Novel pathomechanisms in Chronic Fatigue Syndrome/Myalgic Encephalomyelitis: Do purinergic signalling perturbations and gliosis play a role?

D.R. Staines¹² MBBS, MPH, FAFOM, FAFPHM, E. W. Brenu² HBSc, Grad Dip BMed, S. Marshall-Gradisnik² PhD

1. Queensland Health, Gold Coast Population Health Unit, Southport, Gold Coast, Queensland, Australia.
2. Faculty of Health Science and Medicine, Population Health and Neuroimmunology Unit, Bond University, Robina, Queensland, Australia.

Corresponding author

Ekua Weba Brenu
Faculty of Health Science and Medicine
Bond University
Queensland 4229
Australia
Email: ebrenu@student.bond.edu.au

Dr Donald R. Staines
Associate Professor and Public Health Physician
Gold Coast Population Health Unit
10-12 Young Street,
Southport 4215,
Queensland, Australia
Ph: +61 7 5509 7222
Facsimile: +61 7 5561 1851
E-mail: Don_Staines@health.qld.gov.au
ABSTRACT
CFS/ME is, in some cases, a serious fatigue-related condition exhibiting a range of neurological, immunological and metabolic dysfunctions in symptom presentation. The present paper explores the possibility of perturbations of purinergic signalling (PS) as a pathomechanism of CFS/ME involving glial cell dysfunction, disruption of neuronal transmission, neuroinflammation and possible disturbances in the functioning of the blood-brain and blood-spinal barriers (BBB/BSB). This paper discusses the possibility that the putative neuroinflammatory processes may occur through perturbations of PS involving vasoactive neuropeptide (VN) dysfunction (e.g. through autoimmune mechanisms).

Pituitary adenylate cyclase-activating polypeptide (PACAP) and vasoactive intestinal peptide (VIP) function as neurotransmitters, vasodilators and regulators of immunity, nociception and hypoxic injury. They are important in the central nervous system (CNS) by activating adenylate cyclase (AC) to produce cAMP from ATP. Compromise of ATP metabolism may promote neuronal and glial toxicity through impaired cAMP production or impaired ATP metabolism and these may alter BBB/BSB function.

Although speculative, diagnostic and therapeutic implications may exist for CFS/ME if VN compromise, along with perturbations of PS, do indeed disrupt neurological and glial cell functioning. Treatment opportunities involving phosphodiesterase inhibitors (PDEIs) and purinergic modulators may plausibly exist.