Fatigue in Neurologic Disorders: Pathophysiology, Evaluation, and Intervention

Fatigue and Mobility: The Effect of Fatigue on Mobility in Neurologic Diagnoses

Herb Karpatkin, PT, DSc, NCS, MSCS
Hunter College, City University of New York

Evan T. Cohen, PT, MA, PhD, NCS
Rutgers, The State University of New Jersey

Stefanie DiCarrado, PT, DPT, MSCS
Dominican College, New York

An Overview of Fatigue in Neurologic Populations

Fatigue in Neurologic Disorders

- Common finding throughout all neurologic disorders, both peripheral, central, and interacting components
- Fatigue can occur following progressive and non-progressive conditions, traumatic and non-traumatic conditions
- Common but multifactorial

Fatigue is Multifactorial

- Central Components
- Peripheral Components
- Adaptive/Learned Components
- Iatrogenic Components
- Orthopedic/Musculoskeletal Components
- Psychological/Behavioral components

Course Objectives

1. Identify the evidence for fatigue as a major contributor to disability and a barrier to rehabilitation in persons with neurologic illness
2. Differentiate between primary and secondary fatigue as a symptom of neurologic disease
3. Recognize how fatigue can limit effectiveness of physical therapy interventions for persons with CNS involvement.
4. Examine fatigue in persons with neurologic disability and evaluate its impact on the rehabilitation plan
5. Develop a treatment program for persons with specific neurologic conditions that addresses the effects of fatigue
6. Differentiate fatigue from fatigability, and distinguish the contributors to each

The Role of Fatigue in Neurologic Rehabilitation

- If fatigue is an essential part of neurologic disability, it has to be taken into account in examination, evaluation and intervention
- Part of mobility loss following neurologic disability may be due to fatigue
The Problem

- Patients are referred to PT because of issues with mobility
- PT Interventions are used to address these issues
- A certain amount of volume of practice of these interventions is needed to optimally remediate these issues
- Fatigue prevents achieving that volume
- If fatigue can be addressed, a greater volume of practice can be achieved, and potentially better outcomes.

Fatigue: The Problem for PT

- Fatigue should be an expected part of a neurologic diagnosis
- Clinicians who work with patients with neurologic diagnoses need to be able to
  - Test for the presence of fatigue
  - Determine the type of fatigue
  - Determine its causes
  - Determine its effect on physical function
  - Develop intervention plans for remediating its effects.

Chronic fatigue is a typical symptom of neurological disease (Chaudhuri, 2004)

- Disorders of neuromuscular junction transmission and metabolic diseases cause muscle fatigability, which is characterized by failure to sustain the force of muscle contraction
- Enhanced perception of effort and limited endurance of sustained physical and mental activities are the main characteristics of central fatigue
- Metabolic and structural lesions that disrupt the usual process of activation in pathways interconnecting the basal ganglia, thalamus, limbic system, and higher cortical center are implicated in the pathophysiological process of central fatigue.

A framework for understanding fatigue in CNS disorders for Physical therapists

- Defining fatigue
- Recognizing/describing fatigue
- Examining fatigue
- Interventions for fatigue

Fatigue: Sign vs Symptom

- Sign- an indication of a medical condition that can be objectively observed.
  - Example: slowing of gait over time

- Symptom- a manifestation of the sign subjectively noted by the patient
  - Example: The patient complains that they are too tired to perform exercise

Defining Fatigue

- Fatigue-subjective state of being tired; a feeling of not being able to perform a task or activity either effectively, if at all (symptom)
- Fatigability- Objective measure of how fast someone gets tired. Can be observed (and felt) on any prolonged and/or intensive task for any individual (sign)
- Pathologic fatigue or fatigability-happens faster or more severely than expected than in a non-disabled person
Fatigability vs Fatigue

- **Fatigability** refers to a specific motion or body part that objectively worsens in performance over time.
- **Fatigue** refers to a subjective feeling of tiredness that occurs in an individual that is noted whether the person is engaged in activity or not.
- The sign of fatigability is specific to an action, body part, or physiologic process.
- The symptom of fatigue is general, and often tends to have a global effect.
- Patients can have one without the other, or both.

Fatigue and Fatigability: Definitions

- **Primary fatigue/fatigability**
  - a distinct and particular physiologic change resulting in fatigue or fatigability that is due specifically to the disease process itself
  - reversible only by treating the primary physiologic process
- **Secondary fatigue/fatigability**
  - fatigue that occurs as a result of an adaptation or compensation to the disease pathophysiology
  - Occurs as a result of the disease, not due to the disease itself
  - Reversible if the compensations or adaptations are prevented or limited

Interaction of Primary and Secondary Fatigue

- An activity becomes performed less frequently due to primary fatigue.
- Leads to decreased practice of that activity, and performing that activity becomes harder.
- Leads to further decreased practice of that activity etc etc.

Where can clinicians intervene in this cycle?

Recognizing the Sign of Fatigability

- Progressive slowing of gait
- Progressive weakness of repeated contractions
- Worsening of sensation/speech/vision during a repetitive task
- Decreased performance on a functional measure following exertion
- Physiologic measures- temperature, EMG, cardiovascular
- Patient caregiver complaint/identification

Recognizing the symptom of fatigue

- Patient c/o fatigue
- Patient avoids exercise program
- Caregiver report
- Decreased scores on self-report fatigue measures

Examining fatigue

- Instantaneous measures
  - e.g Visual Analog Scale of Fatigue
- Self report Measures
  - e.g. Fatigue Severity Scale, Fatigue Impact Scale
- Patient caregiver complaint/identification
- Behavioral measures
  - e.g. those related to depression, stress, etc.
Examining fatigability
• 6 minute walk test or other prolonged tests
• Repeated contractions
• EMG
• Change in sensation
• Cardiovascular/cardiopulmonary changes

Subjective fatigue vs objective fatigability
• 2 different constructs
• Separate but overlapping physiologic mechanisms
• Separate and distinct presentations
• Separate tools for evaluation

Taxonomy of fatigue (Kluger et al)

Interventions for fatigability
• Intermittent training
• Temperature manipulation
• Energy conservation
• Removing secondary causes
  — cardiovascular/endurance training
  — strength training
  — flexibility training
  — motor control

Fatigue in Multiple Sclerosis

Fatigue in MS
• Most common symptom in MS
  — Reported by over 80% of all MS patients (Minden, 2006)
• Often occurs prior to diagnosis (Berger, 2013)
• 55% consider one of worst symptoms
Fatigue and fatigability in MS
- Primary: due to the underlying pathology
- Secondary: due to changes, adaptations, and/or compensations in lifestyle that have been caused by the primary changes

Primary causes: Pathophysiology
- Delayed conduction through demyelinated nerves: Motor fatigue (sign of fatigability)
- Cytokine theory: Lassitude (symptom of fatigue)

Secondary causes:
- Deconditioning
- Thermosensitivity
- Sleep disorder
- Infection
- Pain
- Polypharmacy
- Depression
- B&B
- Increased energy cost of movement

Interaction effect
- Primary + secondary fatigue
- As disease progresses, primary fatigue can worsen
- As primary fatigue worsens, the same activity takes a greater amount of energy
- Increased energy cost

Vicious cycle
- As fatigue worsens, movement becomes harder
- As movement becomes more difficult, less is attempted
- Less movement is performed, deconditioning results

Learned non-use
- Persons with fatigue avoid tasks which are too difficult
- Perform compensatory or alternative movements instead
- The avoided task becomes “unlearned”
- Often thought to be part of the primary disability, but can be remediable if avoided task is practiced
Fatigue in MS: Medical management

- Amantadine (Symmetrel)- antiviral/dopaminergic-effective for fatigue
- Dalfampridine (Ampyra)- potassium channel blocker, allows for AP's through demyelinated nerves-effective for fatigability
- Modafinil (provigil)- antinarcopletic-effective for lassitude
- Pemoline (Cylert)- CNS stimulant

Fatigue in MS: PT evaluation and management

- Assume fatigue will be present
- How does it present?
  - As a task progresses, some sx may worsen
- Primary vs. secondary
- Fatigue vs. Fatigability

MS Fatigue scales

- Fatigue Impact Scale (FIS)
- Fatigue Severity Scale (FSS)
- Self report measures of impact of fatigue on various aspects of QOL and performance
- Caregiver support
- Does not give insight into how fatigue affects mobility

Effect of fatigue on balance

- Persons with MS given BBS before and after either 6 minute rest or 6 minute walk
- No change in BBS scores when unfatigued (50.7-51.1)
- Decreased from 51.0 to 47.8 in the fatigued condition (P<.001)

Mobility based measures of fatigability:

6MWT (Karpatkin et al 2014)

- 6 minute walk test
- Distance decreased over time
- Longer test needed to reveal fatigue

MS Fatigue scales

- Visual Analog Scale of Fatigue (VAS-F)
- Looks at fatigue at specific moments

<table>
<thead>
<tr>
<th>Least Fatigue</th>
<th>Most Fatigue</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

6 minute walk test

- Distance decreased
- Longer test needed to reveal fatigue
Fatigability of strength in MS

Interventions for Fatigue

- Fatigue limits the volume of task performance that a person with MS can accomplish
- With less practice of task performance, less motor learning, and less remediation can occur
- What interventions are available to clinicians to address these limitations?

Interventions for Fatigability: Cooling

- Decreased conduction through demyelinated nerves
- Exercise increases core temperature
- Decrease core temp while exercising?

Effect of temperature on gait in MS
(Hunter College 2014)

Interventions for Fatigability: Intermittent exercise

- Taking rest breaks during exercise will result in being able to perform a greater volume of work
- Core temperature may not rise as much
- Because of recovery, overall fatigue may be less severe, resulting a greater total volume
- With greater volume ➔ greater learning

Intermittent walking

- Take breaks when walking
- Instead of walking to fatigue, stop prior to fatigue, recover, then resume
- Allows for greater volume of walking
Results: INT vs CON on Distance
(Karpatkin et al 2015)

Other ideas
• Diminish energy cost of walking
• Weight loss
• Gait efficiency
• Posture

A Case Example:
Fatigue in Multiple Sclerosis

Fatigue in MS
• Highly prevalent
• Definitions not well-agreed upon
• Difficult to differentiate the signs from the symptoms
• Difficult to differentiate areas/constructs affected by fatigue

In essence
• There is evidence that there is a declination in performance after repeated attempts and/or other fatiguing activity.
• This has been found in
  – Reaction time testing
  – Postural control
  – Functional balance testing
  – Gait and walking
  – Speech and communication function

• Although we can quantify fatigue with disease-specific outcome measures, this case focuses rather on fatigability in people with MS
• Check the small body of literature in this area
What does this look like?

What can be done about this?
Our current research gives two leads:

1. Intermittent training
   - Karpatkin, Cohen, DiCarrado et al., 2016

What can be done about this?

2. Maximal Strength Training
   - Karpatkin, Cohen, Klein, et al., 2016

The Summary

- Examine fatigue and fatigability
- Screen for contributors to fatigue
- Refer for pharmacologic management when appropriate
- Utilize techniques that maximize dosing

Fatigue in Stroke

Evan T. Cohen, PT, MA, PhD, NCS
Rutgers, The State University of New Jersey
Doctor of Physical Therapy Program - South

What is Fatigue after Stroke?

Primary vs. Secondary
- As with other pathologies, fatigue may be primary (i.e. a direct consequence of the pathology) or secondary due to related problems (e.g. depression, sleep disorders) or deconditioning.

Fatigue vs. Fatigability
- Differentiating the symptom from the sign
Prevalence of fatigue after stroke

After stroke, fatigue is
- Under reported by our patients
- Not asked about frequently enough by health care providers
- Under represented in the literature regarding medical and rehabilitation interventions
- Not clearly and consistently defined in the literature

Prevalence of fatigue after stroke

- Pooled prevalence estimate 50% (95% CI 43-57%)

Prevalence of fatigue after stroke

- More common even after “minor” stroke (56%) compared to TIA (29%) at 6 months post
  - Persisted even though activity, cognitive and psychosocial factors were no different between groups.

Prevalence of Fatigue After Stroke

Yes
No

Winward, Sackley, Metha, Rothwell, 2009

Fatigue severity

- Fatigue is more severe in ischemic than hemorrhagic stroke

Fatigue severity

Yes
No

Naess, Lunde, Brogger, Waje-Andreassen, 2010

Predicted by

- Independently predicted by depression, low physical functioning, and pre-stroke fatigue

Pathophysiology

Is unclear, but hypothesized causes include:
- Diminished corticomotor excitability
  - Kuppuswamy et al, 2015
- Neuroendocrine dysfunction
  - Silverman et al, 2010
- Post-event inflammation
  - Kelley et al, 2003
Other correlates

Directly related with:
- Pain
- Sleep disorders
- Prescription drug use
  - (e.g. analgesics, antihypertensives, etc)
  (Ponchel et al 2015)

Inversely related with:
- Walking ability (i.e. step count at 1-, 6- and 12-months post-stroke)
  (Duncan et al, 2015)

Other correlates

No/limited evidence for relationships with:
- Polypharmacy
  - Ponchel, 2015
- Number of strokes
  - Glader, Stegmayr & Asplund (2002)
- Location or laterality
  - Ponchel, 2015
- Sex
  - Ponchel, 2015
- Findings on CT
  - Kulkarna et al, 2013

Fatigue as a contributor to disability and barrier to rehab in people with stroke

The presence of post-stroke fatigue predicts:
- Higher mortality
  - Glader et al, 2002
- Institutionalization
  - Glader et al, 2002
- Dependence in ADL/ADL
  - Christensen et al, 2008
- Poorer Physical Function
  - Christensen et al, 2008; Maaijwee et al, 2015
- Slower information processing
  - Maaijwee, 2015

Examining Fatigue

- No fatigue measures recommended by the Stroke EDGE Task Force

  Suggestions
  - Profile of Mood States-Fatigue Subscale (POMS-F) (Elbers et al, 2012).
    - Longer, proprietary
  - Fatigue Assessment Scale (Mead et al, 2007)
    - Brief, open source
  - Simple Visual Analog Scale of Fatigue to measure exertional fatigue
    (Tseng, Gajewski & Kluding, 2010)
    - Very simple, measures immediate feeling of fatigue
  - Many studies use a simple Yes/No to determine presence/absence

Examining Fatigability

- The StrokeEDGE Task Force highly recommended the 6-minute Walk Test across acuity levels and practice settings
- May consider 5-times sit-to-stand test (recommended)
- VO₂ peak/max testing (not recommended – primarily due to low clinical utility) might be considered to examine work tolerance.

Medical Interventions for Fatigue in Stroke

Evidence for pharmacologic management of fatigue is equivocal

The synopsis:
- “There was insufficient evidence on the efficacy of any intervention to treat or prevent fatigue after stroke”
  Wu et al, 2015
Symptomatic interventions may include:
- Anti-depressants
- Pain management
- Address sleep disturbances
  Eskes et al, 2015
Recommendations for PT Management

- **Reduce energy cost of activities?**
  - Use of orthoses or assistive devices as appropriate
  - Obesity management

Recommendations for PT Management

- **Reverse/prevent deconditioning**
  - Facilitating improved respiratory strength?
  - Aerobic/endurance exercise training?

- **Good evidence that cardiorespiratory training** improved functional endurance (Saunders et al, 2016) even early after stroke (Stolier, de Bruin, Knols & Hunz, 2012)

- **Low to moderate evidence that treadmill training** (with or without BWS) improved walking endurance (Mehrota, Polli & Elsner (2014))

- **Must consider safety issue for concurrent cardiovascular system dysfunction**

References


Fatigue in Spinal Cord Injury

Dr. Stefanie DiCarrado PT, DPT, MSCS
Dr. Lawrence Harding PT, DPT

Prevalence

- 25-65% of individuals with SCI report fatigue
  - Described as “Overwhelming sense of tiredness,” “lacking energy”
  - (Olive et al., 2003) found fatigue in individuals with SCI when stimulating a denervated quadriceps muscle
- Causes difficulty with ADL and decreased quality of life
- Greater in individuals with incomplete lesions
  - 21% in complete injuries; 46% in incomplete (Nooijen et al. 2015)
  - Mean FSS 3.55 complete injuries; 4.48 incomplete injuries (Fawkes-Kirby et al. 2008)
- Greater in higher level injuries
  - 21% in paraplegics vs 50% in tetraplegics (Nooijen et al. 2015)

(Loeser et al. 2016, Nooijen et al. 2015, Lohr et al., 2015, Hammell et al., 2019)

Physical vs Chronic Fatigue

Physical Fatigue (Fatigability)
- Fatigue specific to muscle function
- Local muscle or central

Chronic Fatigue (Perception of Fatigue)
- Direct fatigue due to biological, psychological, and aging factors

Tests & Measures
- Subjective perception of fatigue: Questionnaires and fatigue scales, real-time, or retrospective
- Objective fatigability: Decrease in motor performance measured by endurance, strength, cognitive tests

(Fawkes-Kirby et al. 2008, Kluger et al., 2013, Hammell et al., 2009)

Fatigability: Primary & Secondary

PRIMARY FATIGABILITY
- Damage to motor neurons and reduced signal transmission through damaged spinal cord (University of Washington, 2013)
- Motor neuron damage = fewer motor units / muscle fibers stimulated
- Decreased vascular response (Olive et al. 2003)
  - Decreased time to peak blood flow and decrease in return to normal blood flow
- Decreased O2 delivery efficiency
- Increased metabolic waste products
- Sensation disruptions = decreased efferent signals to alpha motor neurons (Bullock-Saxton, 1994)
- Decreased signal transmission = spasticity
- Inefficient movement patterns = increased energy cost of movement

SECONDARY FATIGABILITY
- Disuse atrophy & deconditioning
  - Transition to larger number of fast fatigue muscle fibers with disuse (Dolbow & Gorgey, 2016, Burnham et al. 1997)

FATIGUABILITY: Central

Neurological / Central Fatigue: altered neurotransmitter levels related to poor thermoregulation
- Decreased motor performance while muscle energy supplies remain
- Increased body temperature, increased central fatigue
- Decreased ability to regulate body temperature with spinal cord injury
- Decreasedurogenital function, lack of sweating
- Higher level injuries suggest increased risk of central fatigue
- (Craig et al. 2012, Buhler et al., 2015, Buhler et al., 2016)

Perception of Fatigue: Mental

- Difficulty concentrating
- Increased forgetfulness: feeling like you mind “goes blank” (Craig et al. 2012)
- SCI displayed higher levels of fatigue after performing cognitive tests than controls (Craig et al. 2012)
  - Reported ~ 2x the fatigue as compared to able bodied age matched controls
  - 50% of SCI group demonstrated “excessive” chronic fatigue vs. 20% of able bodied group
  - Highly correlated to increased feelings of depression and poor self efficacy

(Fawkes-Kirby et al. 2008, Fawkes-Kirby et al. 2010)
Perception of fatigue: Emotional

- Depression
- Diminished motivation
  - SCI group found to have higher fatigue scores on item pertaining to altered motivation (Fawkes-Kirby et al 2008)
- Link between fatigue, depression, and self-efficacy
  - Fawkes-Kirby et al 2008: correlation between depression and higher fatigue scores
  - Craig et al 2012: correlation between depression and lower self-efficacy with fatigue
  - Roelands & Meeusen 2010: correlation between neurotransmitter and neuromodulator levels and mood

Factors of Fatigability & perception

- FATIGABILITY
  - Spasticity
  - Activity level: Deconditioning and disuse atrophy
- PERCEPTION OF FATIGUE
  - Social Support
  - Community Participation
  - Time since injury (Roelands, et al. 2013)

A Case Example

Evaluation: Subjective

- Note signs for signs of depression
  - Loss of interest, feelings of worthlessness, insomnia, appetite change, weight loss or gain (Kalpakjian et al 2009)
- Use and timing of medication intake
- Level of social support
- Level of community participation
- Quality of life measures

Evaluation: Objective

- Observation of alertness, attention, emotional expression
- Sensation testing
- ROM
- MMT - perform several repetitions or sustained holds to identify fatigability
  - Myotomes and specific muscles
  - Muscle balance and symmetry
  - Modified Ashworth Scale
  - Fatigability / endurance: Assess with repeated activity
    - Upper Extremity: Encore 6-Minute Arm Test (Hol et al 2007)
    - Walking endurance: 5 min walk for those ambulatory (research is varied in validity and reliability)
  - Wheelchair endurance: Modified walk test (Stavrakakis et al 2015; Leisure Thelney and Turkel 2008)
- Trunk control (Kalpakjian et al 2009)
- The Iowa Fatigue Scale: 4 factors, including cognitive (I have trouble concentrating), perception of fatigue (I feel worn out; I feel energetic), and productivity (I have low output) (Wijesuriya, et al. 2012)

Interventions: Fatigability

- MEDICAL MANAGEMENT - EXERCISE!!! (Nooijen et al 2015; Tawashy et al 2009; Dolbow & Gorgey, 2016
  - Mixed results with Cooling (Griggs et al 2015; Trbovich et al 2014; Webborn et al 2010; Coen et al 2016)
  - Intermittent training: did not help with thermoregulation (Griggs et al 2015)

- Switch muscle groups
  - Change modes of NM interventions: ie muscle reed: proprioceptive reed

- Balance & Posture training: trunk or extremity
  - FES:
    - Reduced fatigue by 60% after 12 weeks NMES resistance training (Dolbow & Gorgey, 2016)
  - Fatigue resistance increased by 43% after 2 weeks of low frequency FES (Ibitoye et al 2016)
Interventions: Mental perception

Mental / Cognitive Strategies
• Vary cognitive challenges
• Use assistive devices to organize
• "Budgeting" energy reserves
• Engage in meaningful activities

Hammell, Miller, Revell, Forman, and Jacobsen (2009)

Interventions: Emotional perception

Emotional Strategies
– Encourage acceptance of capabilities and limitations
– Create meaningful and rewarding achievable activities
– Encourage group activities
• Exercise groups (Kjaer et al 2016)
• Support groups
Hammell et al (2009)

Case study - history

• Name: NH, DOB: 12/03/56, Gender: Female
• Initial Evaluation: 8/18/16: Presents with a diagnosis of SCI C5/6 ASIA D after MVA on 1/5/15. Post ACDF and a posterior laminectomy with titanium plate placement. Followed with In-patient rehab at MSH from 1/13 for 3 months, then with some Home Rehab and Outpatient PT and OT since June 2015.

• Social Hx: Lives with her husband and young...
Case Study - Interventions

- **Therapeutic Exercise**: strengthening of LE musculature
- **Neuromuscular Reeducation**: coordination and timing of proximal stabilizers
- **Gait Training**: endurance training, use of varying assistive devices

Conclusions

- Targeted, goal specific interventions improved objective fatigability but worsened subjective perception of fatigue – Why?
  - Greater perception due to increased activity?
  - No emotional or mental fatigue strategies implemented?
- Treatment plan must be adjusted to include strategies addressing subjective perception

Citations

Fatigue in TBI

- Fatigue is a common and frequently disabling symptom after TBI.
- Reported by 45–73% of patients (Olver, 1996)
- Remains in 73% of patients after 5 years (Olver, 1996).
- Fatigue represents the most disabling symptom for 7% of patients and the first one for 43% of them (LaChapelle, 1998).

Psychological Fatigue

- Psychological fatigue is defined as related to decreased motivation, extended mental activity, or boredom occurring in situations such as effort, concern or chronic depression (Lee).

TBI fatigue: personal statements

- "Anytime I have to focus . . . I'm fatigued."
- "It's like you disconnect – I can't lift my arms, I just can't – I'm not here so I have to go to sleep."
- "I can't finish a project."
- "I just want to sleep, sleep, sleep, just can't come out of it."
- "Like sometimes I feel that I need to be alone, I have to be alone, yes, no more stimulation."
- "If we are thinking in terms of words to describe fatigue – overwhelmed."
- "Responding to noise and light and people, in a restaurant, I know, I have to sit on the end of the table and face the wall."
- "You lose what you were talking about, and you can't hear what anybody else is saying either, and you are trying to grab that thought. It is totally exhausting and fatiguing and it changes your life. It just makes me want to cry thinking about it just because it drives you so easily, you just want to go lay down, you don't want to participate anymore, you quit and a major part of that fatigue is that it changes how you react with everybody . . . but you lose it and its disconnecting on all levels, then you are frustrated with yourself."
Factors associated with fatigue in TBI

- Fatigue at baseline most powerful predictor
- Other predictors:
  - female gender
  - HO depression, marital discord, previous disability

Often high at onset, decreases in first year, and stabilizes or worsens after that

Path: Similar to that of course of rehab?

Suggested causes of fatigue in TBI

Multiple individual and interactive effects of possible causes including:

- Neuroanatomical
- Resource competition/overstimulation
- Skeletal Muscle
- Psychiatric
- Sleep related
- Endocrine

Causes of fatigue in TBI

Central Causes

- Left frontal cortical lesions-organic depression
- Increased basal ganglia activation to perform similar tasks

Suggested causes of fatigue in TBI

- Competition for reduced CNS resources (Van Zommern)
- Increased physiologic measures when performing divided attention tasks.
- Suggests that overstimulation may require utilization of already limited CNS mechanisms
- Is sleepiness in TBI an adaptation to limit overstimulation

Causes of fatigue in TBI

Skeletal Muscle

- Skeletal muscle mitochondrial function is depressed by inactivity
- pwTBI have low levels of activity both acutely and chronically
- Reduction (25-40%) in maximal oxygen uptake and reduced ventilatory threshold seen in pwTBI is consistent with impaired skeletal muscle mitochondrial function.
- Primary or secondary

Possible causes of fatigue in TBI

Neuropsychologic/neuropsychiatric impairment

- Depression- reactive and organic- 29-44% of all TBI patients with depression also CO fatigue
- Cognitive impairment-increased energy to perform the same mental task
- Pain/pain control
Possible causes of TBI fatigue: Sleep disorders

- Sleep disorders are common after TBI-(50-73%)
- Primary sx of insomnia/hypersomnia/apnea
- Some fatigued patients do not have sleep disorders
- Some patients with fatigue do not have sleep disorders
- Is the sleep disorder a symptom of the fatigue or a response?

Possible causes of TBI fatigue- post traumatic endocrine disorders

- Post-traumatic hypopituitarism\(\Rightarrow\) growth hormone dysfunction (15-20% of all TBI)
- Typically associated with self-report of fatigue, decreased exercise tolerance, depression, osteoporosis, hypercholesterolemia and atherosclerosis
- Has lead to treatment with HGH with some cases reporting improvement in ventilatory function

Interventions

- Modafinil-to manage hypersomnia
- High intensity blue light therapy to manage sleep disturbances
- Mindfulness training
- Cognitive behavioral therapy
- Growth hormone replacement
- Counseling for depression
- Earlier mobilization
- Control of stimulation

Fatigue measurement in TBI: The Barrow Neurologic Institute Fatigue Scale (BNI)

Items frequently reported by TBI patients on the BNI:

- “difficulty to perform a complex task without tiredness,”
- “difficulty to hold attention during an entire activity,”
- “difficulty not to go back to sleep during daytime”
- “difficulty not to take a nap during daytime.”

Fatigue in TBI

- There have not been any studies that have specifically assessed the effects of TBI fatigue on physical mobility
- Studies that have examined the effects of interventions have looked at fatigue, and not fatigability (physical performance)

Fatigue in Parkinson’s Disease

- There have not been any studies that have specifically assessed the effects of TBI fatigue on physical mobility
Fatigue in PD

• “sense of exhaustion unexplained by drug effects, other medical, or psychiatric disorders, present for a defined period, and associated with other fatigue-related symptoms, such as reduced motivation and nonrestorative rest, or constraints on activities.” (Friedman 2016)

Fatigue in PD

• I am a 74 year old man. I have had PD for three years. I can live with the PD (not great, but livable), but the fatigue is unbearable. As all my life I was full of superman energy, now I’m good for about an hour or so at a time and between the lightheadedness and the fatigue I’m wasted…I’ve been told to go see a shrink and start on anti-depressants. I don’t think I’m depressed.”

Fatigue in PD

• Common experience in persons with Parkinson’s Disease (pwPD), occurring with a prevalence of 38-53%
• Found to contribute directly and indirectly to restriction in activity and participation in daily activities
• Worsened by physical stressors.
• Motor and Non motor symptoms

Primary and secondary contributions to fatigue in PD

Primary
• Reduced serotonergic function in the basal ganglia and limbic structures
• Altered activation of the hypothalamic-pituitary-adrenal system
• “Sequential effect” - progressive slowness in speed or a decrease in amplitude of sequential movements

Secondary
• Sleep disturbance
• Depression
• Medications
• Increased energy cost of movement

Medical management

• Provigil
• Amphetamines (Methylphenidate)
• Rasagline (Azilect)
• Levadopa -Carbidopa

Parkinson’s Disease Fatigue Scale

• 16-item Self-report measure
• Fatigue over last few weeks
• Binary scoring (0/1)
• Score of ≥8 indicates the presence of significant fatigue
Does fatigue in PD have an effect of mobility?
Increased levels of fatigue associated with
• Decreased leisure physical activity
• Decreased vigorous physical activity
• Less time spent on ADL’s
• Lower diastolic BP and VO2
• Longer TUG

Effect of exercise on PD fatigue
• Limited evidence for positive effect as measured by QOL scales
• Limited examination of whether fatigue contributes to mobility impairment.

Effect of fatigue on mobility in PD
• Has not been examined
• Could be a reason for altered mobility in persons with PD
• How might fatigue affect motor performance in persons with PD?

Ongoing study at Hunter
• Patients with PD dx
• Randomized crossover design
• Mini-BESTest
• 6 minute walk or 6 minute rest
• Mini-BESTest repeated
• One week later, repeated with opposite 6 minute condition

Results by subject

<table>
<thead>
<tr>
<th>Subject #</th>
<th>H&amp;Y MBT</th>
<th>Unfatigued MBT</th>
<th>Fatigued MBT</th>
<th>VAFS Unfatigued</th>
<th>VAFS Fatigued</th>
<th>6MWT 0-3</th>
<th>6MWT 6-9</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1 3</td>
<td>0</td>
<td>-2</td>
<td>-4</td>
<td>+11</td>
<td>769</td>
<td>790</td>
</tr>
<tr>
<td>2</td>
<td>1.5 0</td>
<td>0</td>
<td>+16</td>
<td>+32</td>
<td>904</td>
<td>865</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>1.5 0</td>
<td>0</td>
<td>+8</td>
<td>+12</td>
<td>840</td>
<td>838</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>3 -1</td>
<td>-6</td>
<td>+3</td>
<td>+43</td>
<td>924</td>
<td>908</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>3 0</td>
<td>-3</td>
<td>+37</td>
<td>+63</td>
<td>792</td>
<td>776</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>2 0</td>
<td>1</td>
<td>-14</td>
<td>+5</td>
<td>804</td>
<td>764</td>
<td></td>
</tr>
</tbody>
</table>

Group results

<table>
<thead>
<tr>
<th>MBT Fatigued</th>
<th>MBT Unfatigued</th>
<th>MBT Fatigued</th>
<th>MBT Unfatigued</th>
<th>6MWT Min 0-3</th>
<th>6MWT Min 6-9</th>
<th>VAFS Fatigued</th>
<th>VAFS Unfatigued</th>
</tr>
</thead>
<tbody>
<tr>
<td>19.6</td>
<td>20.2</td>
<td>21.4</td>
<td>19.0</td>
<td>839</td>
<td>823</td>
<td>5.8</td>
<td>6.6</td>
</tr>
<tr>
<td>7.4</td>
<td>36.0</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

• MBT stayed stable in the resting condition, slightly worsened in the fatigued condition
• 6MWT slightly slower in second half (usually faster in non neurologic cases)
• Big increase in VAFS for fatigued condition, indicating that the 6MWT resulted in fatigue
Discussion

- Preliminary results suggest that at higher levels of disability there is worsening of performance with fatigue
- Was the fatigue experienced by the subjects “Parkinsonian” fatigue, or due entirely to the exertion?

A Case Example:
Parkinson’s Disease

Case study- Parkinson’s Disease

- 80 yo MWM dxed with PD 12 years ago
- Hoehn and Yahr 3.0
- BBS 49/56
- Parkinson’s Fatigue Scale -10/16
- Fixed thoracic kyphosis with forward head
- Fixed hip flexion contractures
- Minimal armswing and trunk rotation
- CO walking distance deteriorating over the last several years, with severe fatigue after a few minutes

<table>
<thead>
<tr>
<th>Minute</th>
<th>Cumulative Distance</th>
<th>Per-minute Distance</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>114’</td>
<td>114’</td>
</tr>
<tr>
<td>2</td>
<td>217’</td>
<td>103’</td>
</tr>
<tr>
<td>3</td>
<td>313’</td>
<td>94’</td>
</tr>
<tr>
<td>4</td>
<td>389’</td>
<td>76’</td>
</tr>
<tr>
<td>5</td>
<td>449’</td>
<td>60’</td>
</tr>
<tr>
<td>6</td>
<td>492’</td>
<td>43’</td>
</tr>
</tbody>
</table>

VAS-FΔ- 34mm

Interventions

- Thoracic extension strengthening and thoracic flexor stretching
- Hip flexor stretching/hip extensor strengthening
- Armswing training
  - Rationale: postural impairments and lack of armswing were increasing the energy cost of gait
- Intermittent walking-2 minutes on /2 minutes seated rest. Done once in AM, once in PM
  - Rationale: unable to train at sufficient volume continuously

6- minute walk test 3 weeks later

<table>
<thead>
<tr>
<th>Minute</th>
<th>Cumulative Distance</th>
<th>Per-minute Distance</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>126’</td>
<td>126’</td>
</tr>
<tr>
<td>2</td>
<td>244’</td>
<td>118’</td>
</tr>
<tr>
<td>3</td>
<td>354’</td>
<td>110’</td>
</tr>
<tr>
<td>5</td>
<td>554’</td>
<td>93’</td>
</tr>
<tr>
<td>6</td>
<td>642’</td>
<td>88’</td>
</tr>
</tbody>
</table>

VAS-FΔ- 34mm

VAS-FΔ- 21mm
Fatigue in Neurologic Disorders: Pathophysiology, Evaluation, and Intervention

Summary

- Fatigue is found in most neurologic diseases, and is a significant contributor to disability
- Subjective perceptions of fatigue and objective fatigability can both occur
- Fatigue can have central, peripheral, primary, and secondary components
- By addressing fatigue, clinicians can improve rehab outcomes

Citations


Time for Questions and Discussion

Dr. Herb Karpatkin
herbkarpt@gmail.com

Dr. Evan T. Cohen
cohenet@shp.rutgers.edu

Dr. Stefanie DiCarrado
sdicarrado@gmail.com
