

A patient-oriented multi-modal magnetic resonance imaging study on myalgic encephalomyelitis / chronic fatigue syndrome

Introduction and Background

Myalgic Encephalomyelitis, also known as Chronic Fatigue Syndrome (ME/CFS), is a complex condition that causes long-term, disabling symptoms such as severe fatigue. It mostly affects women and impacts the daily lives of over 580,000 people in Canada and up to 24 million worldwide. Despite how common it is, there is still no clear understanding of what causes ME/CFS, and no effective treatments are available, which can significantly reduce the quality of life for patients.

To help improve understanding of this condition, we conducted a study using advanced brain imaging techniques, including MRI and MRS. Our goal was to see if this new approach could reveal differences in brain function between people with ME/CFS and healthy individuals. We also wanted to explore how these brain changes might be related to common ME/CFS symptoms like fatigue and memory problems.

This study involved MRI scans to look at brain structure and function, a memory task to test thinking abilities, and brain scans that measured chemicals in different areas of the brain. This type of combined approach is one of the first of its kind in ME/CFS research.

Learning community engagement

This project was shaped by the close collaboration of three dedicated patient partners, who played an integral role in every stage of the research. Their lived experience with ME/CFS informed key decisions throughout the study, ensuring that the research stayed focused on the real-world needs and challenges of patients.

- **Study Design:** Helping to shape research questions that addressed key patient concerns, such as fatigue and cognitive challenges.
- **Participant Recruitment:** Guiding recruitment strategies to ensure a patient-friendly process.
- **Execution and Supervision:** Providing input on MRI protocols to enhance patient comfort and supervising research trainees.
- **Findings Interpretation and Dissemination:** Offering valuable insights into the interpretation of results and co-authoring patient-accessible publications.

Methods

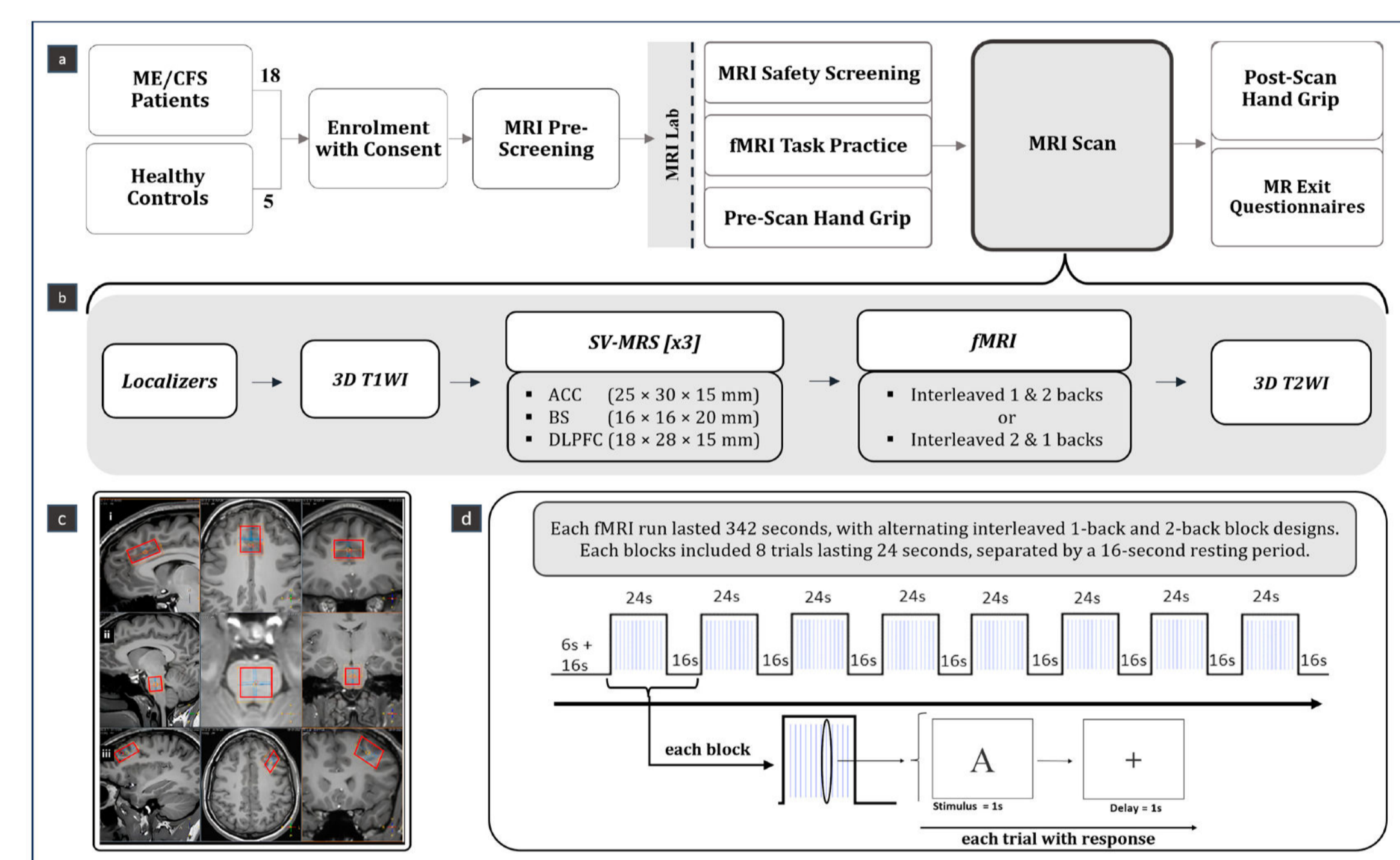


Figure 1. Study design of the multimodal MRI on ME/CFS project. (a) overview of the study design; (b) magnetic resonance imaging (MRI) protocol; (c) single voxel magnetic resonance spectroscopy (SV-MRS): red squares indicate the voxel placements in the following brain regions: (i) anterior cingulate gyrus; (ii) brainstem; (iii) left dorsolateral prefrontal cortex; (d) paradigm of functional MRI (fMRI) task using n-back. MR, magnetic resonance; MRI, magnetic resonance imaging; fMRI, functional MRI; MRS, magnetic resonance spectroscopy; ACC, anterior cingulate cortex; BS, brainstem; L-DLPFC, left dorsolateral prefrontal cortex; 3D, 3 dimensional; T1WI, T1-weighted imaging; T2WI, T2-weighted imaging; SV-single voxel.

Results

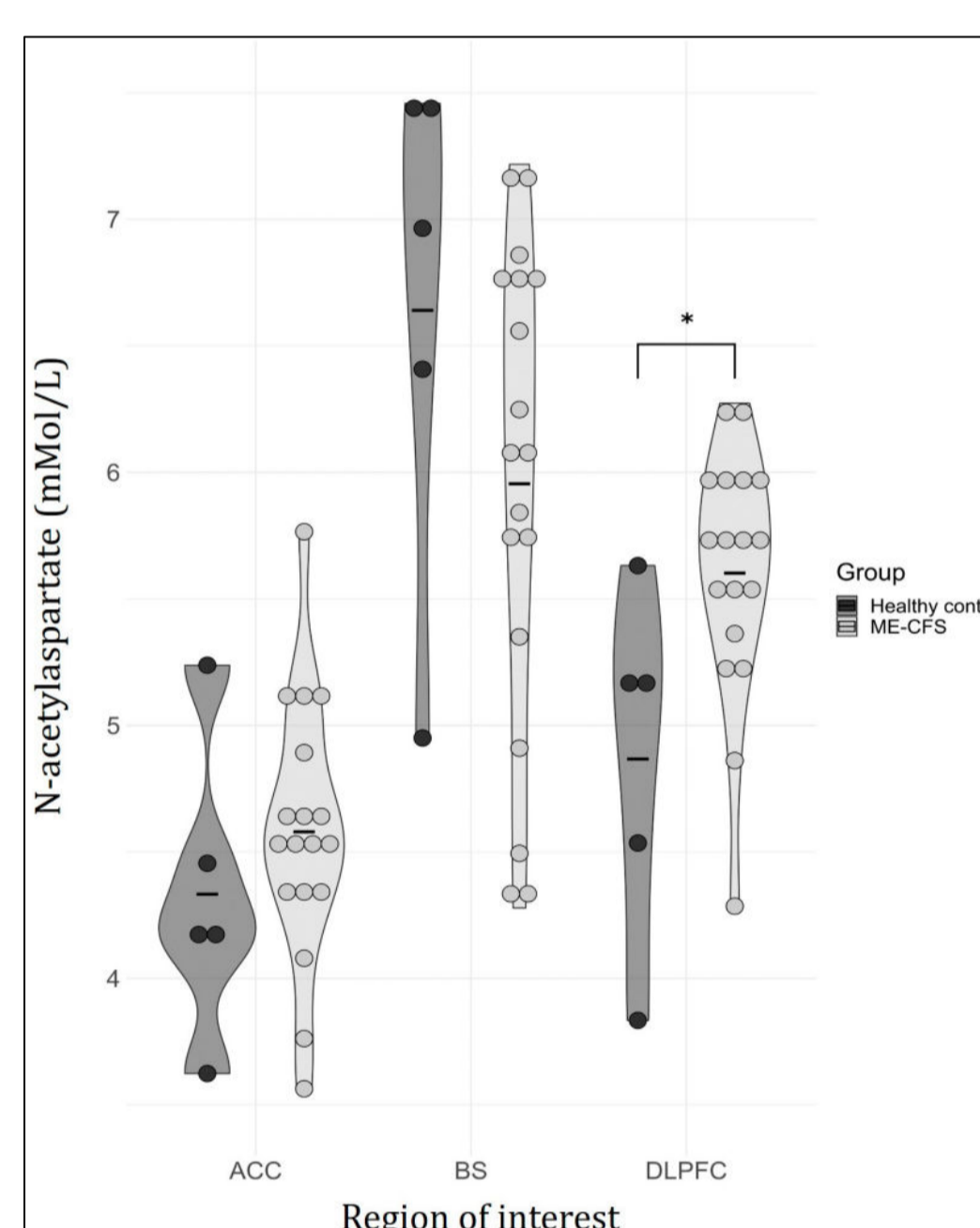


Figure 2. Metabolite N-acetyl aspartate (NAA) concentrations in each region of interest separated by healthy controls (HCs) (black) and ME/CFS (gray). Note: ACC, anterior cingulate cortex; BS, brainstem; DLPFC, dorsolateral prefrontal cortex; ME/CFS, myalgic encephalomyelitis/chronic fatigue syndrome. Black horizontal lines within each plot represent the mean, whereas circles represent individual data points for healthy controls (black) and individuals with ME/CFS (gray). The width of each curve corresponds to the approximate frequency of data points. * indicates a significant difference in NAA was observed in the DLPFC (OR = 8.49, $p = 0.042$, uncorrected).

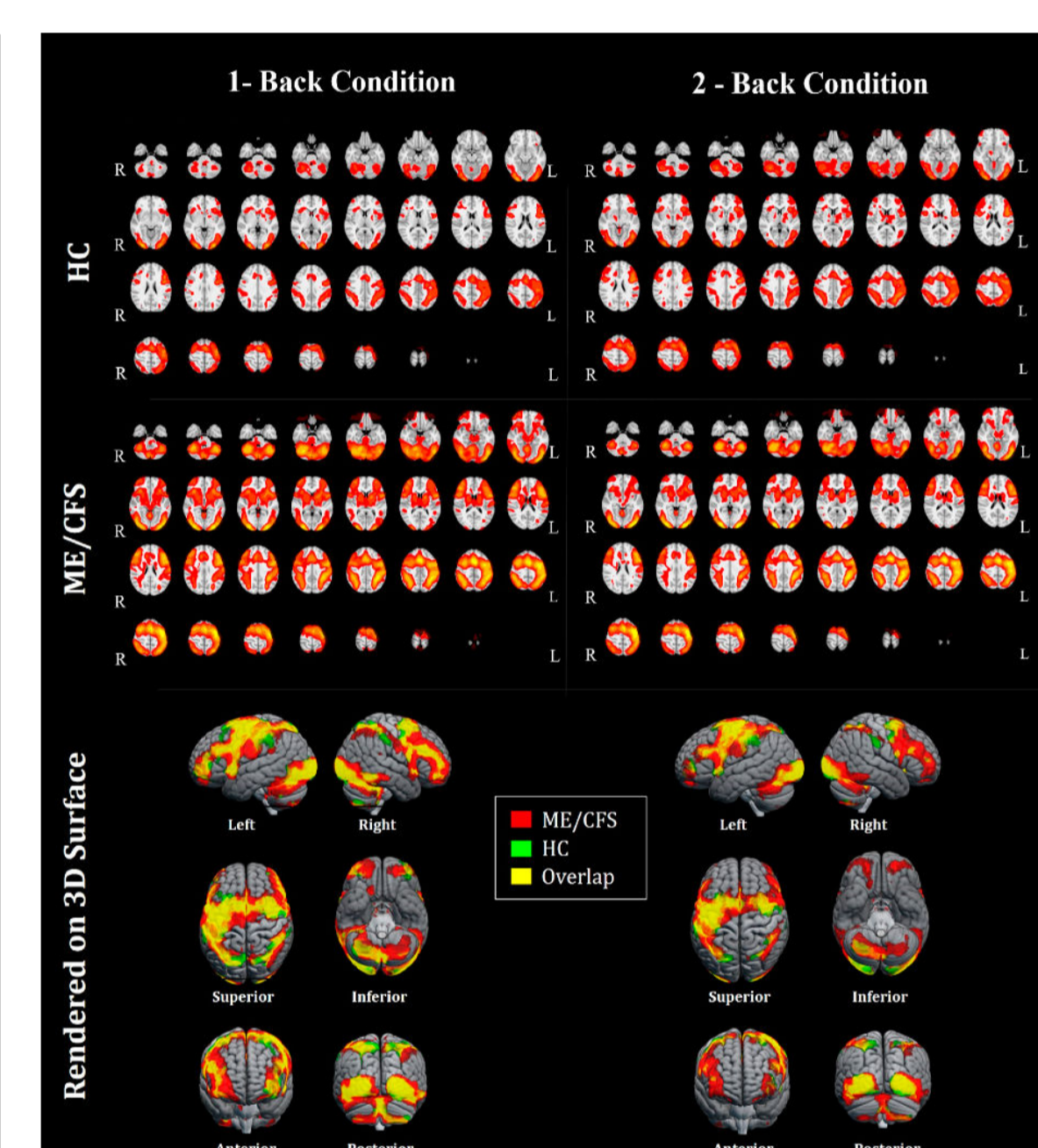


Figure 3: Group mean fMRI activation during the n-back task. The top and middle panels show the group mean activation maps under each condition passing the threshold ($z = 3.4$) for healthy controls (HCs—top panel) and myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS—middle panel). The “R” and “L” indicate the right and left side of the brain, respectively. Levels of significance are shown in red ($p < 0.05$) and yellow ($p < 0.01$), cluster-wise corrected. The bottom panel shows clusters passing the significance threshold ($z = 3.4$) rendered on the standard anatomical space (i.e., MNI 152). Clusters of ME/CFS (red) and HCs (green) groups, and those overlap between the groups (yellow) are displayed.

Conclusions

- The research finding demonstrated the feasibility of combining multiple SV-MRS and fMRI to profile brain metabolites and functional activation in ME/CFS. A 100% completion was seen within the targeted time regardless of patient or control participant group.
- Possible differences in brain metabolite levels and functional activation maps between ME/CFS and HC groups were observed: ME/CFS group showed a higher N-Acetylaspartate in the left DLPFC compared to HC (OR=8.49), This apparent brain metabolite abnormality was correlated with worsened fatigue, pain, and sleep quality scores (p 's $< .015$ corrected for multiple tests).
- An increase of brain functional activation, involving the frontal lobe (the left dorsal lateral prefrontal cortex and the anterior cingulate gyrus) and the brainstem, was also observed in ME/CFS compared to HC ($Z > 3.4$, p 's $< .010$ corrected for multiple tests).
- Our project showcased the successful collaboration between researchers and patient partners throughout the development of patient-oriented research in particular complicated studies involving multimodal MRI and clinical components.
- The project suggests the need of further research with larger cohorts to validate the apparent brain functional and metabolite differences between ME/CFS and HC. The feasibility of combining multiple SV-MRS and fMRI to profile brain metabolites and functional activation in ME/CFS enlightened ongoing efforts adopting this MRI protocol.
- Key findings of the project have been disseminated as a research article in a peer-reviewed scientific journal, co-authored with the patient partners.

References

Acknowledgments

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