

Are We There Yet? Fatigue Management in HIV



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Objectives

- Provide a background of HIV-related fatigue (HRF) including definitions and causes.
- Describe exercise, pharmacological, and behavioral interventions that have some level of evidence
- Discuss future research directions

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HIV-Related Fatigue: Definition

Fatigue is the awareness of a decreased capacity for physical and/or mental activity due to an imbalance in the availability, utilization, and/or restoration of resources needed to perform activity.

- **Tiredness not relieved by rest or sleep**
- **Often associated with physical and psychological symptoms**
- **Can be acute or become chronic across the trajectory of cancer and cancer treatment**
- **May not correspond to patient's level of exertion**



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(Aronson et al., 2007)

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HIV-Related Fatigue: Background

- Most common symptom experienced by adult HIV patients
- Characterized by impaired physical, cognitive, and social function; exhaustion; social withdrawal
- True prevalence unknown due to variations in measurement and domain; estimates between 33-88% of patients; majority of studies agree >50% of HIV patients experience HRF
- Most commonly occurs during HIV treatment; can persist chronically following initiation of treatment and months to years later



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BarrosoJ & Voss, J. G., 2013;
Perazzo, Webel, Boss, & Prince-Paul, 2017

HIV-Related Fatigue: Causes

Multifactorial- no singular cause identified

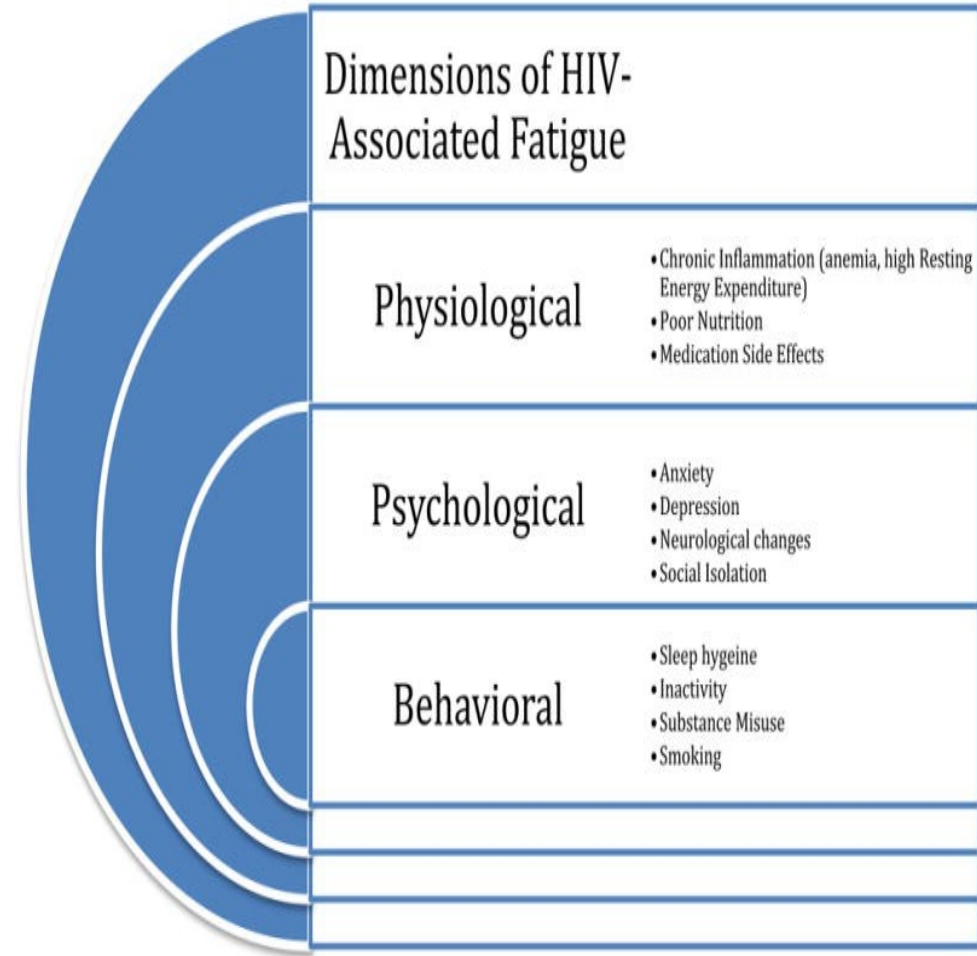
- **Physiological:** altered protein and hormone levels, inflammation, toxicities, pain, anemia, pre-existing conditions
- **Psychological:** depression, anxiety, stress, isolation
- **Behavioral:** decreased physical activity

Unclear:

- Antiretroviral medications
- CD4 counts & viral loads

Symptom Clusters

- Sleep, depression, pain, weakness, and anxiety



How We Assess and Measure Fatigue

- **Self-Report Measures:**
 - Most Common
 - Questionnaires
 - Clinical Interview (e.g. “On a scale of 0 to 10...”)
 - Gives us an idea of the intensity, frequency, and duration of fatigue as reported by a patient at a given time point
- **Limitations:**
 - High variability across studies (e.g. different measures, different intentions to measure fatigue, different ways of asking)
 - Make it difficult to determine true efficacy of interventions
 - Assess different timeframes

Measuring Fatigue

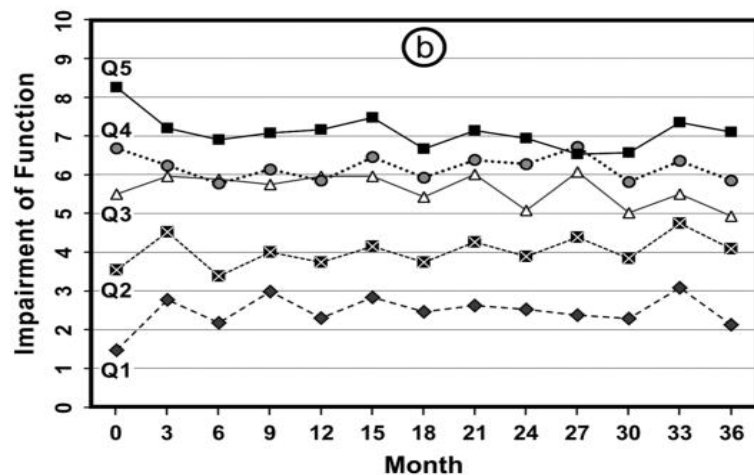
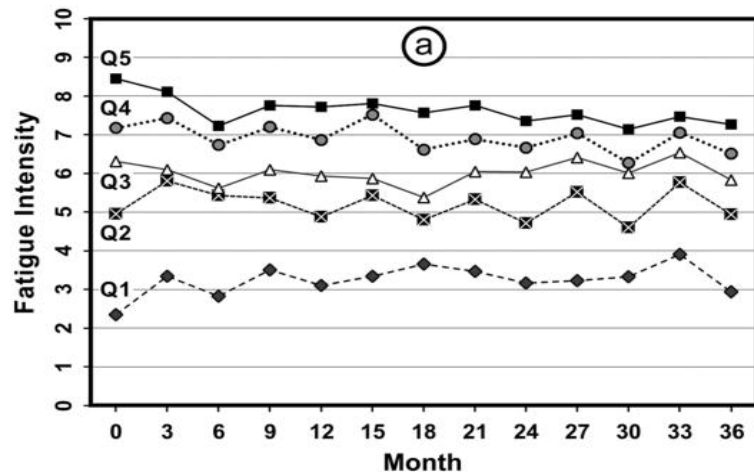
- Fatigue Scale 、 Fatigue Feeling Tone Checklist 、 Symptom Distress Scale 、 Fatigue Scale 、 Fatigue Observation Checklist 、 Piper’s Fatigue Self-Report Scale 、 Lee’s Visual Analog Scale for Fatigue 、 Fatigue Seventy Scale 、 the Multidimensional Assessment of Fatigue



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HIV-related fatigue is chronic and persists for years



- Longitudinal study of 128 PLWH living in North Carolina
- Every three month assessment for 3 years
- Intensity of fatigue, impact on daily living, and consequences were assessed
- Fatigue does not spontaneously remit
- Severity was unchanged after three years
- Stress and depression increased fatigue
- Fatigue interfered most with instrumental activities of daily living
- Fatigue interfered with work, family, and social life.



What interventions are effective for preventing and treating fatigue in People Living with HIV?



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What is the current knowledge of exercise and fatigue?

O'Brien and colleagues (2010) published major review summarizing 14 studies and 30 meta-analyses



Conclude that aerobic exercise, and/or a combination of aerobic exercise with progressive resistance exercise are safe and related to improvements in adults that continuously exercised

- Maximum Oxygen Consumption
- Body Composition
- Psychological status
- Exercise reduces fatigue in cancer populations
- 12-week aerobic exercise program improved time on treadmill (proximarker for physiological fatigue)
- 6-week aerobic/resistance program reduced fatigue but not statistically



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(Smith, Neidig, Nickel, Gladys, Para, & Fass, 2001; Jagers, et al., 2015)

Physical Activity Level in People Living with HIV



- Cleveland prospective study with 90 men and women above and below 50 years of age
- 1 week follow-up at baseline and 7 days later with diary and actigraphy to understand the degree of home-based physical activity
- People with high and low fatigue, increased physical activity was associated to decrease fatigue levels
- No relationship with sleep or gender

- Boston study with 23 HIV+ and 23 HIV- negative men cohort study
- Continuous accelerometer at home for 3 weeks compared to lab-based 6 Minute walk test
- Gait speed was significantly lower in HIV+ despite absence in the 6 Minute walk test
- HIV+ spent the lowest quartile of activity compared with uninfected



Yoga Interventions and HRF Effectiveness



- Indian study with 60 adult participants
- 30 intervention 30 wait-list control RCT
- 8 weeks for 5 days 1 hour of intense yoga practice with meditation, relaxation practices, and a closing prayer
- Both groups were similar in demographics and physical and mental health indicators.
- Fatigue was assessed before after 2 month
- Fatigue severity dropped from 48 to 22 while it stayed the same for the control group.

- Indian study with 18 children/adolescents
- Single pre-post test study
- 6 months for 5 days 1 hour of yoga
- Improved school fatigue and total fatigue scores significantly and increased general fatigue and cognitive fatigue scores but sample was to small to see statistical significance.



What is the current knowledge of pharmacological interventions and HIV-related fatigue?



Weak Evidence

- Thyroid Hormones (no trials)
- Hyperbaric Oxygen Therapy of 20/17 improved in 1994
- Testosterone Therapy in men with hypogonadal syndrome
- Last trial in 2008

Stronger Evidence in HRF patients with depression

- Psychostimulants (mainly in EOL)
 - Modafinil
 - Dextroamphetamine
 - Last trial in 2001



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Derry 1996; Reillo, Altieri, & Neubauer, 1994;
Jordan, 1998; Knapp et al., 2008)

What is the current knowledge of psychological/behavioral interventions and HIV-related fatigue?



- French qualitative study with 50 participants
 - Grounded Theory resulted in three themes
 - Expressing fatigue made HIV visible
 - Gendered fatigue and stigma experiences
 - Uses and effects of expressing HRF
-
- Health education intervention to teach disease self-management skills and information: symptom assessment and management, medication use, physical exercise, relaxation, doctor-patient communication, and nutrition does not improve fatigue



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(Schuft, Duval, Thomas, Ferez, 2018;
Gifford, Laurent, Gonzales, Chesney, & Lorig,
1998)

What is the current knowledge of psychological/behavioral interventions and HIV-related fatigue?



- Secondary analysis of 67 PLWH who completed daily surveys
- Brief scales to measure control beliefs, mood, stress, coping, social support, experience of stigma, and motivation
- Initial fatigue predicted subsequent overall level of control beliefs, mood, stress, coping, and social support
- Bi-directional relationship between stress and stigma predicted later fatigue
- Self-perpetuating cycle of stress, support and fatigue on a daily basis



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(Cook, Hartson, Schmiege, Jankowski, Starr, & Meek, 2016)

What is the current knowledge of psychological/behavioral interventions and HIV-related fatigue?



- Cognitive Behavioral Intervention RCT Study with 33 People Living with HIV in Pennsylvania
- Three CBT session at week 2, 4 and 6
- Measures collected 30, 60 and 90 days
- Fatigue declined significantly after 2 month with an effect size of $-.52$ for usual fatigue and $-.46$ for worst fatigue



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(Doerfler & Goodfellow, 2016)

What are gaps in the current intervention research in HIV-related fatigue?



- Intervention effectiveness
- Dosing of intervention to be appropriate
- Duration of intervention to be effective
- Long term effects and need for booster
- Fatigue happens to a person in an environment
- Biological marker for diagnosis, prognosis, long term follow-up



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Why is this Biomarker research so important?

- We know that inflammation, neuroendocrine dysfunction, and genetic variations occur as part of HIV disease trajectory and treatment
- We know that these factors are related to musculoskeletal dysfunction, sleep disturbance, depression, cognitive disturbance, poor nutrition, and poor functional status

What Biomarkers Could Potentially Contribute:

- Gaining a more complete understanding of the mechanisms that cause fatigue in PLWH
- Predicting PLWH at highest risk for severe fatigue
- Determine who to tailor interventions to based on objective measures that are predictive of fatigue trajectory

Challenges we must address

- Increasing our understanding of these associations
- Examining these associations and how they change over time
- Understanding confounding explanations (e.g. age, other illnesses, medications etc.)



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Current HRF Intervention Studies

Project Title/Grant Type	GrantPIs (Institution)
Impact of physical activity routines and dietary intake on the longitudinal symptom experience of the people living with HIV (PROSPER-HIV) - R01	Webel Allison Case Western Reserve University
Mentoring and research in self-management for health promotion and disease prevention - K24	Schnall Rebecca Columbia University
Return to work RCT: counseling after fatigue treatment in HIV/AIDS - R01	Rabkin Judith New York Psychiatric Institute
Developing resilience intervention for older HIV-infected women – R34	Psaros Christina Massachusetts General Hospital



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