Cognitive Impairment in FM and ME/CFS

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Important Principles of Management: FM and ME/CFS

- 1) Good differential diagnosis to identify and address all aspects of illness and comorbid conditions
- 2) "<u>Pace</u>" activity to prevent symptom escalation (preventive activity management). Avoid push/crash.
- ► 3) Address the major aspects of illness
 - SLEEP: Achieve most restorative
 - MENTAL HEALTH/COGNITION: bolster
 - PAIN: control severe pain and learn to manage chronic pain
 - FITNESS: Achieve best fitness based on tolerance and illness relapse
 - ORTHOSTATIC INTOLERANCE- if applicable



Cognitive impairment is a common complaint of people with FM and ME/CFS.

Patients report:

- brain fog
- trouble word finding
- reduced short term memory, attention and concentration
- mental/cognitive fatigue
- slowed thinking... Reduced processing speed
- mild confusion, disorientation, sensory overload
- inability to process information
- trouble multi-tasking, organizing, reduced "executive function"



Alternate "new" Fibromyalgia Criteria (ACR 2010)

1) Widespread PAIN index (V	VPI)			
(0-19 points—see next slide)		7+	or 3-6	
2) Symptom Score (SS): 0=nor	ne, 1=mild, 2=	mod, 3=severe		
Chronic fatigue	(0-3)			
Unrefreshing sleep	(0-3)			
Cognitive complaints	(0-3)			
Multisystem complaints	<u>(0-3)</u>			
Max SS = 12		<u>5+</u>	<u>and 9+</u>	
		FM	FM	

> 3 months in duration and without other apparent explanation



Wolf F, et al. The American College of Rheumatology Preliminary Diagnostic Criteria for Fibromyalgia and Measurement of Symptom Severity. Arthritis Care & Research. Vol. 62, No. 5, May 2010, pp 600–610

ME/CFS Clinical Diagnostic Criteria:

CORE criteria required for diagnosis:

- 1) Impaired function related to exhaustion/fatigue/fatigability
- 2) **PEM:** post exertional malaise (illness relapse after activity)
- 3) Unrefreshing sleep
- 4) A. Cognitive impairment and/or
 - B. Orthostatic intolerance

*Must be moderate-severe and frequent (present >50% of time)

Other common features of illness include:

- ----Pain: including overlap with FM
- ---Immune manifestations (allergy, inflammation, etc)
- ---Infections



Percentage of ME/CFS patients and healthy controls reporting **neurocognitive manifestations** of at least <u>moderate severity</u> that occurred <u>at least half of the time</u> during the past 6 months





Jason LA, Sunnquist M, Brown A, Evans M, Vernon S, Furst J, Simonis V. Examining case definition criteria for chronic fatigue syndrome and myalgic encephalomyelitis. Fatigue: Biomedicine, Health & Behavior. 2013b;2(1)

ME/CFS and FM cognitive impairment: often difficult to measure objectively

Neuropsychometric testing is expensive and not often covered by insurance. Most of the typical neurocognitive tests are within normal limits. Brain fog is not dementia. IQ intact.

Slowed information processing is the best documented cognitive deficit in ME/CFS

- Difficulty with timed tests
- Difficulty multi-tasking (which is actually moving quickly from task to task)



Neuropsychometric testing 14 year old boy with ME/CFS unable to attend school or do homework

Cognitive Abilities Test:

Verbal

98th percentile 48th

65th

77th

- Quantitative
- Nonverbal
- Composite

Learning and Working Memory:

75th

- Verbal Learning
- Sound Symbol 25th
- Visual learning
 50th

Intellectual:

- Verbal Comprehension 98th
- Perceptual Reasoning 61st
- Working Memory 34th
- Processing speed 21st
- Full Scale 70th

Executive/Neuropsychological Skills:

Planning	<mark>4th</mark>
Simultaneous	58th
Attention	12th
Successive	50th
Full Scale	18th

Brain research in ME/CFS

- Activated microglia and astrocytes (neuroinflammation) were demonstrated in the brain using PET scans in a small study of 10 patients (Nakatomi 2014)
- Functional MRI and spin-echo MRI have demonstrated various changes in the brain but are not all in agreement (numerous studies)
- Lactate is increased in the brain ventricles as imaged by by proton magnetic resonance spectroscopy (MRS) (Murrough 2010, Shungu 2012)
- Quantitative EEG techniques can differentiate ME/CFS from controls (Duffy 2011, Zinn et al 2014, Zeineh et al 2015)
- Spinal fluid of ME/CFS patients showed higher protein and altered cytokines (Spinal fluid abnormalities in patients with CFS. Natelson B, et al. Clin Diagn Lab Immunol. Jan 2005; 12(1`);52.55.)



EEG spectral coherence data distinguish chronic fatigue syndrome patients from healthy controls and depressed patients-A case control study. Duffy...Komaroff. BMC Neurology 2011, 11:82

Microglial "glial" cells are immune cells in the brain and spinal cord.

Inflammation caused by glial cells may:

- cause or contribute to the widespread pain and fatigue of FM
- underlie ME/CFS cognitive slowing, exhaustion, pain
- compromise or reduce normal function in any area of the brain where inflammation occurs



Jarrod Younger MD PhD

The use of low-dose naltrexone (LDN) as a novel anti-inflammatory treatment for chronic pain

Jarred Younger, Luke Parkitny & David McLain

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The use of low-dose naltrexone (LDN) as a novel antiinflammatory treatment for chronic pain. Younger J, et al. Journal Clin Rheumatol. 2014 Apr;33(4):451-9. Epub 2014 Feb 15.

The interaction of naltrexone with microglial cells results in a reduction of proinflammatory cytokines as well as neurotoxic superoxides (Wikipedia)

Deringer

Microglia

http://jonlieffmd.com/blog/are-microglia-the-mostintelligent-brain-cells

Regulation of innate immune responses in the brain. Serge Rivest. Nature Reviews Immunology 9, 429-439 (June 2009)

Microglia are the innate immune cells of the CNS





General Principles of Supportive Management:

> 1) Address all other conditions (complete a good medical work-up)

- i.e. anemia, thyroid, diabetes, sleep apnea, low Vit B12, polypharmacy
- 2) "<u>Pace</u>" to prevent symptom escalation (Preventive activity management. Reduce overload)
- 3) Address the major aspects of illness
 - PAIN: reduce severe pain
 - SLEEP: achieve restorative sleep
 - MENTAL HEALTH: insight and support
 - FITNESS: engage in restorative exercise
 - Orthostatic Intolerance



General Principles of Supportive Management: Possible contributors to cognitive complaints:

- 1) Address all other conditions (complete a good medical work-up)
 - i.e. anemia, thyroid, diabetes, sleep apnea, low Vit B12, polypharmacy
- 2) "<u>Pace</u>" to prevent symptom escalation (NOT pacing, not managing activity leads to overload or PEM)
- 3) Address the major aspects of illness
 - PAIN: unrelenting pain is exhausting to body and brain
 - SLEEP: poor sleep contributes to daytime exhaustion
 - MENTAL HEALTH: anxiety and depression impact cognition
 - FITNESS: sluggish circulation reduces alertness
 - Orthostatic Intolerance reduced brain blood flow



Address potential contributors to "brain fog" and cognitive slowing

- Medications for sleep, pain, anxiety, migraine
- Chronic sleep disturbances
- Secondary mental health conditions---depression, anxiety
- Orthostatic intolerance and other causes of reduced cerebral blood flow and perfusion. "Perfusion" is the circulation or delivery of blood to every cell, bringing oxygen, glucose, everything needed for cell function...
- Cognitive fatigue and fatigability
- Low cellular energy production. Capacity for "function" is reduced.
- PEM—the consequences of exceeding cell energy capacity



Address potential contributors to "brain fog" and cognitive slowing

- Medications for sleep, pain, anxiety, migraine--- minimize meds when possible, especially during the daytime.
- Chronic sleep disturbances ---- continue to improve restorative sleep
- Secondary mental health conditions---depression, anxiety. Address mental health.
- Orthostatic intolerance and other causes of reduced cerebral blood flow and perfusion. "Perfusion" is the circulation or delivery of blood to every cell, bringing oxygen, glucose, everything needed for cell function... Improve cerebral blood flow and perfusion
- Cognitive fatigue and fatigability. Engage in "pacing" cognitively as well as physically
- Low cellular energy production. Capacity for "function" is reduced. Pacing!
- PEM—the consequences of exceeding cell energy capacity. Avoid severe/prolonged PEM



Medications that might help brain fog and cognitive impairment

- Wellbutrin/bupropion 75-300 mg
- Stimulants (examples) ---can lead to crash or PEM
 - methylphenidate (Ritalin)
 - Dexadrine (Adderall) ---can raise BP and HR
- Newer drugs for daytime somnolence
 - Modafinil (Provigil) and armodafinil (Nuvigil) --- can disrupt sleep
- Supplements (a few examples, not supported by strong evidence)
 - Fish oil, omega 3 fatty acids
 - Phosphatidyl serine 100 mg 2x or 3x daily
 - Curcumin (from turmeric)

RESEARCH | CLINICAL CARE | EDUCATION

- B vitamins (B6, B9, B12) related to homocysteine metabolism
- Vitamin E (tocopherol), Vitamin A, Vitamin C

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3311304/

Common dietary supplements for cognitive health. Aging Health. Gestuvo and Hung. 2012

Behavioral strategies for managing cognitive impairment

Cognitive slowing: ME/CFS may recruit more brain areas to accomplish task.

- Behavioral strategies for dealing with cognitive impairment:
 - complete cognitive tasks when more rested or at best time of day
 - allow more time and minimize interruptions
 - utilize day-timer, iphone, other recording/signaling devices
 - dampen or remove other sensory input to the brain
 - quiet room, ear plugs or sound-reducing headphones
 - low or less glaring lights
 - Reduce #people or other chaotic signaling/disruption



PACING and activity management





Thank you and good luck!

Making/Getting the Right Diagnosis
Activity Intolerance, Pacing and PEM
Sleep Disturbances.
Widespread Chronic Pain
Orthostatic Intolerance



