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Welsh Association of ME & CFS Support (WAMES)
Website www.wames.org.uk
Helpline 029 2051 5061 helpline@wames.org.uk
Adviser Dr Nigel Speight
Patron Lord Barry Jones
Charity no. 1144534

The M.E. Brain
an introduction from WAMES

Myalgic Encephalomyelitis (ME), sometimes known as Chronic Fatigue Syndrome (CFS), affects the whole body but the neurological and cognitive symptoms can often be the most debilitating and distressing.

Definition of ME
My muscle
Aligic pain
Encephalo brain
My spinal cord
It is inflammation

While the traditional name for the condition indicates the presence of Myalgia (muscle pain) and Encephalomyelitis (brain-muscle-inflammation disorder) some people prefer to use the more general term encephalopathy (‘brain dysfunction), until more is known about the nature of the inflammation.

Symptoms
The neuro cognitive symptoms that patients experience include:
- confusion
- impairment of concentration
- short-term memory consolidation
- disorientation
- difficulty with information processing, categorising and word retrieval
- perceptual and sensory disturbances – e.g. spatial instability and disorientation and inability to focus vision.
• ataxia, muscle weakness and fasciculations are common.
• there may be overload phenomena: cognitive, sensory – e.g. photophobia and hyper sensitivity to noise - and/or emotional overload.

Research findings
Numerous research studies have been undertaken, helped by recent technological advances, to assess neuro-cognitive impairments. These confirm both structural and functional brain abnormalities.

There is, however, a lot that is still unknown about the role of the brain in ME and some past studies have suffered from methodological problems (e.g. differences in ME and CFS criteria used in various studies, and the fact that most research definitions are so wide that they contain a variety of patient groups). The terminology used by researchers (ME, ME/CFS or CFS) does not necessarily reflect the selection criteria or illness definition.

Since the central nervous system (CNS) is the “master con-trol” of all body functions, and much of the research points to damage and dysfunction of the CNS, it is reasonable to deduce that all body systems - immune, cardiovascular, endocrine, musculoskeletal – will experience dysfunction, which will in turn affect others, including the CNS.

Brain abnormalities

- Brain-stem hypoperfusion (decreased blood flow) was confirmed in all ME/CFS patients. Patients with ME/ CFS have a generalised reduction of brain perfusion, with a particular pattern of hypoperfusion of the brain-stem.

Costa 1988, 1995 (3)

- MRI scans show brain stem dysfunction and altered homeostasis.

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Numerous studies, including neuroimaging, have shown that there is a low incidence of psychologically-related problems in ME/CFS patients, that the disease is not caused or maintained by psychological factors, that it is distinct from clinical depression, and depression rates in ME/CFS are comparable to those with other chronic illnesses.

- Greater effort is needed by people with ME/CFS to process auditory information as effectively as demographically similar healthy adults.  
  **Lange 2005** (24)

- Plasma neuropeptide Y: a biomarker for symptom severity in chronic fatigue syndrome.  
  **Fletcher 2010** (25)

- A research review of studies that have shown generalised hyperalgesia (an increased sensitivity to pain throughout the body) in ME for a variety of sensory stimuli, including electrical stimulation, mechanical pressure, heat and histamine, concluded that there is good evidence that ME/CFS patients have a generalised hyperalgesia.

- Furthermore, patients’ pain sensitivity increases after stressors, such as harmful heat pain, and following exercise – an unusual observation since sensitivity to pain normally decreases in the general population during physical activity.  
  **Nijs 2012** (26)

- Differences were found in the neuropsychological performance of twins with CFS in comparison to their healthy co-twin.  
  **Claypoole 2007** (27)

- In the absence of sensory/motor abnormalities, impaired acquisition of the classically conditioned eye-blink response indicates an associative deficit suggesting organic brain dysfunction within a defined neural substrate in CFS patients.  
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- Differences found between CFS and depression  
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- Exercise – induced changes in cerebrospinal fluid miRNAs in Gulf War Illness and CFS show they are distinct disorders  
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- Significant reductions were found in global gray matter volume which was linked to the reduction in physical activity in CFS patients.  
  **De Lange 2005** (10)  
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- In separate but possibly related work, there are reports of subcortical “white matter hyperintensities” areas of bright intensity - on MRI scans in CFS patients.  
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"...now there's proof that inflammation occurs in the brain and there's evidence that patients with this illness experience a level of disability that's equal to that of patients with late-stage AIDS, patients undergoing chemotherapy, or patients with multiple sclerosis."

Dr. Nancy Klimas
Encephalitic symptoms, Brain and CNS inflammation
Lumbar punctures and autopsies have shown definite signs of inflammation in the brain and spinal cord.

- Evidence consistent with chronic infections affecting the nervous system in ME/CFS, or the inflammation as a result of the infections.  
  Komaroff 2011 (18)

- This research review concludes that CFS is likely to be a disease of long-term inflammatory processes of the brain.  
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- Distinct cerebrospinal fluid proteomes differentiate post-treatment Lyme disease from CFS.  
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- Spinal fluid abnormalities in patients results support two hypotheses: that some patients have a neurological abnormality that may contribute to the clinical picture of the illness and that immune dysregulation within the central nervous system may be involved in this process.  
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- The significant differences observed in a number of key putative CNS 5-HT and dopaminergic modulators, coupled with the exacerbated perception of effort, provide further evidence for a potentially significant role for CNS mechanisms in the pathogenesis of CFS.  
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Monoamine abnormalities
Monoamine neurotransmitter disorders mimic the symptoms of neurological disorders such as cerebral palsy and thus are frequently misdiagnosed.

Cognitive Dysfunctions Neurocognitive studies (i.e. studies of how the patient proc-esses information) have shown that patients have difficulty with memory, concentration and many other thought processes, that they require more energy to process information, and that their ability to process information worsens with physical exercise or prolonged mental tasks.

Factors which might contribute include vascular insufficiency, metabolic dysregulation, or an ongoing infectious process.
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Brain abnormalities

Neuroimaging of ME/ CFS brains has shown objective evidence of poor and abnormal oxygenation, abnormal energy metabolism, small lesions in various areas of the brain, and significant reduction in gray matter. These have been identified using PET, MRI, BEAM, SPECT and SPET scans.  

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