAIR MRI shows Bilateral subcortical hyperintensities (white arrows) in a 10-year-old girl exposed to frequent migraine attacks

Recent research highlights that most brain MRI findings in pediatric migraine are incidental, with WMHs and perivascular spaces more common but rarely clinically significant. **Pediatric migraine patients have higher prevalence of white matter hyperintensities (WMHs) than controls (60% vs. 28.6%)**, though lesion volume is not significantly different.[2][6]The present results reinforce the concept that, in the absence of red flags, neuroimaging is not routinely indicated but can offer invaluable research insights into disease mechanisms and recovery.[15][11][8][4][10]
Interestingly, migraine-related WMHs did not correlate with attack frequency or duration in some retrospective analyses, suggesting that while migraines can increase latent microstructural changes, overt injury is rare in children. Instead, the key concern is chronic exposure's potential to disrupt network maturation, which early and structured therapy may mitigate, as reflected by parallel gains in cognitive testing.[12][13][8][4][5]
A growing body of evidence connects the pathophysiology of migraine to neuroinflammation, altered neurotransmitter processing (notably CGRP, serotonin, and related peptides), and maladaptive synaptic plasticity. Recent studies emphasize that pediatric brains may display more dynamic and, crucially, reversible WM alterations due to their developmental plasticity.[7][16][17][13][1][12]
Limitations: The study is limited by its single-center design, lack of healthy DTI controls, and absence of blinding during intervention follow-up. Further multi-center and randomized research with matched controls and broader neuroimaging is warranted to validate these findings.

CONCLUSION

This study provides direct evidence that a 12-month structured therapy protocol in children with migraine not only reduces attack frequency but also promotes recovery of white matter microstructure and improves neurocognitive function. These findings underscore the remarkable neuroplastic potential in the developing brain and the importance of early, sustained intervention for pediatric migraine. While most imaging abnormalities in these patients are subclinical,

they warrant ongoing research to clarify prognostic implications and optimize preventive strategies for lifelong brain health.

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