

NCNED Research: Two New Studies on the Brain and Immune System in ME

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Microstructural alterations in brain tissue of ME/CFS and long COVID using diffusion tensor imaging and diffusion kurtosis imaging

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37 ME, 19 long COVID and 27 healthy controls (HC).
Data were acquired using a 3 Tesla (3T) Prisma MRI scanner.

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Findings in ME

Compared with HC, people with ME showed microstructural alterations in:

Cingulum (*pathway linking memory, emotion, and focus)*
Involved in emotional processing, memory and attention — differences here may relate to brain fog and mood.

Supplementary motor area (*A planning region for movement)*
Helps plan and coordinate voluntary movement and speech — may relate to the heaviness and motor slowing many describe.

Parts of Corpus callosum (*The bridge between brain hemispheres)*
The main connector between the brain's left and right sides — differences may relate to cognitive and sensory symptoms.

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Findings in ME

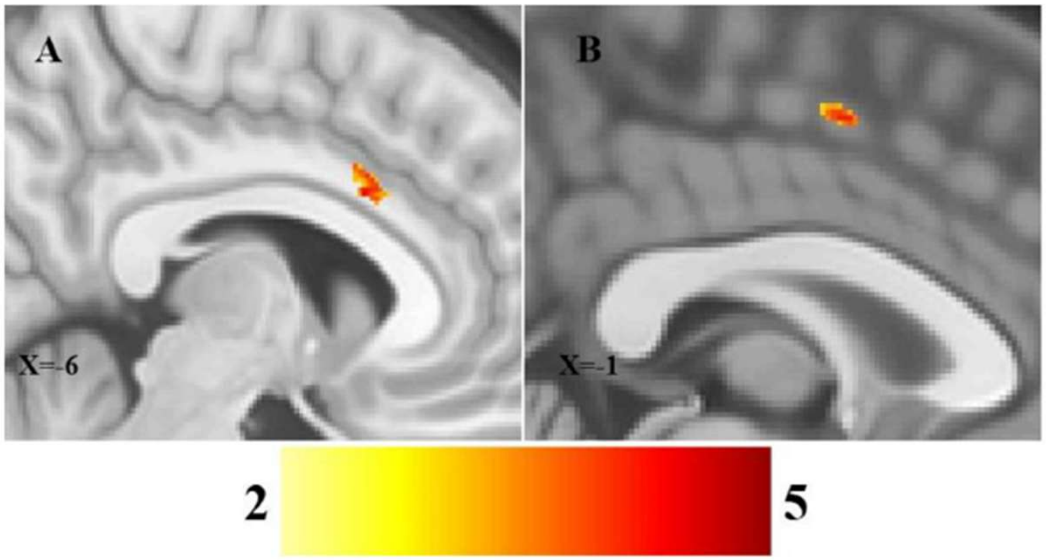


FIGURE 1
Findings of DTI in ME/CFS compared to healthy controls (HC). **(A)** significantly increased fractional anisotropy (FA) in the left cingulum (ME/CFS > HC) and **(B)** significantly decreased mean diffusivity, axial diffusivity and radial diffusivity in the left medial supplementary motor area/ medial frontal gyrus (ME/CFS < HC).

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Findings in long COVID

Compared with HC, people with long COVID demonstrated microstructural alterations in:

Fusiform gyrus (*Involved in visual processing & face recognition)*
Some people with Long COVID have described trouble recognising faces or visual overload — this may be a related clue.

Precentral gyrus (*The brain's main movement-control strip)*
Directly controls voluntary movement — differences here may connect to fatigue and motor symptoms.

Corona radiata & forceps minor (*Major connecting pathways deep in the brain)*
These carry signals across the brain and have been linked in other studies to fatigue and cognitive complaints.

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ME vs. Long COVID

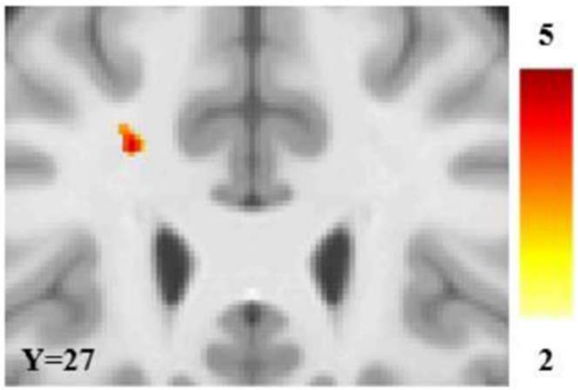


FIGURE 2
Comparison of ME/CFS and long COVID (ME/CFS < long COVID) showing significant increase in axial kurtosis (AK) in the left corona radiata.

ME has significant increase in the left corona radiata.

- Possibly compensatory denser cell packing or neuroinflammation.
- Important pathways for voluntary movement, motor coordination, and sensory filtering.
- Changes may be related to motor difficulties, altered sensory processing, cognitive difficulties in ME.

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Study impact

This study identifies distinct tissue microstructural alterations in ME and long COVID and offers a vital insight into the neuropathological basis of shared symptoms in both conditions.

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BMC Immunology

RESEARCH Open Access

Deficient TRPM3-linked mitochondrial Ca^{2+} influx in natural killer cells associated with myalgic encephalomyelitis/chronic fatigue syndrome

Chandi Tabeth Magawa[1,2,3*], Natalie Eaton-Fitch[1,2], Katsuhiko Muraki[2,4] and Sonya Marshall-Gradisnik[1,2]



Fluorescence live-cell imaging was used to investigate Ca^{2+} mobilisation in NK cells of (*N* = 10) ME, classified using Canadian Consensus Criteria, and (*N* = 10) healthy control (HC) participants.

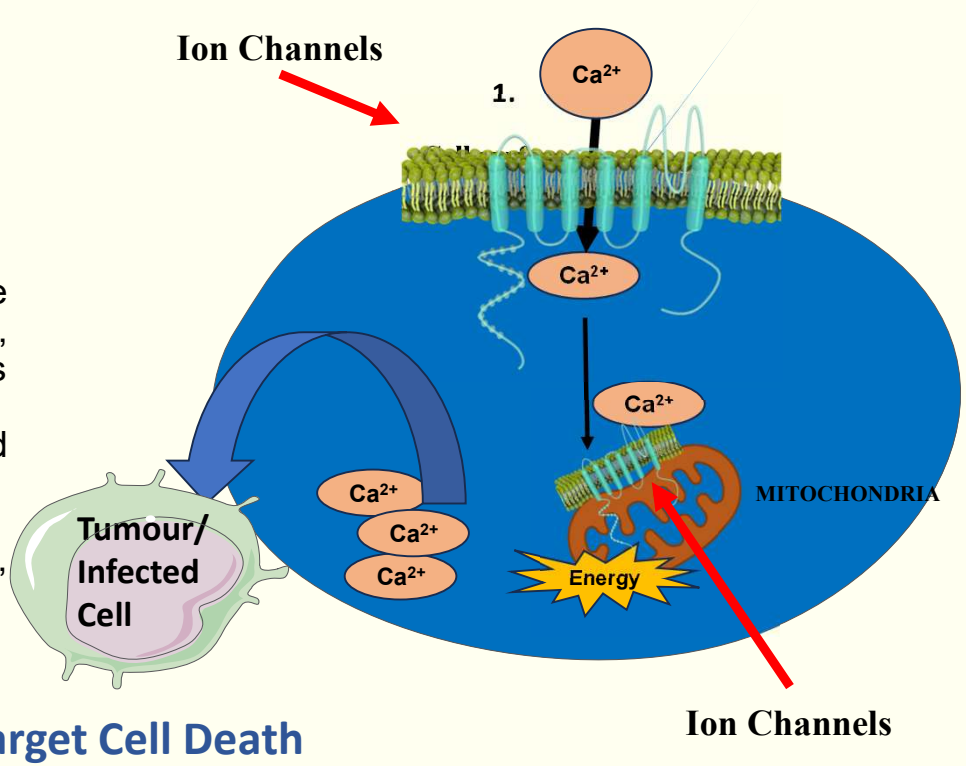
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Natural Killer Cell

TRPM3

- Expressed in many cells including the brain, spinal cord, kidneys, pancreas, immune cells, vascular smooth muscle cells
- Respond to external stimuli, threats and stress
- Participate in several signalling pathways, including Ca^{2+} signalling



Grimm et al., 2003; Lee et al., 2003; Fonfria et al., 2006

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Ion channels and calcium influx: other sites in the cell

1. Normal function: Ion channels move calcium into cell to perform normal function.

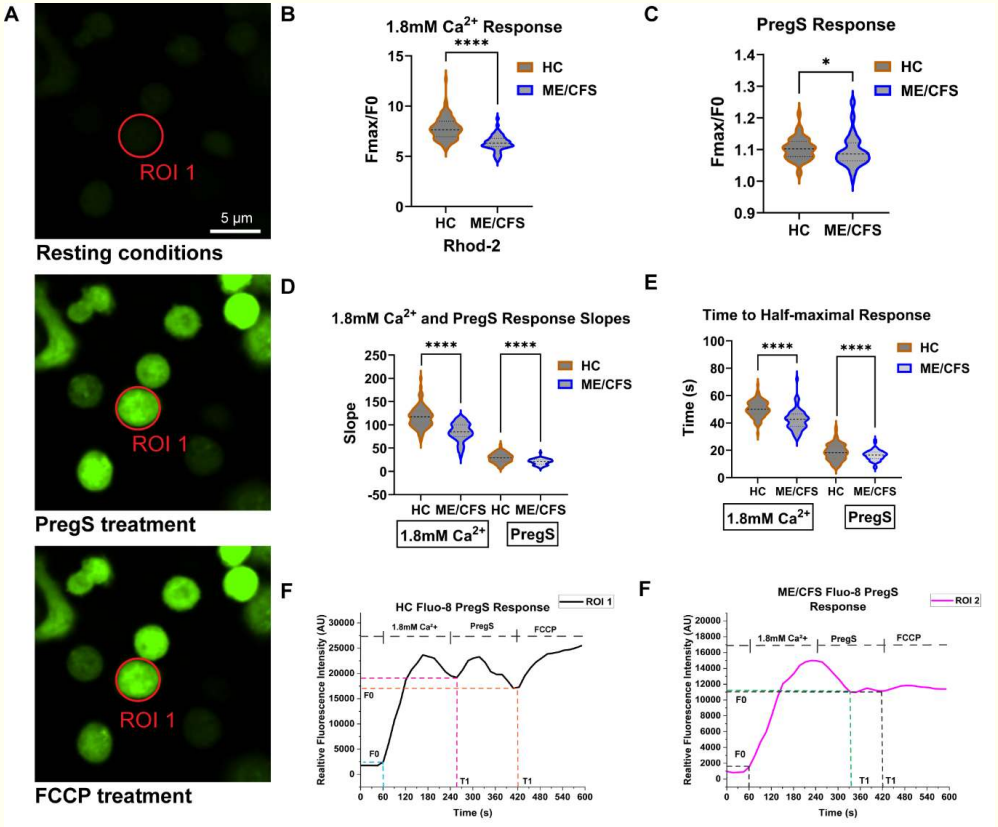
2. NCNED now examining ion channel function and calcium influx after ion channel activation in other sites of the cell in ME patients and healthy controls.

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Impaired TRPM3-dependent cytosolic Ca^{2+}

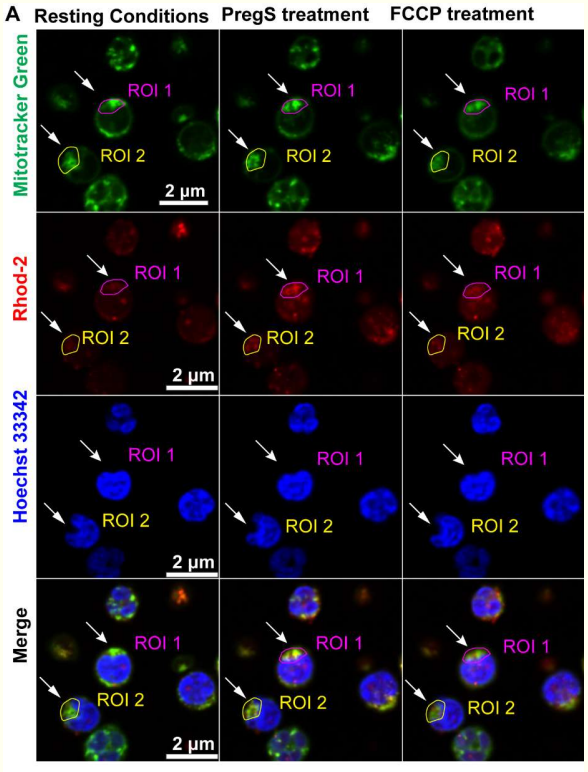
- Confirmed previous findings of cytosolic Ca^{2+} influx is significantly reduced in ME.
- Significant reduction in store operated Ca^{2+} in ME
- Ca^{2+} influx response is slower in people with ME compared with HC

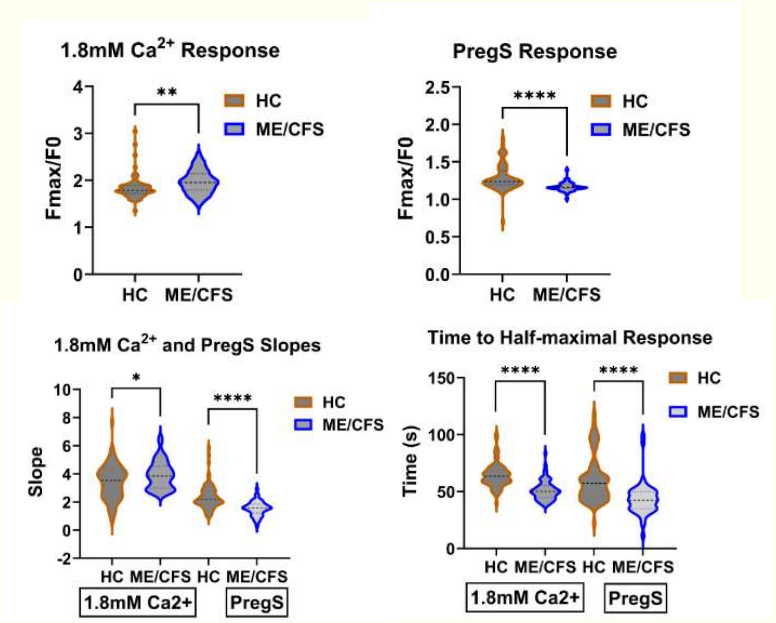


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Magawa et al. 2026

Impaired TRPM3-dependent mitochondrial Ca^{2+}





- Increased store operated calcium entry - mitochondrial Ca^{2+} uptake in ME
- Reduced TRPM3-mitochondrial Ca^{2+} uptake in ME

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Magawa et al. 2026

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Summary



Consistent TRPM3 ion channel dysfunction

→ Reduced Ca^{2+} mobilisation



Directly reported TRPM3-dependent Ca^{2+} mobilisation dysfunction in cellular compartments

→ Mitochondria



Future investigations aimed to elucidate other TRP ion channel family members

→ TRPM2, TRPM7, TRPM8

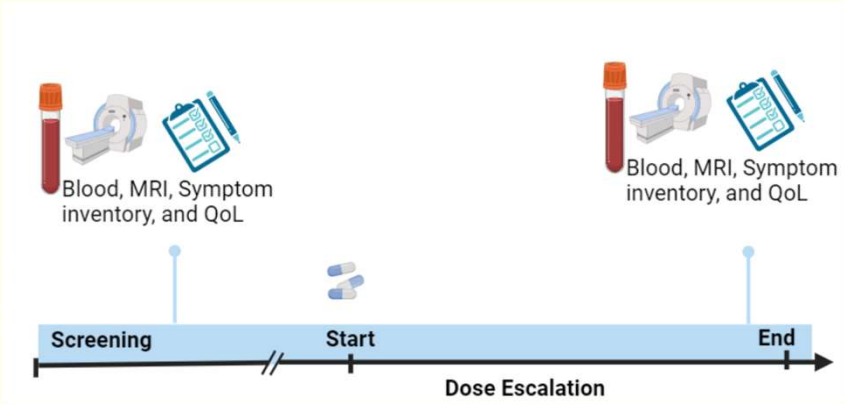
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Low Dose Naltrexone for the treatment of ME and Long COVID Condition - TreatMELC Study

Randomised double-blind placebo-controlled 12-week clinical trial

Health condition(s) studied: ME and long COVID

Treatment: Low-dose Naltrexone (LDN) or placebo



Project aims

The aim of this randomised controlled trial is to determine if **treatment with LDN improves ion channel and brain function, fatigue, cognitive and neurological symptoms, and health-related quality-of-life** (HRQoL) in people living with **ME and Long COVID**. If this is the case, LDN may offer a cost-effective treatment for ME/CFS and Long COVID.

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Post COVID-19 condition (Long COVID)

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Thank you

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Questions

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