A 6-month Ibudilast Treatment Regimen Aimed to Improve Brain Function in Patients with Myalgic Encephalomyelitis/Chronic Fatigue syndrom: A Case Study.

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ABSTRACT

Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS) represents a complex condition whose onset is potentially linked to viral infections or immune-mediated disturbances, instigating inflammatory processes with repercussions on brain interconnectivity. Ibudilast, originally developed for Amyotrophic Lateral Sclerosis (ALS), demonstrates the potential to stimulate myelin growth.

This case study explores the intricate relationship between viral infections and vector markers within diverse brain networks, employing Fractional Anisotropy (FA) imaging as a primary investigative tool. A comprehensive analysis of 120 brain volumes is conducted, tracking changes over time and capturing unique characteristics. Automated fibre quantification facilitates the comparison of FA along 12 specific tracts.

The study encompasses two ME/CFS patients subjected to a six-month Ibudilast regimen, alongside two untreated ME/CFS patients. Diagnoses are meticulously established through clinical evaluation, self-reported assessments, alignment with the Canadian Consensus Criteria for CFS, and ICD-10 coding.

These findings illuminate the potential implications of Ibudilast in managing ME/CFS and underscore the imperative need for further research into this complex syndrome.

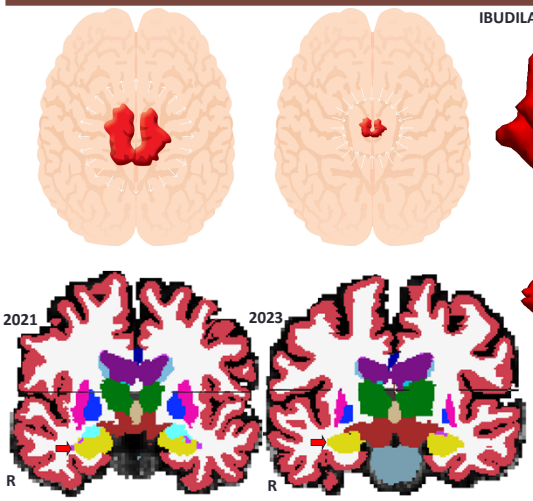
METHODS

- We examined 12 primary fibre tracts from a total of 42 available in the Diffusion MRI Atlas.
- The tract atlas, obtained from the Center for Biomedical Imaging at Massachusetts General Hospital and Harvard Medical School, was manually annotated.
- TRACULA software was employed to reconstruct the tracts based on the atlas.
- DTI, a variant of magnetic resonance imaging, was used to measure water molecule movement in the brain, allowing visualization of nerve fibres in white matter.
- Data processing involved importing DCM files into Horos and converting them for analysis with TRACULA and FreeSurfer.
- Fractional Anisotropy (FA) measured the diffusion of water molecules in the tissue, indicating anisotropy.
- Additionally, Radial Diffusivity (RD), representing myelin sheath inflammation, and Axial Diffusivity (AD), reflecting axonal damage, were analysed.
- Brain regions including the hypothalamus, lateral ventricles, cerebellum white matter volume, cerebellum cortex, hippocampus, amygdala, thalamus, and fornix were examined.
- Ibudilast was initially administered at 10mg/day and increased to 30mg/day after 3 months due to its phosphodiesterase inhibition and anti-inflammatory effects.

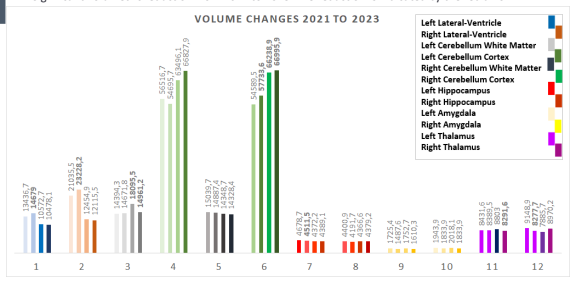
RESULTS

- Unexpectedly, ME/CFS patients showed a deterioration over a 3-year period, suggesting a progressive decline in neuronal processes.
- Comparing baseline measurements, a 10-30% decrease in axial diffusivity was observed in 12 brain regions.
- Ibudilast treatment led to improved brain coherence and reduced high fibre activity in axial diffusivity in 8 brain network areas.
- Treatment-naïve patients exhibited a 10-20% increase in axial diffusivity in the right cerebellum.
- Heart rate variability and hypothalamus volume normalized within the treatment group.
- No significant volume changes were noted in the test group.
- In ME/CFS individuals, increased right anterior arcuate and highly elevated inferior longitudinal fasciculus (ILF) fibre crossings were observed when considering insular cortex fibres.
- Axial diffusivity changes in the right cerebellum were detected in both ME/CFS and LC patients, possibly impacting body awareness and peripheral neuromuscular impulse feedback.
- These findings could provide insights into the persistent symptoms of LC and ME/CFS, but further patient data is needed for validation.

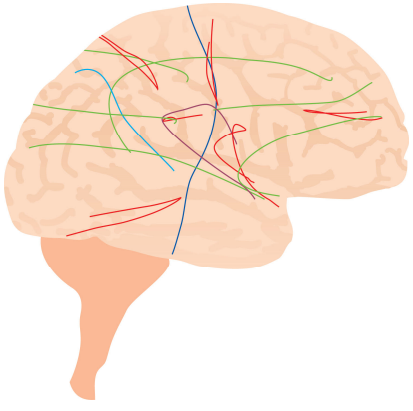
RESULTS



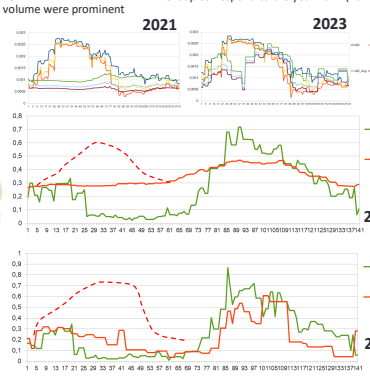
- Fig. 2 The right Hippocampus of the Control Group is represented in olive color, highlighting its significant volumetric reduction from 2021 to 2023. The reduction is indicated by the red arrow.



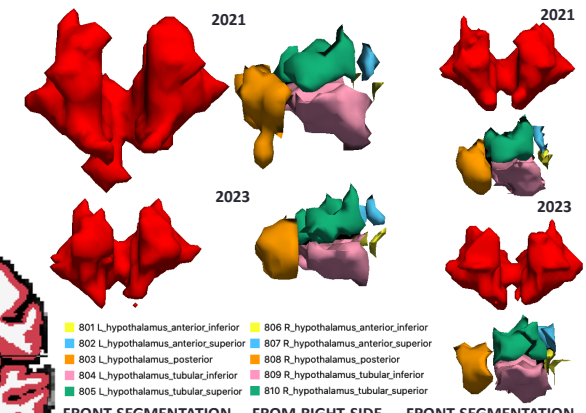
- Fig. 1 depicts volumetric changes across 12 distinct areas, organized into twelve groups. In Group 1, the two front bars highlighted in light blue represent the Control Group, while the dark blue bars within Section 1 pertain to the Intervention Group following Ibudilast application. Notably, substantial volumetric changes were observed, especially within the Control Group, where increases in volume were prominent in the left Amygdala, right Cerebellum Cortex, and right Lateral Ventricle areas.

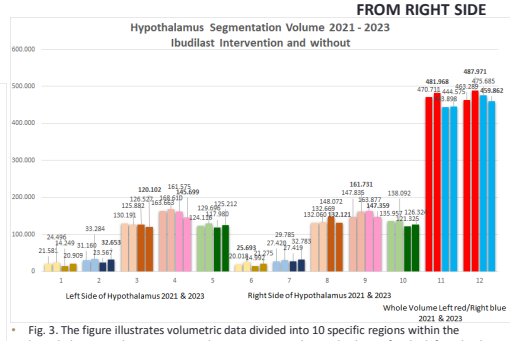


- Fig. 5 Shows the 12 Fibre Sections examination of the fractional anisotropy.



- Fig. 4 Shows the serious deterioration of the Control Group without intervention, over time of the FA_Avg's in the Fornix area. The front rise is completely missing (marked by the dashed line).





- Fig. 3. The figure illustrates volumetric data divided into 10 specific regions within the hypothalamus, with Sections 11 and 12 representing the total volumes for the left and right sides. The X-axis consists of 12 sections, each representing four categories within two groups. The lighter-shaded bars at the front depict the Control Group, with the first bar for the year 2021 and the second bar for the year 2023. In contrast, the rear bars in the Experimental Group correspond to the year 2021 (no intervention) and 2023 (with Ibudilast intervention).

CONCLUSIONS

- The results obtained in this study raise the possibility that Ibudilast could be a viable option for enhancing brain function among individuals with ME/CFS. Furthermore, these findings present fractional anisotropy as a potential biomarker that holds promise for diagnosing both ME/CFS and LC, offering a valuable tool for identifying and distinguishing these conditions.

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