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) “Pace” 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 (WPI)
   (0-19 points—see next slide)  
   7+ or 3-6

2) Symptom Score (SS): 0=none, 1=mild, 2=mod, 3=severe
   Chronic fatigue (0-3)
   Unrefreshing sleep (0-3)
   **Cognitive complaints** (0-3)
   **Multisystem complaints** (0-3)
   Max SS = 12  
   5+ and 9+
   FM FM

> 3 months in duration and without other apparent explanation

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 moderate severity that occurred **at least half of the time** during the past 6 months.

<table>
<thead>
<tr>
<th>Manifestation</th>
<th>ME/CFS</th>
<th>Controls</th>
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<tbody>
<tr>
<td>Problems remembering</td>
<td>80%</td>
<td>7%</td>
</tr>
<tr>
<td>Difficulty expressing thoughts</td>
<td>73%</td>
<td>2%</td>
</tr>
<tr>
<td>Difficulty paying attention</td>
<td>69%</td>
<td>7%</td>
</tr>
<tr>
<td>Slowness of thought</td>
<td>66%</td>
<td>2%</td>
</tr>
<tr>
<td>Absent-mindedness</td>
<td>68%</td>
<td>5%</td>
</tr>
<tr>
<td>Difficulty understanding</td>
<td>55%</td>
<td>2%</td>
</tr>
</tbody>
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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

<table>
<thead>
<tr>
<th>Cognitive Abilities Test:</th>
<th>Learning and Working Memory:</th>
</tr>
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<tbody>
<tr>
<td>Verbal 98th percentile</td>
<td>Verbal Learning 75th</td>
</tr>
<tr>
<td>Quantitative 48th</td>
<td>Sound Symbol 25th</td>
</tr>
<tr>
<td>Nonverbal 65th</td>
<td>Visual learning 50th</td>
</tr>
<tr>
<td>Composite 77th</td>
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</tbody>
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Intellectual:
- Verbal Comprehension 98th
- Perceptual Reasoning 61st
- Working Memory 34th
- Processing speed 21st
- Full Scale 70th

Executive/Neuropsychological Skills:
- Planning 4th
- 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)


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

The interaction of naltrexone with microglial cells results in a reduction of proinflammatory cytokines as well as neurotoxic superoxides (Wikipedia)
Microglia are the innate immune cells of the CNS.

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

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) **“Pace”** 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) **“Pace”** 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)
  - 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/
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

ORTHOSTATIC INTOLERANCE…

PAIN reduction

Restorative SLEEP

FITNESS

MENTAL HEALTH

CHRONIC UNWELLNESS
Thank you and good luck!

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