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
Algic	pain
Encephalo	brain
Mye	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 indicative of such dysfunction are as characteristic of the condition as postexertional malaise (PEM). The major Canadian [1] and International [2] definitions require that patients have at least two of a list of six 'neurological/ cognitive manifestations' before a diagnosis of ME can be made.

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 sys-tem (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

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 identi-fied using PET, MRI, BEAM, SPECT and SPET scans.

- 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)

Natelson 2017 (30)

- MRI scans show brain stem dysfunction and altered homeostasis.

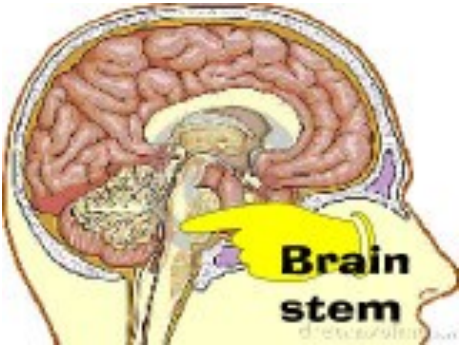
Barnden 2011 (4)

- EEG can be used to distinguish between ME/CFS patients, depression patients and healthy people.

Duffy 2011 (5)

- Deficits in motor preparatory areas of the brain have a neuro-physiological basis.

Davey 2003 (6)



- 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)*

  Okada 2004 *(9)*

- In separate but possibly related work, there are reports of subcortical "white matter hyper -intensities" areas of bright intensity - on MRI scans in CFS patients.

  Natelson 1993 *(8)*

  Lange 1999 *(7)*

- Changes were shown in the chemistry of the brain in patients with CFS, especially in relation to raised free choline levels.(9)

  Tomoda 2005 *(13)*

  Puri 2002 *(14)*
  Chaudhuri 2000 *15)*

- Patients with CFS were found to have reduced absolute cortical blood flow which supported earlier findings that patients devoid of psychopathology are the group most at risk of having some of the symptoms of CFS due to brain dysfunction.

  Yosiuchi 2006 *(16)*

- Reduced responsiveness in the brain to stimuli found by fMRI was found to be an essential feature of ME/CFS

  Tanaka 2006 *(17)*

- CFS brains have diminished white matter and white matter abnormalities in the right hemisphere.

  Zeineh 2014 *(33)*
  Finkelmeyer 2017 *(34)*

- Progressive changes in white matter were found with longitudinal MRI over 6 year period and were found to correlate with patients' symptom scores.

  Shan 2016 *(35)*

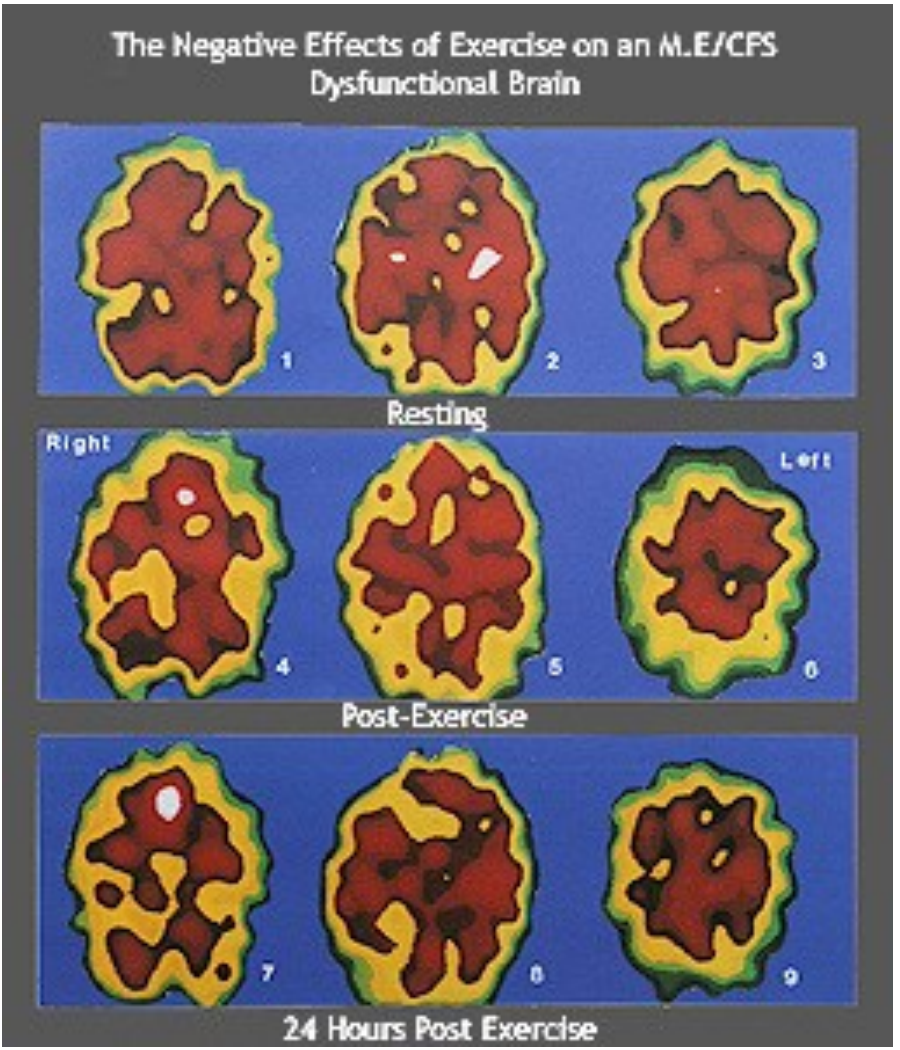
- Abnormal blood flow & connectivity found in ME/CFS

  Gay 2015 (36)
  Barnden 2016 (37)
  Boissoneault 2016 *(38)*

- Acute exercise affect brains function abnormally and was related to increased impairment in symptoms ***Cook 2017*** *(39)*

"***...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



Dr Byron Hyde (29) in Canada routinely takes SPECT scans of patients and has found that at any one moment there may be a large area of the brain that is completely non-functioning. Dr Hyde believes that if a patient's illness is not measurable on a SPECT scan, then it cannot be ME.

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.

Arnott 2011 *(19)*

- Distinct cerebrospinal fluid proteomes differentiate post-treatment Lyme disease from CFS.

Schutzer 2011 *(20)*

- 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.

Natelson 2005 *(21)*

- 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.

Georgiades 2003*(22)*

- Prevalence in the Cerebrospinal Fluid of the Following Infectious Agents in a Cohort of 12 CFS Subjects: Human Herpes Virus-6 and 8; Chlamydia Species; Mycoplasma Species; EBV; CMV; and Coxsackievirus.

Levine 2001 (*23)*

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.

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 eyeblink response indicates an associative deficit suggesting organic brain dysfunction within a defined neural substrate in CFS patients.

Servatius 1998 *(28)*

- Differences found between CFS and depression

Barnden 2015 *(31)*

- Exercise – induced changes in cerebrospinal fluid miRNAs in Gulf War Illness and CFS show they are distinct disorders

Baraniuk 2017 *(32)*

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ME is classified by the World Health Organisation WHO) as a neurological disorder at ICD-10 G93.3

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