PRIME – building infrastructure for **P**atients, **R**esearchers and **I**ndustry for **ME**/CFS

PRIME Webinar 4: The Neurology of ME/CFS

Wednesday 28th October, 2026 2-5pm GMT

Online: Register here

General abstract:

Join leading international researchers for an online workshop exploring the advancing field of **neurology in ME/CFS**. This event will showcase the latest discoveries into how the brain and nervous system are affected in ME/CFS, highlighting research that might transform our understanding of the condition.

Through presentations from experts at the forefront of the field, attendees will learn how imaging techniques, alongside other approaches to generating and analysing neurological data, are providing new insights into the mechanisms underlying ME/CFS. The workshop will explore why neurology has become such an important area of research, how these findings are shaping future studies, and their potential to improve diagnosis, identify therapeutic targets, and ultimately lead to better outcomes for people living with ME/CFS.

As the latest webinar in the **PRIME** project's series of ME/CFS-focused events, this workshop offers an opportunity to hear from internationally recognised researchers in neurological ME/CFS research. Whether you are a researcher, healthcare professional, person with ME/CFS or simply interested in the latest scientific advances, you'll gain insights into one of the most promising areas of ME/CFS research and the potential it holds for improving patients' lives.

Speakers:

- **James Cox -** Professor of Human Pain Genetics in the Wolfson Institute for Biomedical Research (WIBR), University College London
- **Felipe Correra de Silva -** Netherlands Institute of Neuroscience, Amsterdam UMC
- **Keyla Santos Guedes de Sá -** Pew Latin American Fellow and postdoctoral researcher in the Department of Immunobiology at Yale School of Medicine
- **Beata Godlewska -** Senior Clinical Scientist, Honorary Consultant in General Adult Psychiatry, University of Oxford
- **Jarred Younger** – Professor & Director of the Neuroinflammation, Pain, and Fatigue Laboratory, University of Alabama at Birmingham

Programme: **Talks 20mins + 10mins questions**

2-2.05pm
Welcome from the Chair (Prof. Chris Ponting, University of Edinburgh)

2.05-2.35pm
Talk 1: *Exploring the role of carbonic anhydrase 10 (CA10) in ME/CFS and chronic pain*
James Cox - Professor of Human Pain Genetics in the Wolfson Institute for Biomedical Research (WIBR), University College London
Abstract: The DecodeME genome-wide association study has found eight loci with a significant association for ME/CFS. One of these loci, close to the *CA10* gene, also has significant associations in multi-site chronic pain and neck/shoulder pain cohorts. *CA10* encodes carbonic anhydrase X, a highly evolutionarily conserved gene with an important, but under-researched, role in synaptic function. CA10 binds directly to neurexins (presynaptic cell-adhesion molecules), helping to regulate synapse formation and neural connectivity. We will describe our initial experiments and future plans that aim to determine the potential role of *CA10* in ME/CFS and chronic pain.

2.35-3.05pm
Talk 2: *Investigation of neuroendocrine and neuroimmune alterations in ME/CFS*
Felipe Correra de Silva - Netherlands Institute of Neuroscience, Amsterdam UMC
Abstract: Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS) is a severe disabling disorder whose underlying neurobiology remains elusive, largely due to a lack of tissue-based evidence. To address this, we established a brain donor program focused on ME/CFS within with the Netherlands Brain Bank, enabling the interrogation of cellular and molecular changes in the ME/CFS central nervous (CNS) system. Here, we combined machine learning-driven analyses of clinical datasets with histological, endocrinological, and molecular characterization of postmortem brains from ME/CFS cases compared to well matched controls. We identified a reduction in hypothalamic corticotropin-releasing hormone (CRH)-expressing neurons, accompanied by altered pituitary signalling and reduced cerebrospinal fluid cortisol levels, consistent with multi-level suppression of the hypothalamic–pituitary–adrenal (HPA) axis.
Given the prominence of neuroinflammation in ME/CFS models, we next assessed whether a (microglial) neuroinflammatory profile could underlie the observed hypothalamic alterations. Microglia were comparable among controls and ME/CFS, and altered morphology characterized by an increased proportion of dystrophic cells in ME/CFS. Furthermore, these cells did not show elevations in classical activation markers and altered phagocytic capacity. Together, these findings do not support a sustained, classically activated neuroinflammatory state in ME/CFS.
Collectively, our findings define the neurobiological basis for well documented endocrine alterations in ME/CFS and suggest that these changes are not driven by classical neuroinflammation but are associated with a distinct, potentially dysfunctional microglial state.

3.05-3.35pm
Talk 3: *Autoantibodies Analysis in Long COVID and ME/CFS*
Keyla Santos Guedes de Sá - Pew Latin American Fellow and postdoctoral researcher in the Department of Immunobiology at Yale School of Medicine
Abstract: Acute SARS-CoV-2 infection triggers the de novo production of diverse, functional autoantibodies (AABs) that remain elevated in long COVID (LC), but their pathogenic role remains unclear. Using tissue-based immunofluorescence, ELISA, human protein array, and mass spectrometry assays, we identified a broad range

of AAB targets among individuals with LC. Individuals with neurocognitive symptoms showed increased AABs against central nervous system (CNS) and peripheral nervous system proteins. Purified immunoglobulin G (IgG) reacted with human locus coeruleus, thalamus, adrenal gland, and thyroid and cross-reacted with mouse sciatic nerve and meninges. CNS-reactive AABs correlated with several neurological symptoms. MED20-targeting IgG from patients with LC showed enhanced antibody-dependent phagocytosis. Passive transfer of IgG from individuals with LC into mice induced fatigue-like behavior, loss of balance/coordination, thermal hyperalgesia, small fiber nerve damage, and increased pain-related neuronal activity, recapitulating patients' symptoms. These findings suggest that targeting AABs might offer therapeutic benefits for this LC subgroup.

3.35-3.50pm - BREAK

Chair (Slawomir Kajawski - Assistant Professor at The Nicolaus Copernicus University in Toruń, Bydgoszcz, Poland)

3.50-4.20pm

Talk 4: *When the brain is challenged: energy metabolism in ME/CFS*

Beata Godlewska - Senior Clinical Scientist, Honorary Consultant in General Adult Psychiatry, University of Oxford

Abstract: In this talk, I will discuss the hypothesis that ME/CFS is characterised by reduced cerebral oxidative metabolic reserve - the capacity of the brain to meet increases in energetic demand through oxidative metabolism. Growing evidence implicates altered cellular energy metabolism in ME/CFS, but most neuroimaging studies have examined the brain at rest. This is particularly relevant in a condition defined by worsening symptoms following exertion. We therefore asked whether abnormalities in brain energy metabolism become more apparent when energetic demand increases.

Using functional MRS at 7 Tesla, we measured changes in lactate in the visual cortex during stimulation with a flickering checkerboard. Lactate is particularly informative because it lies at the interface between glycolytic and oxidative metabolism and links astrocytic and neuronal energy metabolism. Rather than asking simply whether brain metabolism is abnormal at rest, this allowed us to ask a different question: how does the brain in ME/CFS respond when its energy requirements increase?

Lactate concentrations did not differ between groups at rest, but visual stimulation produced a substantially greater increase in ME/CFS than in healthy controls (22.2% versus 10.6%). Greater lactate responses were also associated with lower self-reported energy and vitality. These findings suggest that altered brain energy metabolism in ME/CFS may be demand-dependent, becoming apparent when energetic requirements increase.

4.20-4.50pm

Talk 5: *Is the ME/CFS brain trapped in a pathologic state of energy conservation?*

Jarred Younger – Professor & Director of the Neuroinflammation, Pain, and Fatigue Laboratory, University of Alabama at Birmingham

Abstract: Recent human neuroimaging studies have identified intriguing abnormalities in the brains of individuals with ME/CFS, including increased brain lactate, transitions of microglia toward inflammatory phenotypes, impaired glymphatic function, and reduced availability of adenosine triphosphate (ATP). In this talk, we discuss the hypothesis that ME/CFS involves a persistent disturbance in the systems that estimate physiological threat and available energy, causing the central nervous system to adopt a state of abnormally constrained autonomic, cognitive, and motor output. This abnormal constraint of activity may be particularly evident under conditions of increased physiological demand

4.50-5.00pm - Concluding Remarks

Speaker Bios:

James Cox

Prof James Cox is based in the Molecular Nociception Group in the Wolfson Institute for Biomedical Research (WIBR), UCL. After studying Medical Science as an undergraduate in Birmingham, he studied for his PhD in Molecular Genetics in Cambridge where he worked with patients with X-linked learning disability. He then joined Prof Geoff Woods (in Cambridge) and Prof. John Wood (at UCL) as a post-doc before establishing his own research team in 2011 at UCL with an MRC Career Development Award. His team investigates the genetics and underlying biology of inherited pain disorders and ME/CFS.

Felipe Correra de Silva

Postdoctoral fellow at the University of Amsterdam and Netherlands Institute for Neuroscience, under guidance of prof. dr. Lucassen, prof. Dr. Huitinga and dr. Hamman. My work investigates the molecular and cellular alterations in the central nervous system (CNS) in ME/CFS, using human postmortem samples. My long-term goal is to provide a detailed map of the CNS alterations in ME/CFS, providing advances in identification of therapeutic targets and biomarker discovery.

Keyla Santos Guedes de Sá

I am a Pew Latin American Fellow and postdoctoral researcher in the Department of Immunobiology at Yale School of Medicine, under the guidance of Dr. Akiko Iwasaki. My work investigates how pathogenic autoantibodies emerge after infections and contribute to chronic diseases such as Long COVID and ME/CFS. I integrate large-scale proteomics, immunology, and translational approaches to uncover mechanisms of neuro-immune interactions and identify therapeutic targets. My long-term goal is to establish an independent research program focused on autoantibody-mediated neurological chronic diseases and precision medicine.

Beata Godlewska, PhD, MBBS

Senior Clinical Researcher at the University of Oxford's Department of Psychiatry, and Honorary Consultant Psychiatrist with Oxford Health NHS Foundation Trust. Her research focuses on understanding the neurobiology of ME/CFS and fatigue, with a particular interest in brain energy metabolism and mitochondrial function. She uses advanced neuroimaging approaches, including ultra-high-field magnetic resonance spectroscopy (MRS) and functional MRS, to investigate brain metabolism in vivo and how it changes in response to energetic demand. Her broader goal is to translate mechanistic understanding of ME/CFS into biomarkers and new therapeutic approaches.

Jarred Younger

Professor in the departments of Psychology, Clinical Immunology and Rheumatology, and Anesthesiology and Perioperative Medicine at the University of Alabama at Birmingham (UAB). Dr. Younger received his doctorate in Experimental Psychophysiology in 2003 from the University of Tennessee, Knoxville and completed postdoctoral fellowships at Arizona State University and Stanford University. Dr. Younger joined the Stanford faculty in 2009 and moved to UAB in 2014 where he directs the Neuroinflammation, Pain, and Fatigue Laboratory. Dr. Younger's work focuses on using neuroimaging, immunological, and pharmaceutical scientific approaches to better understand brain inflammation. He is currently funded by the National Institutes of Health, Department of Defense, and ME Research UK foundation. His group develops diagnostics and treatments for myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS), fibromyalgia, Long-COVID, and Gulf War Illness.