UNIVERSITY OF LEICESTER

Physiotherapy

Fatigue : **Potential Causes, Management** and Special Populations including Post Viral Fatigue Syndrome and Myalgic Encephalomyelitis

Dr Nicola Clague-Baker

My background

PhD research:

- use of CR in stroke population – 4 phase feasibility study funded by Stroke Association
- Phase 4 – cohort took part in adapted CR – fatigue measured before and after and interviews

Post grad research:

- Feasibility of investigating oxygen consumption (VO_2), Heart rate, Blood pressure, lactic acid levels and activity levels of people with Myalgic Encephalomyelitis during normal daily activities.

- Physio for 30 years
- Lecturer for 14 years

Objectives

- Incidence of fatigue in neurological conditions
- Define fatigue
- Explain the potential causes of fatigue
- Discuss the management of fatigue
- Focus on PVFS and ME
- Explain ME
- Discuss problems with exercise in ME population
- Alternative management strategies for ME

Incidence in neurological conditions

- Stroke - 43% (Drummond et al., 2017) to 57% of the stroke population (Choi-Kwon et al., 2005).
- MS – approx. 40% to 70% (Fiest et al 2016, Krupp et al 1988)
- PD – 33 – 81% (Kostic et al 2016, Siciliano et al 2018)
- TBI – 21 – 73% (Mollayeva et al 2014)
- related to poor neurological recovery, reduced functional ability, decreased quality of life and, possibly, high mortality (O'Connell and Stokes, 2007: p.321)
- Linked to poor social participation, less return to work and increased mortality rate (Glader et al 2002, Naess et al 2012)

Fatigue

- Decreased mental and physical endurance
- Decreased motivation
- Depletion of reserves
- Lassitude (Krupp 2003)

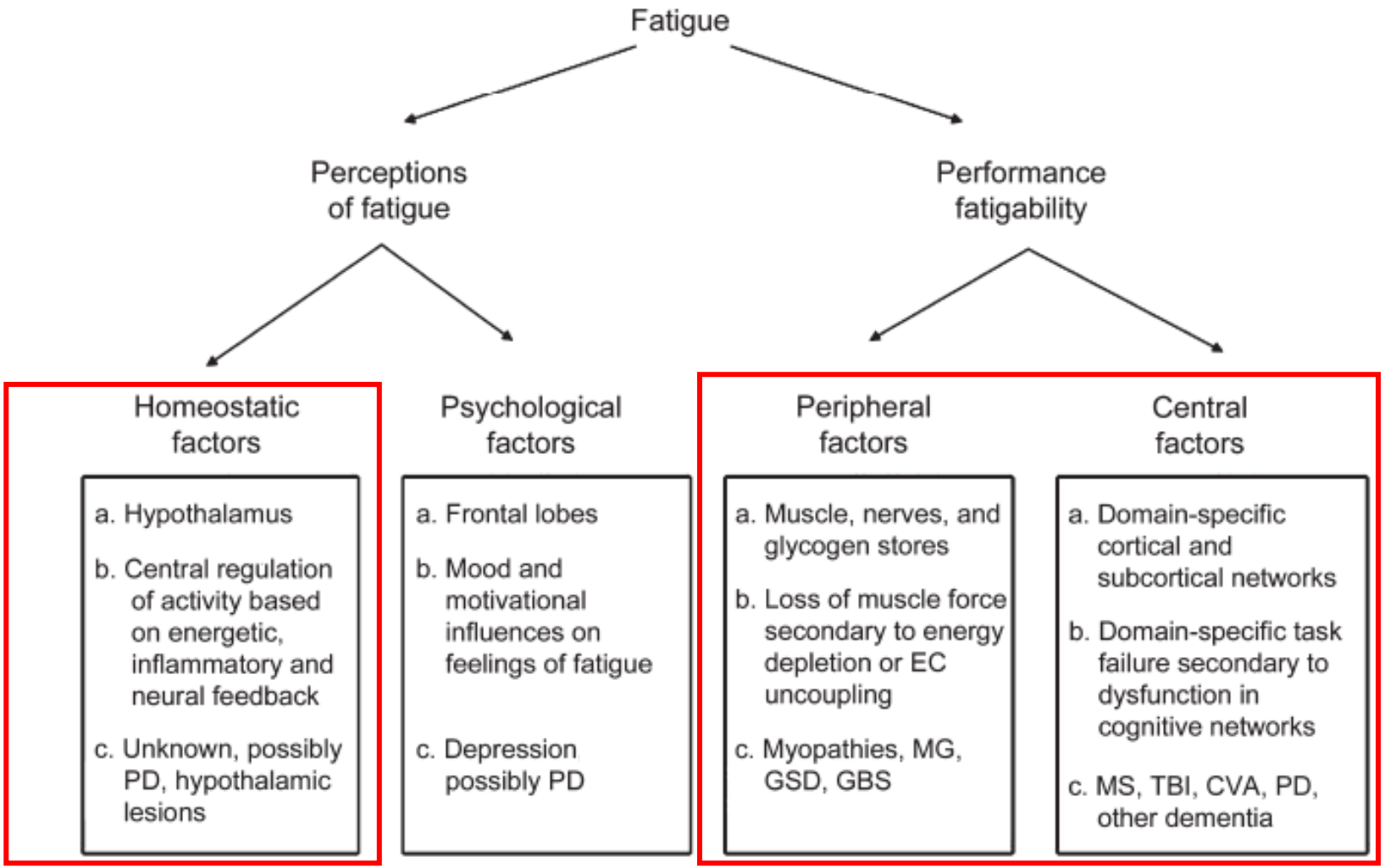
Overwhelming sense of tiredness, weakness, lack of energy, and exhaustion (subjective fatigue);

or as a mismatch between expended effort and actual performance;

or as a reduction in the capacity to either initiate or sustain voluntary activities (objective fatigue) (Kostic 2016)

https://www.mssociety.org.uk/about-ms/signs-and-symptoms/fatigue

Perception versus fatiguability?



Kluger et al 2013

Possible causes of fatigue:

Central

- CNS
- Endocrine dysfunction
- Immunological
- ANS

Peripheral

- Neuromuscular

Primary – related to pathology of the condition or
Secondary – related to other conditions such as sleep disturbances, depression etc

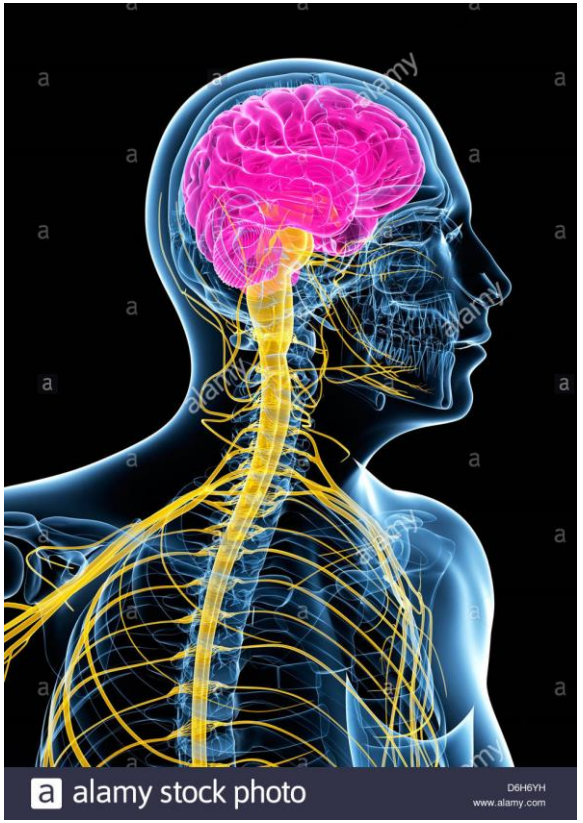
. **Other**

- Hypothyroidism or other gland disorders
- Respiratory
- Cardiac
- Cancer
- Arthritis
- Infections/Inflammation
- Anaemia, B12 deficiency
- Diabetes
- Pain
- Medications
- Sleep
- Diet
- Cardiovascular fitness
- The list goes on…

Central - Central Nervous system causes:

- Failure in the integration of the limbic input and the motor functions within the basal ganglia affecting the striatal–thalamic–frontal cortical system.

  (Chaudhuri and Behan 2000)



- Lesions in basal ganglia on MRI associated with increased fatigue.

(Krupp 2003)

Central - Central Nervous system causes:

- Dysfunction in areas related to hypothalamus and endocrine system
- Reduced frontal lobe activity and deficits in perfusion and glucose uptake shown on PET scans.

(Krupp 2003)

- Reduction in brainstem perfusion.

(Costa et al 1995)

Central - Central Nervous system causes:

- Diminished motor cortical excitability is associated with high levels of poststroke fatigue.

  (Kuppuswamy et al, 2015)

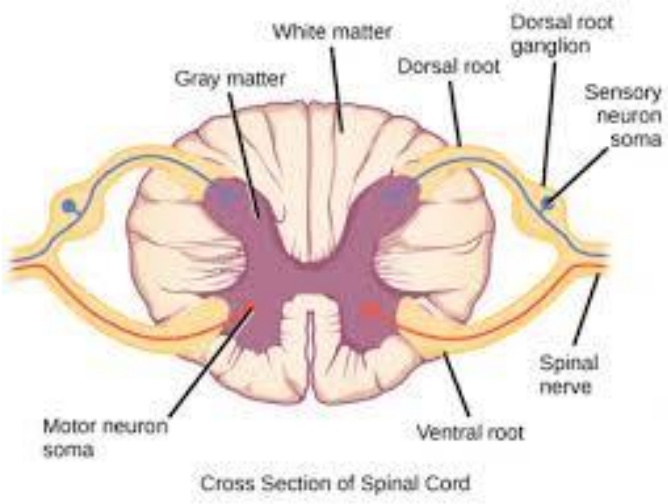
- Perceptual fatigue arises from mis-calibration of effort mediated by poor sensory attenuation ie. perceive too many sensory inputs = more perceived fatigue.

  (Kuppuswamy, 2017)

Central - Central Nervous system causes:

- Dorsal root ganglion neurons have been discovered that specifically respond to low pH, ATP and ammonia.

  (Kluger et al 2013)



Cross Section of Spinal Cord

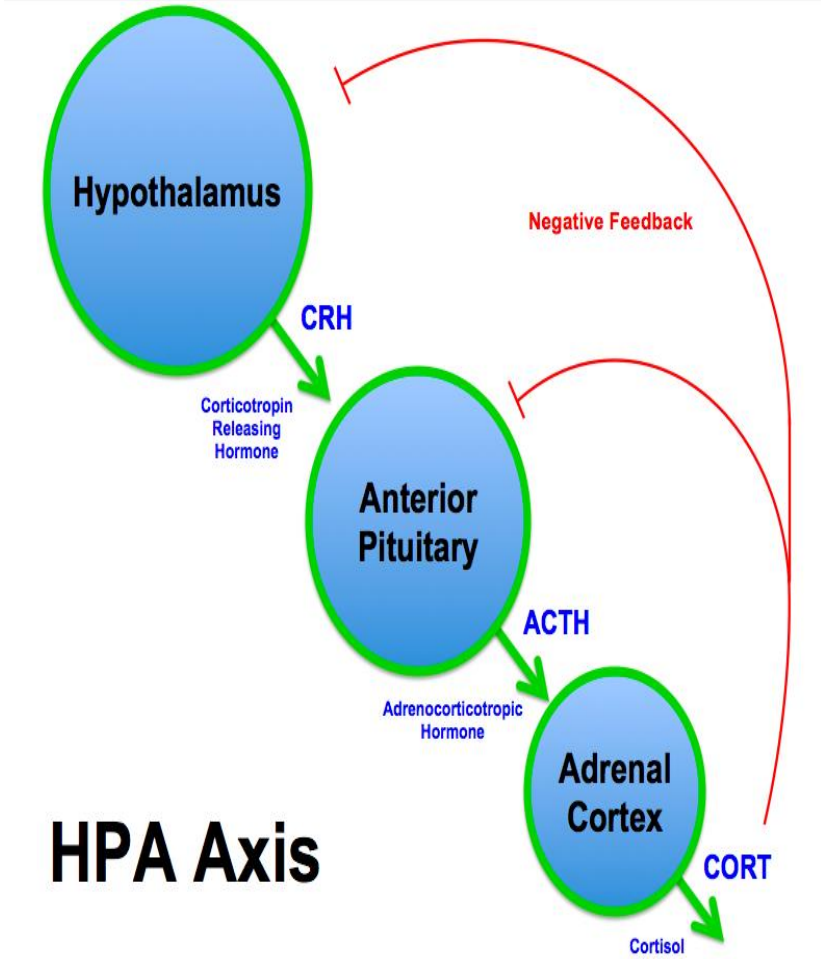
- Increased brain temperature, accumulation of ammonia, increases in serotonin, and decrements in dopamine

  (Kluger et al 2013)

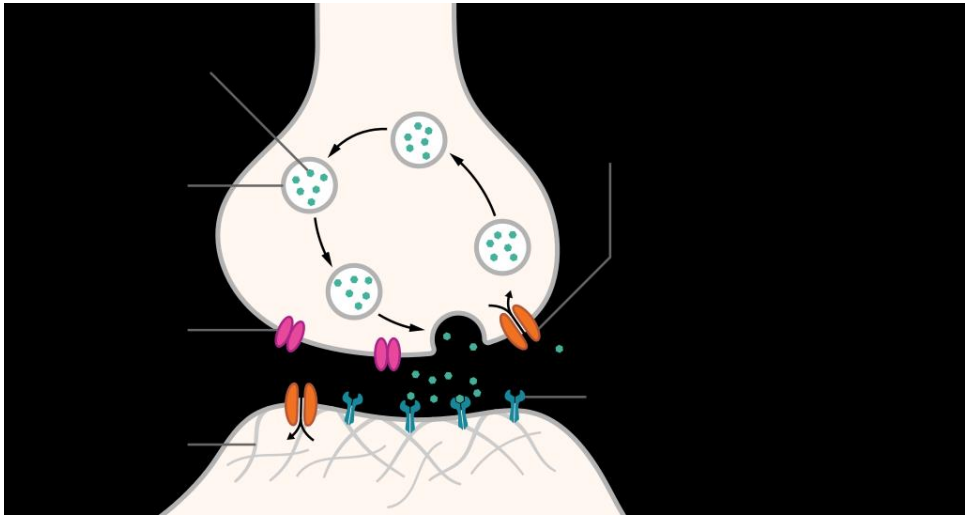
Central - Endocrine dysfunction

- Hypothalamic-pituitary-adrenal axis
- Normally stress leads to release of cortisol which reduces stress response.
- In abnormal systems – low levels of cortisol so highly sensitive to stress.

(Krupp 2003)



Central - Endocrine dysfunction



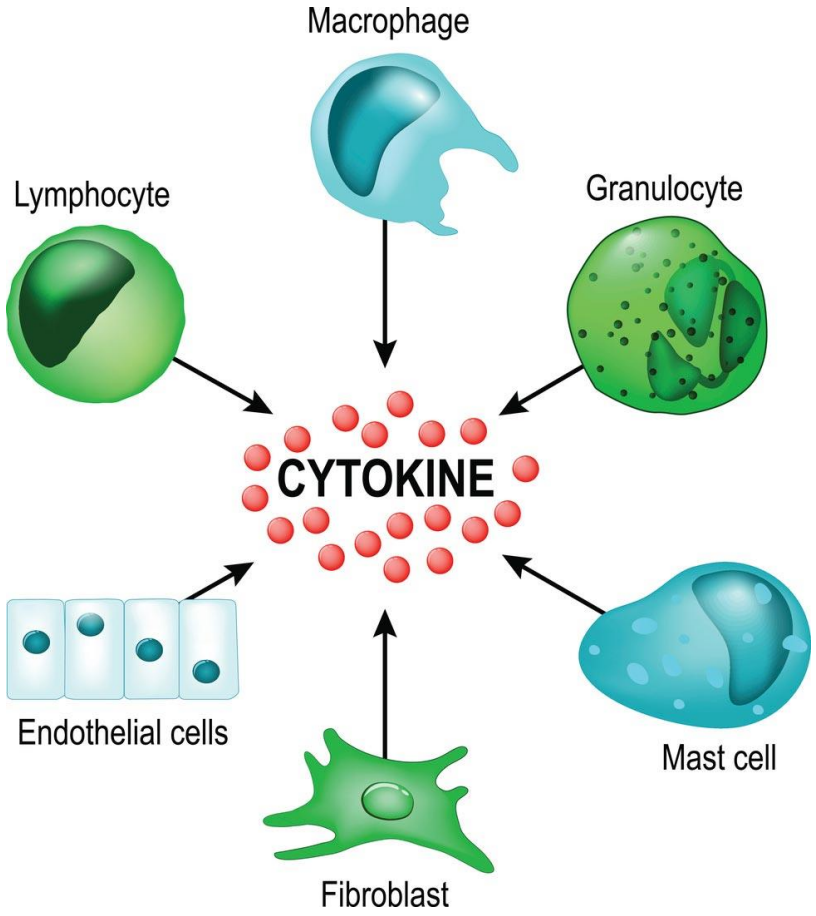
- Interaction between neuroendocrine and neurotransmitter systems
- Dopamine and serotonin innervate the hypothalamus - with widespread actions in the brain

(Taylor et al 2016)

Central - Immunological

- Increased cytokines (cell signaling) e.g. Interleukin-2 and interferon induce fatigue and T lymphocytes affect sleep.

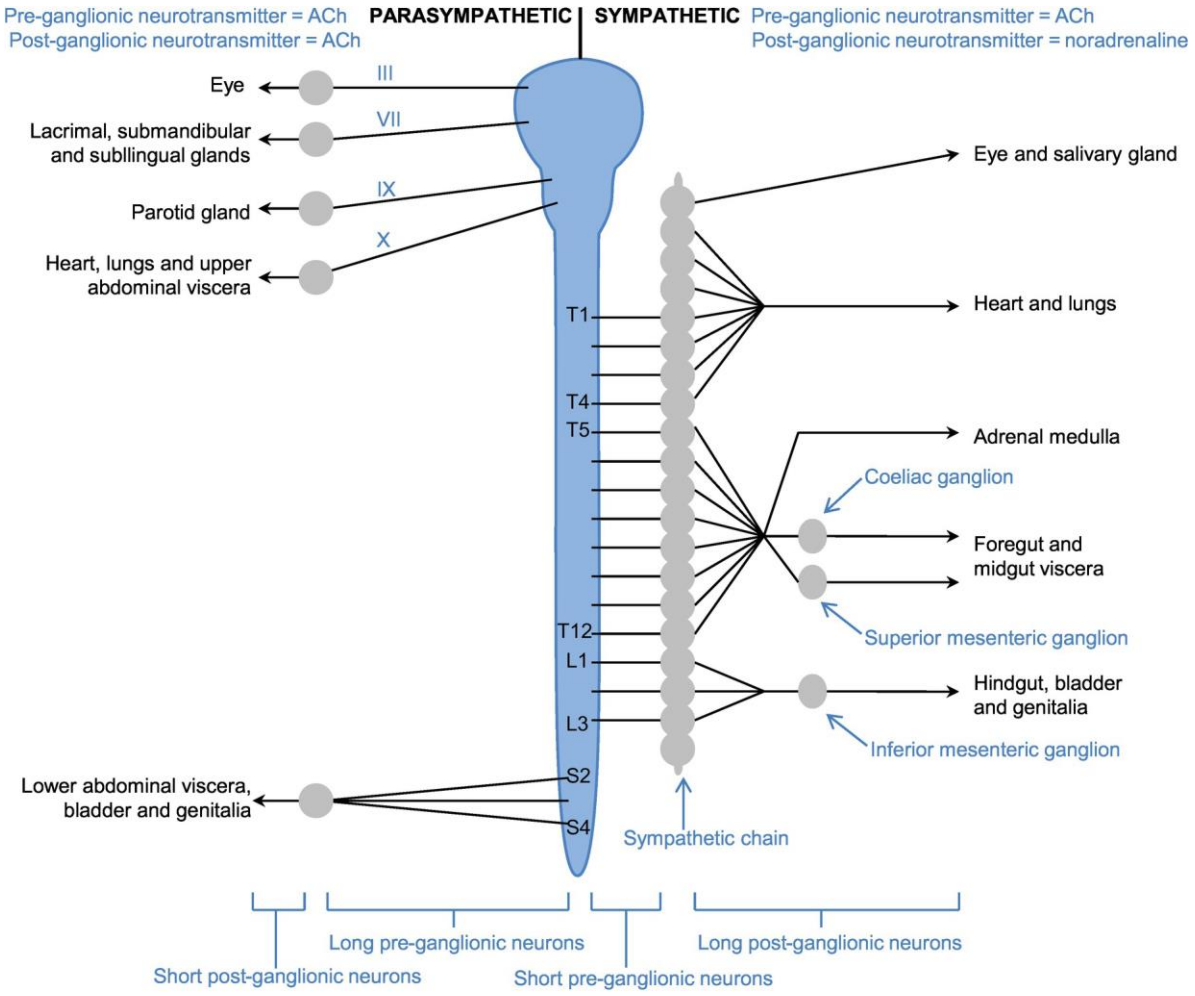
(Krupp 2003)



Central - Autonomic Nervous System

- Autonomic Nervous System –
- reduced activity leads to fatigue due to effect of lowering BP, RR, HR.

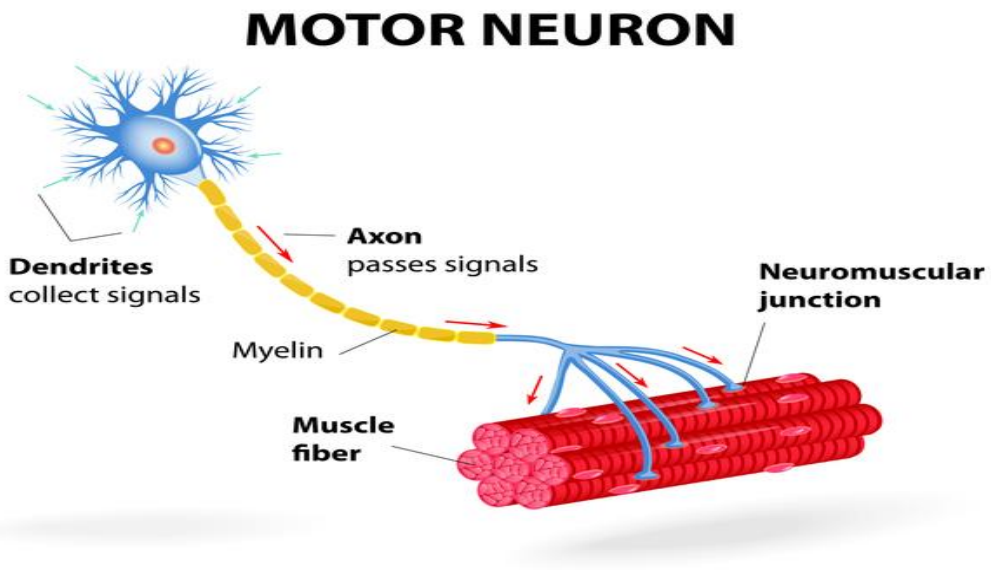
(Krupp 2003)



Peripheral - Neuromuscular causes

- Axonal damage/ peripheral nerve dysfunction?
- Changes in the Na pump at the nodes of Ranvier can result in nerve conduction block.

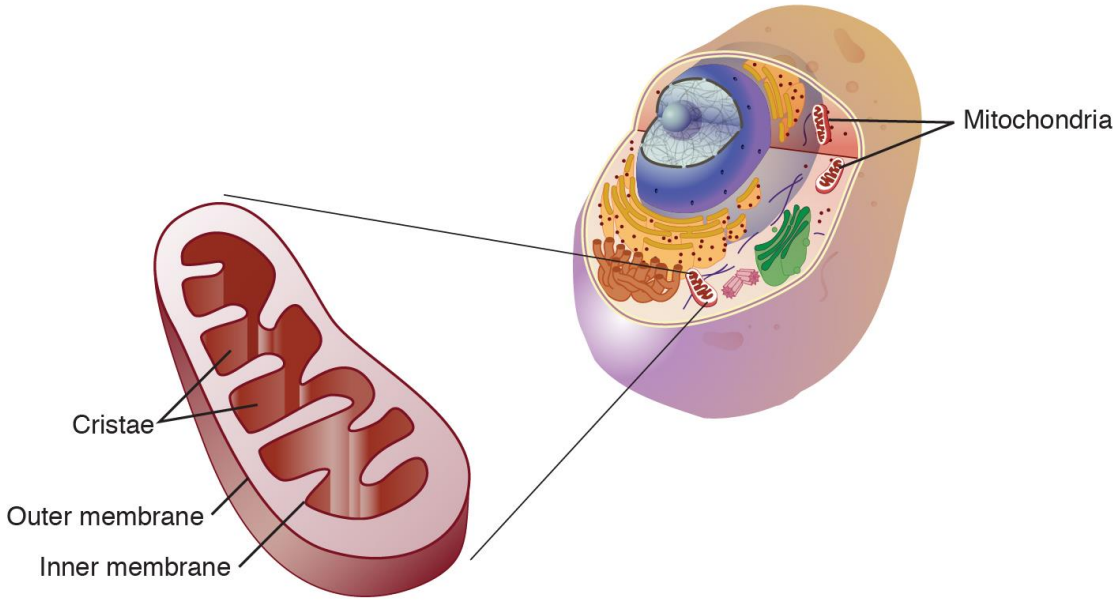
(Krupp 2003)



Peripheral - Neuromuscular causes

- Impaired muscular excitation, contraction and metabolism.
- Fall in muscle PCr, accumulation of H+ ions and reduced pH.

(Krupp 2003)



Treatment of fatigue – medical management

Thorough medical assessment to rule out other conditions:

- **Routine laboratory investigation**: □ CBC, □ ESR, □ CA, □ P, □ RBC Mg, □ vitamin D3, □ B12 & folate, □ ferritin, □ zinc □ FBS, □ PC, □ Hb A1C, □ serum electrolytes, □ TSH, □ protein electrophoresis screen, □ CRP, □ creatinine, □ ECG (U+ T wave notching), □ CPK and liver function, □ rheumatoid factor, □ antinuclear antibodies, □ urinalysis, □ essential fatty acids, □ CoEnzyme Q10, □ immunoglobulins, □ diurnal cortisol levels, □ TTG, □ serotonin
- **Additional laboratory investigation**: (as indicated by symptoms, history, clinical evaluation, lab findings, risk factors)□ 24 hour urine free cortisol, □ DHEA sulphate, □ ACTH, □ chest x-ray, □ hormones including free testosterone □ panoramic x-ray of dental roots, □ amino acid profile, □ abdominal ultra sound, □ lactose/fructose breath test.
- **Pathogen Tests**

(Carruthers and van de Sande 2011)

Treatment of fatigue – medical management

Thorough medical assessment to rule out other conditions:

- **Immune system profiles**: □ *↓NK cell function & ↑ cytotoxicity; □ B & T-cell function: □ IgG, □ IgG subclasses 1-4; □ IgA, □ IgM (shift from T1 to T2), □ cytokine/chemokine profile panel (94% accuracy): IL-8, IL-13, MIP-1β, MCP-1, IL4,□ flow cytometry for ↑ lymphocyte activity, □ ↑ 37 kDa 2-5A RNase L immunoassay – defect/ratio & bioactivity, □food sensitivity panel, □ chemical sensitivities, □ stool for WCB - D-lactic acid bacteria balance, ova & parasites, □autoimmune profile, Intestinal dysbiosis: □ IgA & IgM for intestinal aerobic bacteria in serum, □↑ leukocyte elastase activity in PBMCs, □ IgG food intolerance test, □ toxoplasmosis
- **Neurological & static testing**: □ *SPECT scan with contrast - ↓ cortical/cerebellar region cerebral blood flow (rCBF) in the frontal, parietal, temporal and occipital & brain stem regions □ MRI of spine (dynamic disc bulges/herniation , stenosis), □ sleep study (↓ stage 4 sleep, sleep pattern &rule out treatable sleep dysfunctions – upper airway resistance syndrome, sleep apnea, etc.)

Treatment of fatigue – medical management

Thorough medical assessment to rule out other conditions:

- **Energy metabolism/ion transport**: □ ATP profile – identifies insufficient energy due to cellular respiration dysfunction □ further ATP related parameters, superoxide dismutase and cell-free DNA Respiratory: □ pulmonary function test Cardiovascular: □ Tilt table test to confirm OI (70 -80% tilt, measure HR continuously, BP periodically – 30 min or presyncope); □ Cardiac output decreases - left ventricular dysfunction in the heart; □ 24-Hour Monitor for suspected arrhythmia, NMH/POTS, myocarditis

(Carruthers and van de Sande 2011)

- Be aware of the importance of differential diagnosis of fatigue

Treatment of fatigue – Medical management – MS and PD

If progressive:

disease modifying medication can help

eg. **glatiramer acetate** or **interferon beta** for MS or **levodopa** for PD

- **Modafinil** (affects arousal through dopamine pathways)
- **Aspirin**
- **Amantadine** (increases dopamine release)
- **Methylphenidate** (Ritalin) (used for ADHD through dopamine pathways)

Limited effectiveness

Treatment of fatigue – Medical management – CVA and TBI

- **Enerion** (Vitamin B12)(Gurak 2005)
- **(-)-OSU6162** (dopamine stabilizer)(Johansson 2012)
- **Citicoline and a combination of Chinese herbs** (dopamine and hypothalamus)(Guo 2012)
- **Fluoxetine** (anti-depressant, SSRI)(Choi-Kwon 2007)

Insufficient evidence

Evidence for nonpharmacology treatment -

MS – Cochrane review - RR (Heine 2015), Systematic review – progressive (Rooney 2019)

- Exercise (Andreasen et al 2011)
- Mindfulness (Grossman et al 2010)
- Energy management strategies (Hugos et al 2010)
- Neurocognitive approach (Catalan et al 2011)

Insufficient evidence

PD – Systematic review (Siciliano et al 2018), Cochrane review (Elbers 2015)

- Exercise (RuiPing et al 2017)
- Exercise (Elbers et al 2015)

May improve quality of life

Evidence for nonpharmacology treatment -

TBI -

- Systematic review (Cantor 2014) – CBT, physical activity
- Systematic review (Xu 2017) – mindfulness, CBT, aquatic/exercise, computerized working memory training

May be beneficial

Stroke – Systematic review (Su 2020)

- Fatigue education programme (Clarke 2012)
- Mindfulness-based stress reduction programme (Johansson 2012)
- Physical training (Zedlitz 2012)
- Traditional Chinese medicine, CBT, Community health management (Su 2020)

Develop more clinically effective interventions

Nonmedical treatment of fatigue –
Physio objective assessment

Thorough neurological assessment to determine potential neuromusculoskeletal contributors to fatigue:

- Strength
- Tone
- Sensation
- Coordination
- Pain

Measurement of fatigue (over 50 scales)

- Fatigue Severity Scale (MS, SLE)
- Fatigue Impact Scale (MS, CFS)
- FACIT (Fatigue Scale) (Chronic illness)
- Multidimensional Fatigue Symptom Inventory (cancer)
- Brief fatigue Inventory (cancer)
- Fatigue Assessment Scale (workers)
- Neurological fatigue index-MS (NFI-MS) in stroke
- Fatigue Descriptive Scale
- Visual Analogue scale for fatigue
- And many more

Subjective assessment add questions on:

Pain

Rest and relaxation

Sleep

Diet

Mental health

Leisure time

Cognitive activities

Physical Activity

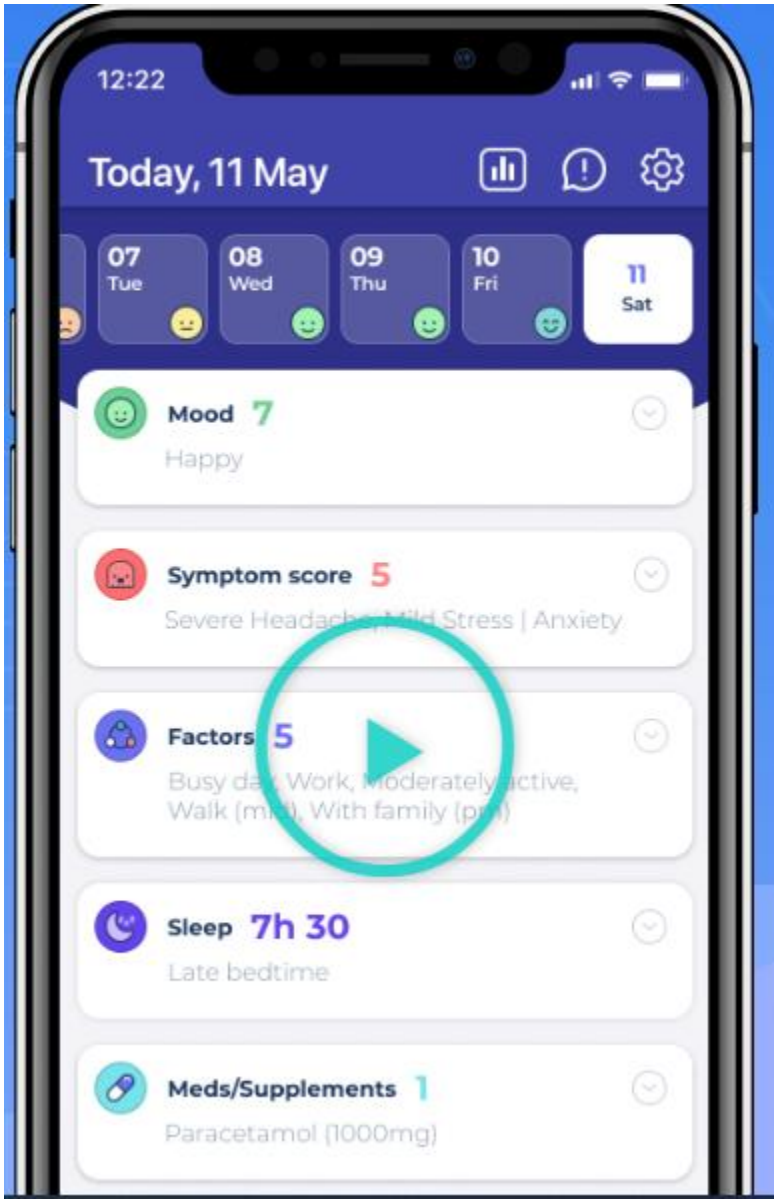
Fatigue diary

Weekly Diary

Week Starting:

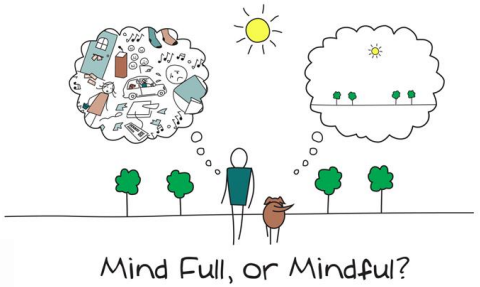
	Sunday	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday
7	(Sleep)	Breakfast	Breakfast	Breakfast	Breakfast	Breakfast	(Sleep)
8	(Sleep)	Chores	Shopping	Chores	Chores	Computer	(Sleep)
9	Breakfast	Phone	Phone	Phone	Phone	Rest	Breakfast
10	Computer	Computer	Computer	Computer	Computer	Rest	Laundry
11	Rest	Rest	Rest	Rest	Rest	Doctor	Rest
Noon	Lunch	Lunch	Lunch	Lunch	Lunch	Lunch	Lunch
1	Visit friends	Work	Work	Work	Work	Chores	Phone
2	Friends	Work	Work	Work	Work	Computer	Shopping
3	Computer	Work	Work	Work	Work	Rest	Rest
4	Phone	Work	Work	Work	Work	Rest	Housecleaning
5	Rest	Rest	Rest	Rest	Rest	Phone	Rest
6	Dinner	Dinner	Dinner	Dinner	Dinner	Dinner	Dinner out
7	Call parents	Computer	Computer	Computer	Rest	Computer	Dinner out
8	TV	Walk, TV	Walk, TV	Walk, TV	Walk, TV	TV	Rest
9	TV	TV	TV	TV	TV	TV	TV
10	Bath & Bed	Bath & Bed	Bath & Bed	Bath & Bed	Bath & Bed	Bath & Bed	Bath & Bed (11 pm)

Bearable app



Fatigue management

- 3Ps – Pace, Prioritise and Plan
- Rest and relaxation
- Sleep
- Food and nutrition
- Emotional health
- Cognition
- Leisure time
- Pain management
- Physical activity and exercise



UNIVERSITY OF LEICESTER

3ps - pacing, prioritizing, planning

- **Pacing** is all about balancing activity and rest
- The word ‘activity’ - includes mental, emotional and physical activity
- **Prioritising** – do you really need to do it, can you delegate.
- **Plan** your day/week

Research related to pacing

Very little – mainly related to pain management

- The Parkwood Pacing and Planning™ App –TBI research

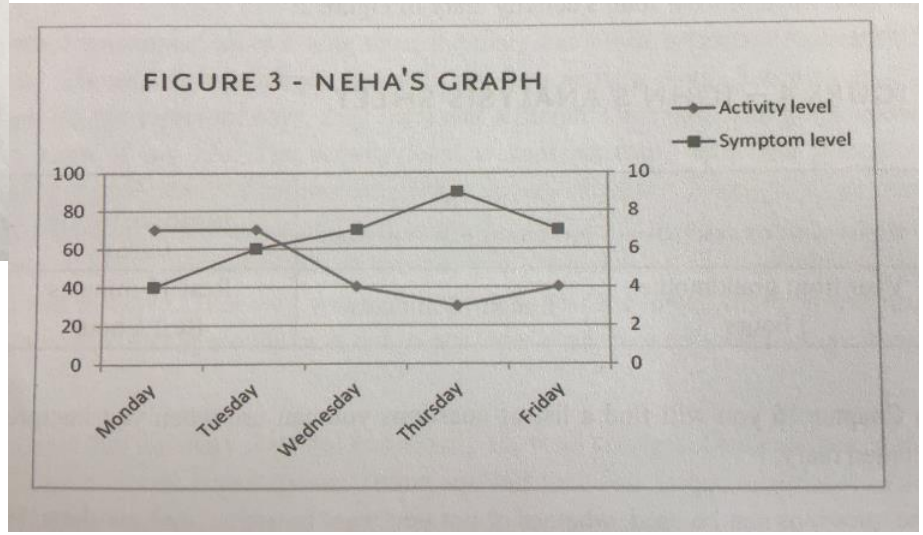
- number of useful websites:
- http://www.cfsselfhelp.org/library/how-i-use-pacing-manage-cfs
- https://www.rcot.co.uk/conserving-energy
- https://myhealth.alberta.ca/Learning/early-concussion/pacing-and-energy-conservation

How to pace, plan, prioritise:

1. Establish a baseline ie. record your activity and symptoms over 2 weeks
2. Remember this is **physical** and **cognitive** activity – you can then recognize any activities that are particularly fatiguing

FIGURE 1 – NEHA'S SIMPLE DIARY

	ACTIVITY LEVEL	SYMPTOM LEVEL	NOTES
MONDAY	70	4	Good day
TUESDAY	70	6	Wired, hard to relax
WEDNESDAY	40	7	Pretty tired
THURSDAY	30	9	Completely exhausted
FRIDAY	40	7	Little better today



Dahl 2018

How to pace, plan, prioritise:

3. Regular small rests throughout the day

4. Change activities – cognitive to physical

5. Break down activities – cleaning – get cleaning things out, wipe sink…

6. Energy conservation –

Think body positions, use aids – electric toothbrush, wheeled shopper and appliances – wheelchairs, office chairs with wheels and brakes, shower seats.

7. Timers - can help to prevent over exertion

8. Prioritise – what needs to be done rather than what could be done

9. Plan – what activities are you going to do, what will you need

http://www.cfsselfhelp.org/library/how-i-use-pacing-manage-cfs

Rest and relaxation

- Short, regular rest periods throughout the day
- Fully relax and properly rest the brain.
- For healing rest, be quiet and still, both physically and mentally
- better to avoid sleeping during the day, as this may disrupt night time sleep cycle.

- **Repairing rest** – if done too much body needs to recover
- **Healing rest** – already rested but resting more

Dahl 2018

Sleep

- At least 7 hours per night
- Stick to a calm routine
- Avoid getting overtired
- Avoid caffeine
- Resolve pain
- Positioning for relaxation
- Instead of lying in bed awake, after 15 minutes of not sleeping get out of bed and do something
- Mindfulness – Calm app, Headspace app
- Melatonin – released about 9pm as gets dark
- Amitriptyline – sedative
- Magnesium – muscle spasms

Togo et al 2008

Food and nutrition

- Avoid junk food
- 1 – 1.5 l water per day
- Healthy diet includes:

5 – 7 portions of fruit and veg a day

Low animal fats

High omega-3 fats – fish and plants

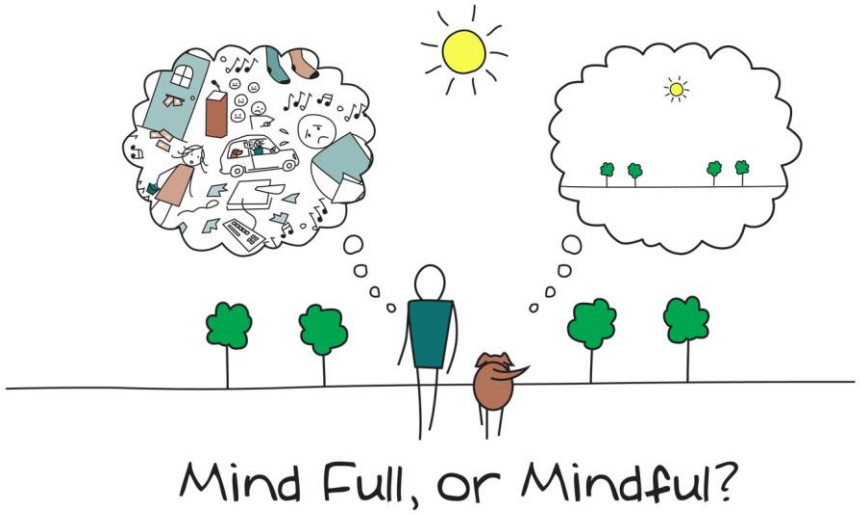
Low sugars/carbohydrates (<50g/day)

Low salt (<2g/day)

Calcium, magnesium – (Pommerich 2018)

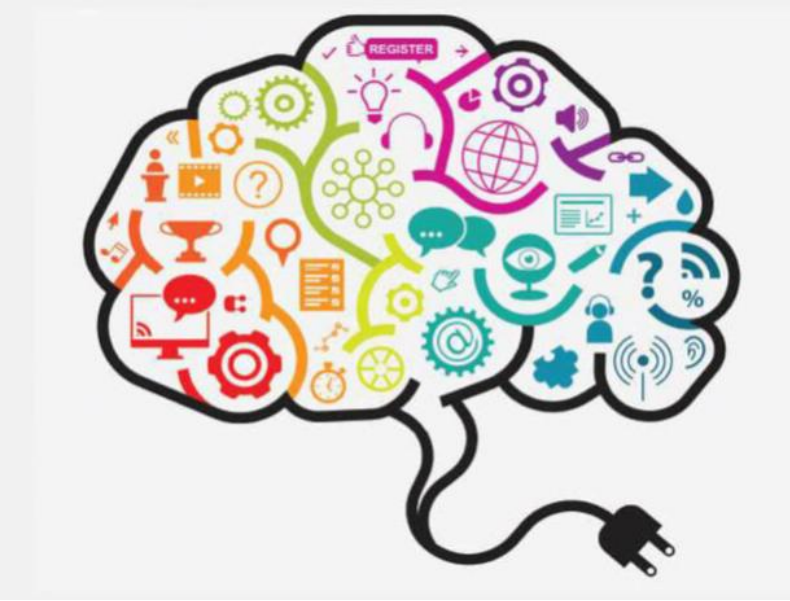
Emotional health

- doing enjoyable things,
- talking issues through with others
- actively seeking out information and advice about issues that are worrying
- finding ways to think more positively
- Relaxation techniques



Cognitive activity

- Be aware of the cognitive energy requirements
- Cognition means anything that involves thought processes: planning, problem-solving, having a conversation, writing, reading etc
- Energy requirements for thinking: approximately 20% of the energy consumed in the body
- Strategies: Do one thing at a time, use checklists, charts, diaries, electronic reminders, cue cards
- Cognitive fatigue affects physical fatigue (Mcmorris 2018)



Leisure time

- Important to include leisure time, but this needs to be considered in energy consumption.

- Each person will have different ways that they like to spend in leisure time

Physical activity – Graded Exercise Therapy

- **Not for PVFS and ME**
- Starts at 5-6 days out of 7 days a week
- **Duration** - Starts at a comfortable baseline (might be just 2 mins a day) and increases slowly until reaches 30 minutes a day. Monitor Borg rating scale and heart rate.
- Progress duration by 20% only per week. Don't want an increase in heart rate
- **Intensity** – starts low then progresses slowly to target heart rate once can manage 30 minutes of exercise 5-6 days per week. HR can be increased by 10-20% at a time until reach target heart rate.
- Final stage – introduce into community/social interaction

https://www.mssociety.org.uk/about-ms/signs-and-symptoms/fatigue/managing-fatigue

Cardiorespiratory exercise

- **Not for PVFS and ME**
- Some evidence to show that exercise could reduce fatigue in people with:
- **MS** (Heine et al 2015)
- **CVA** (Barritt and Smithard, 2011)
- **TBI** (Xu et al, 2017)

- Our study - mild to moderate stroke in subacute phase –
- All 32 had fatigue
- CR exercise - decreased fatigue (MFIS) 11 to 4

(Clague-Baker 2020 under review)

Our study

"*This was a wall where I've got to sleep, I can't move, I physically can't move, I've got to rest*" (P21)

"*I have felt tired, very tired and very achy*" (P31)

- Over half felt exercise reduced their fatigue:

"*I could sleep more once I'd been exercising*" (P22).

- Two felt that exercise made them worse:

"*It made it worse just because I had to have a sleep every day*" (P5).

(Clague-Baker 2020 under review)

Summary

- Fatigue is an overwhelming symptom common to many neurological conditions
- Incidence of fatigue can be as much as 80% in people with neurological conditions
- Potential causes relate to the neurological damage (central or primary fatigue) or the consequences of the damage (peripheral or secondary fatigue)
- Choose a fatigue outcome measure that is validated for the condition
- Management of fatigue includes: pacing, rest and relaxation, sleep, food and nutrition, emotional health, cognition, leisure time and physical activity and exercise
- Exercise is not appropriate for all neurological conditions **particularly PVFS and ME**

UNIVERSITY OF LEICESTER

Fatigue : Potential Causes, Management and **Special Populations including Post Viral Fatigue Syndrome and Myalgic Encephalomyelitis**

Comparison of symptoms between "Post Viral Fatigue post COVID19", Post Viral Fatigue Syndrome and Myalgic Encephalomyelitis

PVF (COVID*)	PVFS (+ 1 month**)	ME (+ 4 months**) (ICC Criteria)
Decreased exercise tolerance /fatigue	Activity induced fatigue (physical and mental)	A. Post exertional malaise (PEM) or Post-Exertional Neuroimmune Exhaustion (PENE): Physical and/or cognitive fatigability in response to exertion. Substantial reduction in pre-illness activity level. Post-exertional symptom exacerbation - recurring flare of viral symptoms. Recovery period is prolonged.
Decreased function/work/ADLs	Unable to maintain previous levels of activity	B. Neurological impairments: neurocognitive, pain, sleep disturbances, neuro sensory/perceptual/motor disturbances
Breathlessness or silent hypoxia	Intermittent and recurring flare of viral symptoms	C. Immune, Gastro-intestinal & Genitourinary Impairments: eg. flu like symptoms, sensitivities etc
Cognitive issues (memory, attention)	Unrefreshing sleep	D. Energy Metabolism/Ion Transportation Impairments: Cardiovascular - (OI), neurally mediated hypotension (NMH), postural orthostatic tachycardia syndrome (POTS), Resp or thermostatic
Swallow issues	Cognitive problems	
Muscle weakness & pain	Orthostatic intolerances	www.physiosforme.com

RCOT advice for post viral fatigue

How to manage post-viral fatigue after COVID-19

Practical advice for people who have been treated in hospital

Post-viral fatigue is when you have an extended period of feeling unwell and fatigued after a viral infection.

Fatigue is a normal part of the body's response to fighting a viral infection such as COVID-19, it's also common after any serious or critical illness that requires being admitted to hospital. Fatigue is likely to continue for some time after the infection has cleared. It can make you sleep more, feel unsteady on your feet, make standing for long periods difficult, as well as affecting your ability to concentrate and your memory.

How to conserve your energy

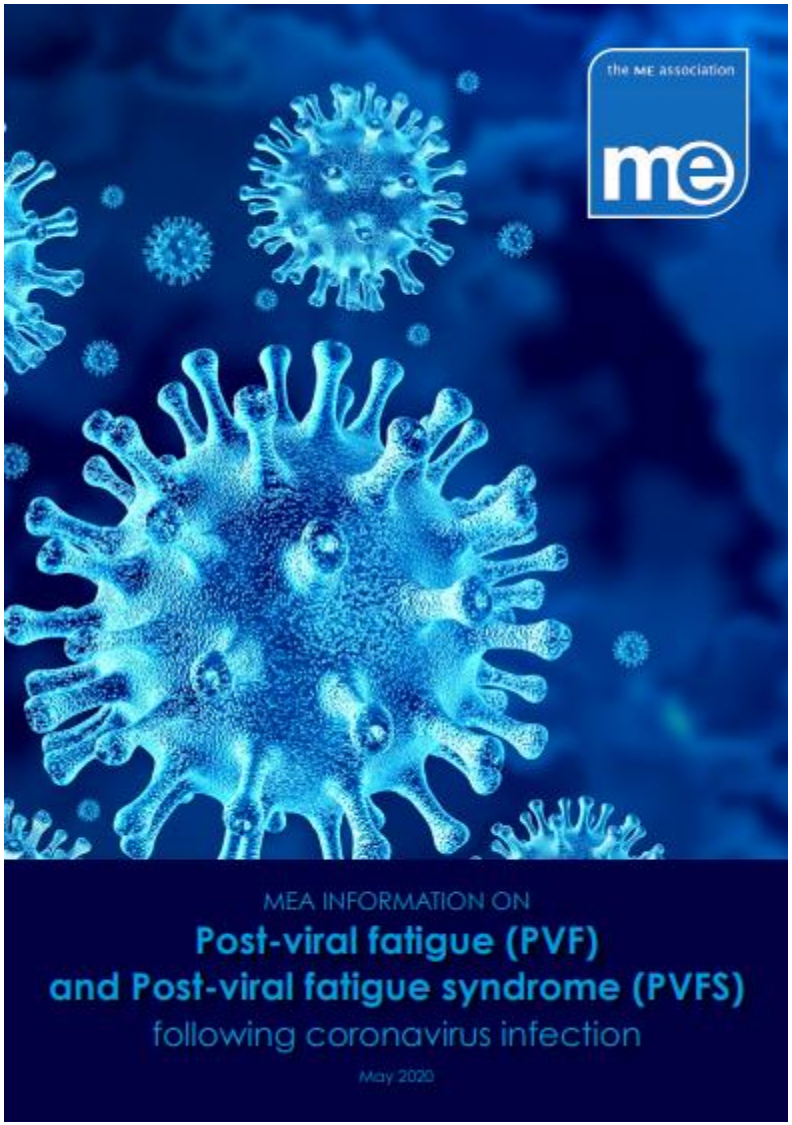
Practical advice for people during and after having COVID-19

When you are ill or recovering from an illness, you are likely to have less energy and feel tired. A simple task, such as putting on your shoes, can feel like hard work. This guide will help you to find ways to conserve your energy as you go about your daily tasks. By making these small changes you'll have more energy throughout the day.

The 3 Ps principle (Pace, Plan and Prioritise)

Learning to pace, plan and prioritise your daily activities will help you to save energy.

ME Association advice for post viral fatigue



https://meassociation.org.uk/wp-content/uploads/MEA-PVF-and-PVFS-Following-Coronavirus-Infection-30.04.20.pdf

UNIVERSITY OF LEICESTER

Main advice for PVFS

- Rest
- Pace
- Prioritise
- Plan
- Hydration
- Nutrition

- **Not GET (NICE statement), not CR exercise, not exercise in any form**

Myalgic Encephalomyelitis

Incidence of ME

- Myalgic – muscles
- Encephalopathy – brain symptoms

- 2 : 1,000 adult population
- or 150,000 to 250,000 in UK (MS 100,000)

- Rare below age 7 and >60
- Age of onset – 13 – 15 years, early 20s and mid 40s
- Female: male 2:1

(Carruthers et al 2011)

Diagnosis of ME (not CFS)

- Really difficult – by exclusion of other disorders
- Canadian or London or International consensus criteria, not the Oxford criteria

4 or more symptoms (not just fatigue): primary symptom Post Exertional Malaise (PEM)

PEM lasting more than 24 hours – delayed onset	Muscle pain
Unrefreshing sleep	Signs of flu – headaches, tender lymph nodes, Sore throat
Impairment of short-term memory, other cognitive dysfunctions	Autonomic symptoms – orthostatic intolerance
Pain in joints	Activity-induced muscle fatigue

(Carruthers et al 2011)

PEM – not just fatigue

- Fatigue
- Poor concentration
- Difficulty thinking
- Muscle pain
- Sleep disturbance
- Poor memory
- Flu-like symptoms
- Joint pain
- Headache
- Sore throat
- Tender lymph nodes

Delayed onset – up to 24 to 72 hours after exertion

Can persist for days, weeks, months, or years.

(Chu et al 2018)

Other common symptoms

- Disturbed thermoregulation (temperature control),
- sensory disturbances including paraesthesia (abnormal skin sensations),
- photophobia (sensitivity to light)
- hyperacusis (sensitivity to noise),
- headaches,
- shakiness,
- balance problems,
- nausea,
- gastrointestinal problems,
- alcohol intolerance and chemical sensitivities,
- recurrent sore throats,
- shortness of breath,
- vision problems.

(Carruthers et al 2011)

Possible causes of ME symptoms:

Possible causes:

1. Endocrine dysfunction
2. Immunological
3. ANS
4. Neuromuscular
5. Cardiac function
6. Gut dysbiosis

Symptoms:

- PEM 2,4,6,
- Unrefreshing sleep 1, 3,
- Muscle pain/Joint pain 2,4,6
- Cognitive dysfunction 2,4,
- Flu-like symptoms 2,
- High/low BP/HR 1,3,5
- Muscle fatigue 2,4,6
- Disturbed thermoregulation 1,2,3,
- sensory disturbances 1,2,

Symptoms:

- photophobia (sensitivity to light) 1,2
- hyperacusis (sensitivity to noise) 1,2
- Headaches 2
- Shakiness 2,4
- balance problems 1,2,4
- Nausea 2
- gastrointestinal problems 2,6
- alcohol intolerance and chemical sensitivities 2,6
- shortness of breath 2,3,4,5

Co-morbidities

- Fibromyalgic-type pain
- Atypical facial pain and temporomandibular jaw dysfunction
- Gynaecological conditions
- Hypermobility syndromes - such

as Ehlers-Danlos Syndrome (EDS)

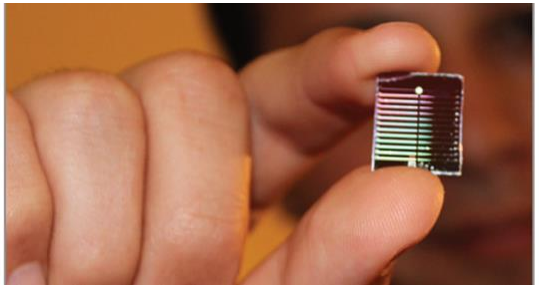
- Interstitial cystitis/bladder pain
- Gastrointestinal complaints
- Migraine type headaches
- Postural Orthostatic Tachycardia

(Carruthers et al 2011)

Diagnosis

No established test for diagnosis. Some promise with:

- Biomarkers
- https://jamanetwork.com/journals/jama/article-abstract/2737657?fbclid=IwAR0R6Kvo34nA4J73ghNC5ej1cYbmEEgFDphC6TVI9aZfEjLcVS-s-GHWI9M



Diagnosis – promise with:

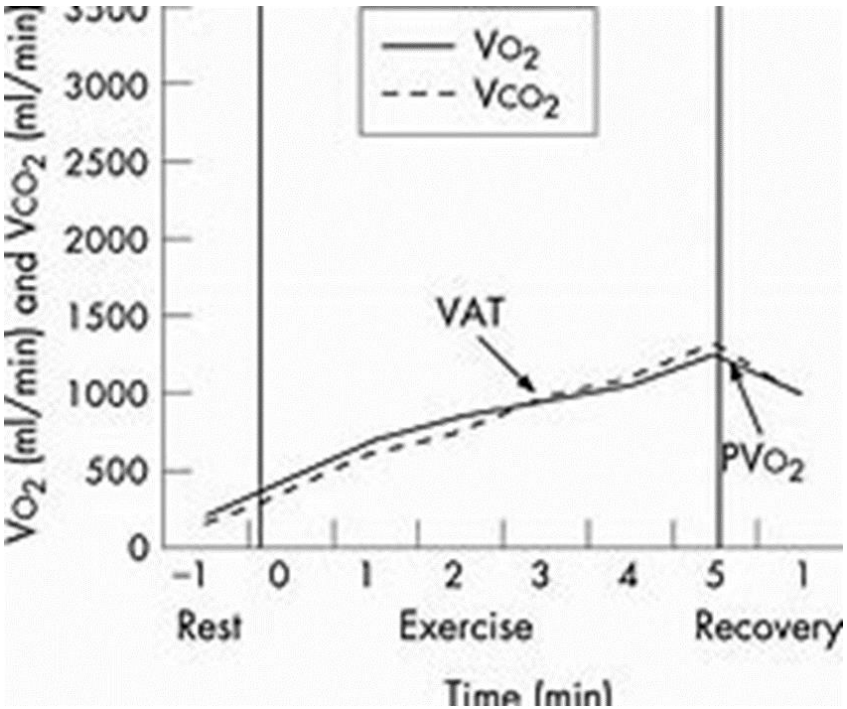
2 day Cardiopulmonary (CPET) test – @4WorkWell

- https://www.healthrising.org/blog/2019/01/17/decoding-2-day-cpet-chronic-fatigue-syndrome/

- CPET test is the gold standard for cardiovascular testing
- Measure VO_2 max or VO_2 peak while exercising on a treadmill or bike

CPET

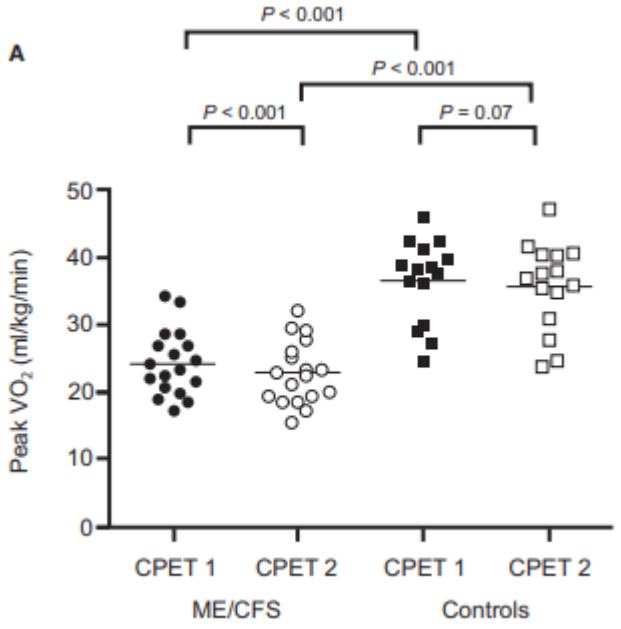
- Amount of oxygen consumed and CO_2 produced is measured
- VO_2 max is when the patient can no longer push themselves due to fatigue
- Aiming to reach anaerobic threshold when amount of oxygen taken in is equal to the amount of CO_2 produced
- Switching to anaerobic respiration. Point at which lactic acid production increases.

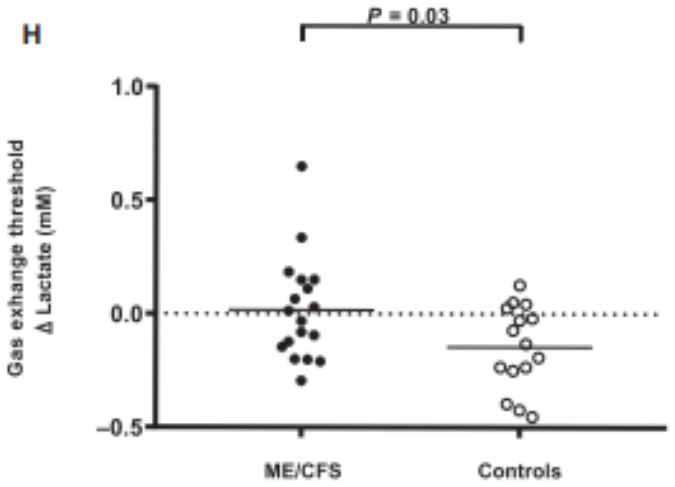


2 day CPET test for pwme

- On all tests all pwme had lower VO_2 peak

On the second tests all pwme had higher levels of lactic acid production





Could this explain PEM?

Lien et al 2019

Abnormal responses to exercise – metabolism

- **reduced maximum oxygen consumption and anaerobic threshold**

Causes?

- Oxygen carrying capacity – red blood cells affected
- Mitochodrial damage – aerobic metabolism affected, rely on anaerobic metabolism. Reduced ATP production. Increased intracellular acidosis

(Davenport et al 2019)

Abnormal responses to exercise – circulatory system

- Based on ex phys research over last 20 years - CPET testing
- SR – 36 studies/ 2000 people with ME

- **reduced maximum heart rate – Chronotropic Intolerance (CI)**
- **reduced cardiac output, insufficient blood pressure increase on exertion**
- **Also orthostatic intolerances** – POTS and NMH

- Cause - ? Autonomic Nervous system? Or beta-2 adrenergic receptors in blood vessels? Or hypermobility – relaxing of collagen

(Davenport et al 2019)

Types of ME

- Mild - 50% reduction in pre-illness activity levels
- Moderate - mostly housebound
- Severe - mostly bedbound
- Very severe - totally bedridden and needing help with the basic functions of living

- Some people start with mild and progress to severe, others start with severe and can change to mild

- Not clear why some people progress and others do not

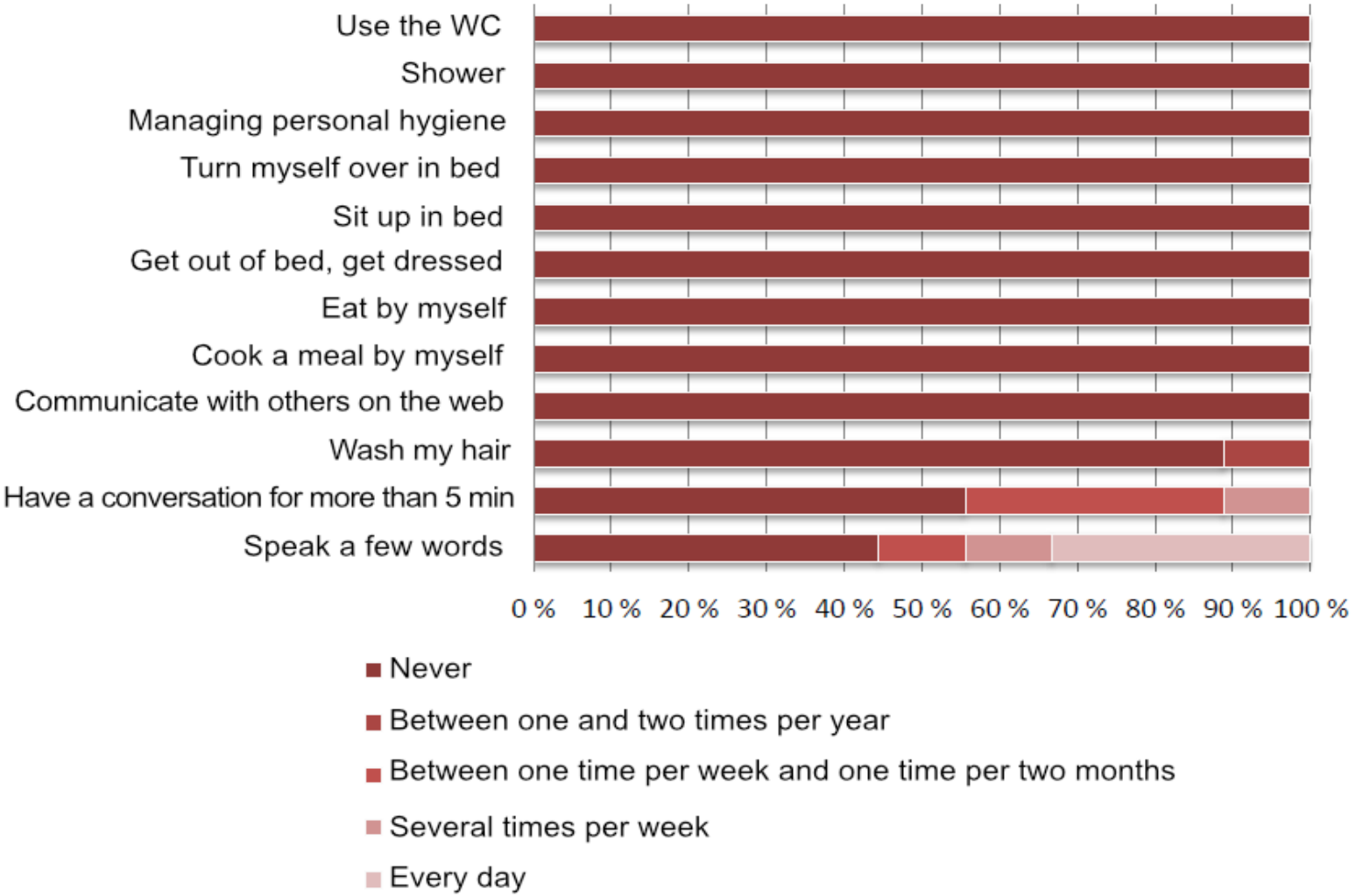
Severe and very severe

- *My name is Emily. I developed the neurological condition Myalgic Encephalomyelitis (ME) when I was 6 years old. In April 2011 I turned 30.*

I still have ME.

- *My reaction to small exertions and sensory stimulation is extreme. Voices wafting up from downstairs, a brief doctor's visit, a little light, all can leave me with surging pain, on the verge of vomiting, struggling with each breath and feeling I'll go mad with the suffering.*
- *My days and nights are filled with restless sleep interspersed with injections, needle changes (for a syringe driver), nappy changes (as well as experiencing transient paralysis and at times being blind and mute, I am doubly incontinent) and medicines/fluid being pumped into my stomach through a tube.*
- https://alifehidden.com/2019/08/07/emilysappeal/amp/?__twitter_impression=true

Functional level, extremely severely ill



http://www.me-foreningen.info/ressurser/me-foreningens-rapporter/de-sykeste-me-pasientene/

Severe and very severe – potential physio support

- Less is more
- Maybe gentle massage or myofascial release
- Trigger points
- Positioning
- Maybe passive movements depending on pain
- ? Oxygen therapy
- ? Perrin technique
- Supporting family and carers

- **Not GET**

Fatigue management

- 3Ps – Pacing, Prioritizing, Planning
- Rest and relaxation, Sleep
- Food and nutrition
- Emotional health
- Cognition
- Leisure time
- Pain management
- HR monitoring

- **Not GET**

Weekly Diary

Week Starting:

	Sunday	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday
7	(Sleep)	Breakfast	Breakfast	Breakfast	Breakfast	Breakfast	(Sleep)
8	(Sleep)	Chores	Shopping	Chores	Chores	Computer	(Sleep)
9	Breakfast	Phone	Phone	Phone	Phone	Rest	Breakfast
10	Computer	Computer	Computer	Computer	Computer	Rest	Laundry
11	Rest	Rest	Rest	Rest	Rest	Doctor	Rest
Noon	Lunch	Lunch	Lunch	Lunch	Lunch	Lunch	Lunch
1	Visit friends	Work	Work	Work	Work	Chores	Phone
2	Friends	Work	Work	Work	Work	Computer	Shopping
3	Computer	Work	Work	Work	Work	Rest	Rest
4	Phone	Work	Work	Work	Work	Rest	Housecleaning
5	Rest	Rest	Rest	Rest	Rest	Phone	Rest
6	Dinner	Dinner	Dinner	Dinner	Dinner	Dinner	Dinner out
7	Call parents	Computer	Computer	Computer	Rest	Computer	Dinner out
8	TV	Walk, TV	Walk, TV	Walk, TV	Walk, TV	TV	Rest
9	TV	TV	TV	TV	TV	TV	TV
10	Bath & Bed	Bath & Bed	Bath & Bed	Bath & Bed	Bath & Bed	Bath & Bed	Bath & Bed (11 pm)

HR monitoring

- http://livewithcfs.blogspot.com/2011/02/heart-rate-and-post-exertional-crashes.html

- People with ME have a lower anaerobic threshold ie. they move into anaerobic respiration a lot quicker than healthy individuals.
- Therefore they need to calculate their anaerobic threshold at 50% of their MHR
- (220 - your age) * 0.5 = anaerobic threshold or AT, in beats per minute

- HR monitoring aims to keep any activity below this threshold

Objectives

- Incidence of fatigue in neurological conditions
- Define fatigue
- Explain the potential causes of fatigue
- Discuss the management of fatigue
- Focus on PVFS and ME
- Explain ME
- Discuss problems with exercise in ME population
- Alternative management strategies for ME

Websites - Fatigue

- https://www.mssociety.org.uk/about-ms/signs-and-symptoms/fatigue
- https://www.stroke.org.uk/effects-of-stroke/tiredness-and-fatigue
- http://sci.washington.edu/info/forums/reports/exercise_2013.asp
- https://spinalcordinjuryzone.com/info/7270/fatigue
- https://www.spinal.co.uk/about-us/
- https://www.krysalisconsultancy.co.uk/resources/item/fatigue-and-brain-injury
- https://biau.org/fatigue-and-traumatic-brain-injury%E2%80%A8/
- https://www.verywellhealth.com/about-fatigue-in-parkinsons-disease-2612183
- https://www.parkinsons.org.uk/information-and-support/fatigue

References - Fatigue

Andreasen AK, Stenager E, Dalgas U. (2011) The effect of exercise therapy on fatigue in multiple sclerosis. Mult Scler;17, pp.1041–1054.

Barritt, AW and Smithard, DG (2011)Targeting Fatigue in Stroke Patients. ISRN Neurology, Article ID 805646, 6 pages

Carruthers BM, van de Sande MI, De Meirleir KL, Klimas DG, Broderick G, Mitchell T, Staines D, Powles ACP, Speight N, et al. (2011) Myalgic encephalomyelitis: International Consensus Criteria. J Intern Med; 270 pp. 327-338. Reprinted with permission of John Wiley & Sons. Some notes are slightly modified.
http://onlinelibrary.wiley.com/doi/10.1111/j.1365-2796.2011.02428.x/full
http://onlinelibrary.wiley.com/doi/10.1111/j.1365-2796.2011.02428.x/pdf

Chaudhuri, A and Behan, PO (2000) Fatigue and basal ganglia, Journal of the Neurological Sciences 179(S 1-2) pp.34-42

Choi-Kwon, S., Han, S.W., Kwon, S.U., Kim, J.S. (2005) 'Poststroke fatigue: characteristics and related factors'. Cerebrovascular Disease, 19, pp. 84–90

Clague-Baker, N, Robinson T, Gillies, CL, Drewry S, Hagenberg A, Singh S (2020) Adapted cardiac rehabilitation for people with sub-acute, mild-to-moderate stroke: a mixed methods feasibility study. (under review)

Costa DC, Tannock C, Brostoff J. (1995) Brainstem perfusion is impaired in chronic fatigue syndrome. QJM; 88 pp. 767-773.

References - Fatigue

Dahl I (2018) Classic pacing for a better life with ME. Writersworld.

Drummond, A., Hawkins, L., Sprigg, N., Ward, N., Mistri, A., Tyrrell, P., Mead, G. E., Worthington, E. and Lincoln, N. (2017) 'The Nottingham Fatigue after Stroke (NotFAST) study: Factors associated with severity of fatigue in stroke patients without depression'. Clinical Rehabilitation, 31(10), pp. 1406-1415

Elbers RG, Verhoef J, van Wegen EEH, Berendse HW, Kwakkel G. (2015) Interventions for fatigue in Parkinson's disease. Cochrane Database of Systematic Reviews, Issue 10. Art. No.: CD010925.

Fiest, KM, Fisk, JD, Patten, SB, Tremlett, H, Wolfson, C, Warren, S, McKay,KA, Berrigan, LI, Marrie, RA (2016) Fatigue and Comorbidities in Multiple Sclerosis. Int J of MS care. 18, pp.96–104.

Finlayson M, Preissner K, Cho C, Plow M. (2011) Randomized trial of a teleconference-delivered fatigue management program for people with multiple sclerosis. Mult Scler; 17, pp.1130–1140.

Glader EL, Stegmayr B, Asplund K. (2002) Poststroke fatigue: a 2-year follow-up study of stroke patients in Sweden. Stroke.;33(5), pp.1327-33

Gousmit, EM, Nijs,J, Jason LA & Wallman, KE (2011) Pacing as a strategy to improve energy management in myalgic encephalomyelitis/chronic fatigue syndrome: a consensus document. Disability & Rehabilitation, 1–8, Early Online

References - Fatigue

Grossman P, Kappos L, Gensicke H, et al. (2010) MS quality of life, depression, and fatigue improve after mindfulness training: a randomized trial. Neurology;75, pp.1141–1149.

Hammell et al (2009) Fatigue and spinal cord injury: a qualitative analysis. Spinal Cord, 47, pp.44–49

Heine M, van de Port I, Rietberg MB, van Wegen EEH, Kwakkel G (2015) Exercise therapy for fatigue in multiple sclerosis (Review) Cochrane Database of Systematic Reviews, Issue 9. Art. No.: CD009956.

Hugos, CL, Copperman,LF, Fuller BE, Yadav V, Lovera J, Bourdette DN. (2010) Clinical trial of a formal group fatigue program in multiple sclerosis. Mult Scler;16, pp.724–732.

Kluger,BM, Krupp, LB and Enoka, RM (2013) Fatigue and fatigability in neurologic illnesses. Proposal for a unified taxonomy. American Academy of Neurology. 80; pp. 409-416

Kostic et al (2016) The Pathophysiology of Fatigue in Parkinson's Disease and its Pragmatic Management. Movement Disorders, pp 323- 330

Krupp, L. B. Alvarez, L. A. LaRocca, N. G. and ScheinbergL. C. (1988) Fatigue in multiple sclerosis, Archives of Neurology, vol.45, no. 4, pp. 435–437

References - Fatigue

Krupp, L.B. (2003) Fatigue (The most common complaints series). Butterworth-Heinemann

Krupp, L.B. (2004) Fatigue in Multiple Sclerosis: A Guide to Diagnosis and Management. Demos Medical

Kuppuswamy A, Clark E, Turner IF, et al. (2015) Post stroke fatigue: a deficit in cortico-motor excitability? Brain;138(Pt 1), pp.136–48.

Kuppuswamy A (2017) The fatigue conundrum, Brain 140, pp. 2240–2245

Mollayeva et al. (2013) Fatigue in adults with traumatic brain injury:mpredictors and consequences. A systematic review of longitudinal study protocols. Systematic Reviews, 2, pp.57

Naess, H, Lunde L, Brogger J, Waje-Andreassen U. (2012) Fatigue among stroke patients on long-term follow-up. The Bergen Stroke Study. J Neurol Sci., 312(1-2), pp.138-41.

RuiPing X et al. (2017) “Effectiveness of Exercise on Reducing Fatigue in Parkinson’s Disease: A Systematic Review”. EC Neurology. 9.1, pp.12-19.

References - Fatigue

Siciliano, M, Trojano, L, Santangelo, G, De Micco, R, Tedeschi, G and Tessitore, A. (2018) Fatigue in Parkinson's disease: A systematic review and meta-analysis. Movement Disorders. 33, Issue11 pp1712-1723

Su, Y, Yuki ,M and Otsuki, M. Non-Pharmacological Interventions for Post-StrokeFatigue: Systematic Review and Network Meta-Analysis J. Clin. Med. 2020, 9, pp. 621

Taylor JL, Amann M, Duchateau,J, Meeusen, R and Rice, CL (2016) Neural Contributions to Muscle Fatigue: From the Brain to the Muscle and Back Again. Med Sci Sports Exerc. 48(11), pp. 2294–2306.

Togo,F, Natelson,BH, Cherniack,NS, FitzGibbons,J, Garcon C and Rapoport, D,M (2008) Sleep structure and sleepiness in chronic fatigue syndrome with or without coexisting fibromyalgia. Arthritis Research & Therapy, 10:R56

van den Akker LE, Beckerman H, Collette EH, Eijssen IC, Dekker J, de Groot V. Effectiveness of cognitive behavioral therapy for the treatment of fatigue in patients with multiple sclerosis: a systematic review and meta-analysis. J Psychosom Res. 2016;90, pp.33-42.

References - Fatigue

Wu S, Kutlubaev MA, Chun HY, Cowey E, Pollock A, Macleod MR, et al. (2015) Interventions for post-stroke fatigue. Cochrane Database Syst Rev.(7):CD007030.

Xu , Gang-Zhu, et al. (2017) Complementary and alternative interventions for fatigue management after traumatic brain injury: a systematic review. Xi'an, China : Therapeutic Advances in Neurological Disorders

References - ME

Carruthers, B. M. MD, CM, FRACP (C) & Van de Sande, M.I. B ed.(eds) (2012), International Consensus Primer For Medical Practitioners, International Consensus Panel, available from http://www.investinme.org/Documents/Guidelines/Myalgic%20Encephalomyelitis%20International%20Consensus%20Primer%20-2012-11-26.pdf

Chu, L, Valencia, IJ, Garvert, DW, Montoya, JG. (2018) Deconstructing post-exertional malaise in myalgic encephalomyelitis/ chronic fatigue syndrome: A patient-centered, cross-sectional survey. PLoS ONE 13(6): e0197811.

Cleare, A. J. et al (2015). Chronic Fatigue Syndrome, BMJ Clinical Evidence, 1101. Available from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4585442/

Davenport TE, Lehnen M, Stevens SR, VanNess JM, Stevens J and Snell CR (2019) Chronotropic Intolerance: An Overlooked Determinant of Symptoms and Activity Limitation in Myalgic Encephalomyelitis/Chronic Fatigue Syndrome? Front. Pediatr. 7, pp.82.

Jason, L. PhD, (2019) CDC Empirical Case Definition and Prevalence of CFS, International Association for Chronic Fatigue Syndrome and Myalgic Encephalomyelitis. Available from – http://iacfsme.org/ME-CFS-Primer-Education/Pages/CDC-Empirical-Case-Definition-and-Prevalence-of-CF.aspx

References - ME

Lien et al (2019) Abnormal blood lactate accumulation during repeated exercise testing in myalgic encephalomyelitis/chronic fatigue syndrome. Physiological reports. 7, 11, pp.1-14

M.E. Association, (2019) Seven Key Symptoms for Making a Diagnosis of ME/CFS. Available from https://www.meassociation.org.uk/about/the-symptoms-testing-assessment-mecfs/#Part%201

M.E. Association, (2019) Symptoms, Testing and Assessment https://www.meassociation.org.uk/about/the-symptoms-testing-assessment-mecfs/

M.E. Association (2017), Pace Trial – the making of a medical scandal, Press release: Journal of Health Psychology, Special Issue on The PACE Trial, Vol. 22, No 9, Aug. 2017. Available from https://www.meassociation.org.uk/2017/07/the-pace-trial-the-making-of-a-medical-scandal-29-july-2017/

M.E. Association (2011) Disability Scale (downloadable pdf) https://www.meassociation.org.uk/wp-content/uploads/2012/02/MEA-Disability-Rating-Scale.pdf

References - ME

Younger, J., (2018), The Open Medical Foundation, How brain inflammation causes ME/CFS, YouTube https://youtu.be/8XrdSlpUQTE

World Health Organisation (2016) G93.3 classification https://icd.who.int/browse10/2016/en#/G93.3 ICD: 10 version:2016

Websites - ME

Shepherd, C., Dr. (2017) NHS Choices, YouTube – https://youtu.be/hLeDEgo6Pd0
Available from: https://www.nhs.uk/conditions/chronic-fatigue-syndrome-cfs/

http://livewithcfs.blogspot.com/2011/02/heart-rate-and-post-exertional-crashes.html

www.thegracecharityforme.org

http://www.shoutoutaboutme.com/about-me/7293/

https://www.healthrising.org/blog/2019/01/17/decoding-2-day-cpet-chronic-fatigue-syndrome/

https://alifehidden.com/2019/08/07/emilysappeal/amp/?__twitter_impression=true

https://www.meassociation.org.uk/2019/04/forward-me-and-oxford-brookes-university-announce-results-of-patient-survey-on-cbt-and-get-in-me-cfs-03-april-2019/

https://journals.sagepub.com/doi/abs/10.1177/1359105319847261

https//www.physiosforme.com

Websites - ME

https://www.facebook.com/notes/nz-carers-of-kids-with-mecfsrelated-illnesses/you-and-me-an-update-on-myalgic-encephalomyelitis-for-psychologists-by-rose-silv/210275105308663 7/

https://www.bbc.co.uk/news/uk-scotland-48770748#

https://www.youtube.com/watch?v=208JacsB5kM&feature=youtu.be

https://www.meaction.net/2019/07/24/uk-teenager-with-severe-me-threatened-with-forced-institutionalized/

www.thegracecharityforme.org

http://www.shoutoutaboutme.com/about-me/7293/

Films

- Unrest
- Voices from the shadows