Recommendations from the 3rd Stroke Recovery & Rehabilitation Roundtable: A roadmap for research in post-stroke fatigue

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on behalf of the Fatigue Task Force

https://strokerecoveryalliance.com/

Acknowledgments & Disclosures

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The third Stroke Recovery and Rehabilitation Roundtable (SRRR3) is an initiative of ISRRA.

The World Stroke Organisation (WSO) endorses the goals of the Stroke Recovery and Rehabilitation Roundtable research activity which are consistent with the mission of the WSO.

Affects half of all people living with stroke

Thinking

Planning /

(Lancet 2022)

4th highest research priority for people with stroke

Physical fatigue

Emotional fatigue

Review

International Journal of Stroke WSO

Global prevalence

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66 studies, n=11,697

Pooled global prevalence

47% (95% CI 43 to 50)

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SRRR | Stroke Recovery and Rehabilitation Roundtable

Guidelines

A roadmap for research in post-stroke fatigue: Consensus-based core recommendations from the third Stroke Recovery and Rehabilitation Roundtable

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Abstract

Rationale: Fatigue affects almost half of all people living with stroke. Stroke survivors rank understanding fatigue and how to reduce it as one of the highest research priorities.

Methods: We convened an interdisciplinary, international group of clinical and pre-clinical researchers and lived experience experts. We identified four priority areas: (1) best measurement tools for research, (2) clinical identification of fatigue and potentially modifiable causes, (3) promising interventions and recommendations for future trials, and (4) possible biological mechanisms of fatigue. Cross-cutting themes were aphasia and the voice of people with lived experience. Working parties were formed and structured consensus building processes were followed.

Results: We present 20 recommendations covering outcome measures for research, development, and testing of new interventions and priority areas for future research on the biology of post-stroke fatigue. We developed and recommend the use of the Stroke Fatigue Clinical Assessment Tool.

Review Article

Mechanisms of Post-Stroke Fatigue: A Follow-Up From the Third Stroke Recovery and Rehabilitation Roundtable

Annapoorna Kuppuswamy, PhD[1,2], Sandra Billinger, PhD[3], Kirsten G. Coupland, PhD[4], Coralie English, PhD[5], Mansur A. Kutlubaev, PhD[6], Lorimer Moseley, DSc[7], Quentin J. Pittman, PhD[8], Dawn B. Simpson, PhD[9], Brad A. Sutherland, PhD[10], Connie Wong, PhD[11], and Dale Corbett, PhD[12]

Abstract

Background. Post-stroke fatigue (PSF) is a significant and highly prevalent symptom, whose mechanisms are poorly understood. The third Stroke Recovery and Rehabilitation Roundtable paper on PSF focussed primarily on defining and measuring PSF while mechanisms were briefly discussed. This companion paper to the main paper is aimed at elaborating possible mechanisms of PSF. *Methods.* This paper reviews the available evidence that potentially explains the pathophysiology of PSF and draws parallels from fatigue literature in other conditions. We start by proposing a case for phenotyping PSF based on structural, functional, and behavioral characteristics of PSF. This is followed by discussion of a potentially significant role of early inflammation in the development of fatigue, specifically the impact of low-grade inflammation and its long-term systemic effects resulting in PSF. Of the many neurotransmitter systems in the brain, the dopaminergic systems have the most evidence for a role in PSF, along with a role in sensorimotor processing. Sensorimotor neural network dynamics are compromised as highlighted by evidence from both neurostimulation and neuromodulation studies. The double-edged sword effect of exercise on PSF provides further insight into how PSF might emerge and the importance of carefully titrating interventional paradigms. *Conclusion.* The paper concludes by synthesizing the presented evidence into a unifying model of fatigue which distinguishes between factors that pre-dispose, precipitate, and perpetuate PSF. This framework will help guide new research into the biological mechanisms of PSF which is a necessary prerequisite for developing treatments to mitigate the debilitating effects of post-stroke fatigue.

Identification of 4 priority areas

How do we **measure** fatigue?

What are the most likely causes of fatigue?

How do we **differentiate** fatigue from other conditions?

What are the most promising **interventions**?
How do we **develop and test** them?

Overarching considerations:
What are the priorities/perspectives of people with lived experience?
How are people with aphasia included/considered in all key areas
How do we define, describe and explain fatigue?

Recommendation: Definition

"Post-stroke fatigue is a feeling of lack of energy, weariness, or exhaustion that can be overwhelming, and which involves physical, perceptual, emotional and cognitive aspects not relieved by rest and affecting a person's daily life"
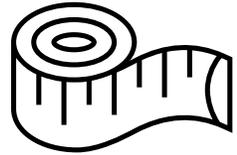
How do we measure fatigue?

The challenge:
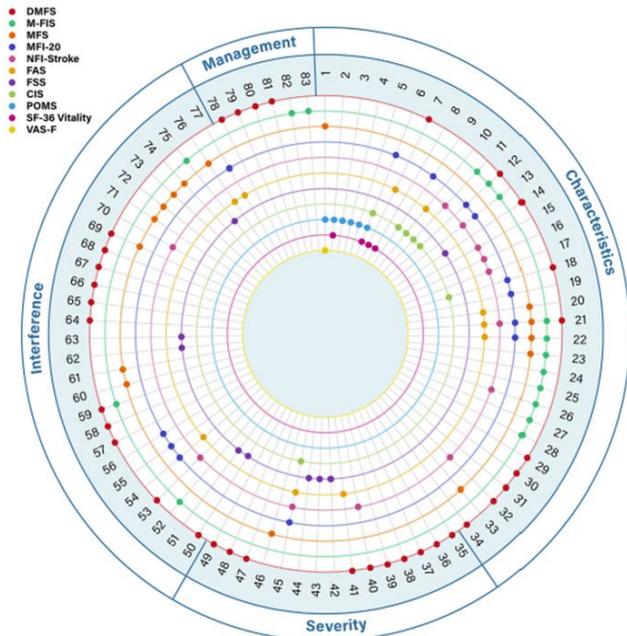
Shortlist of 6 measures:

- Frequency of use

- Scales for stroke fatigue
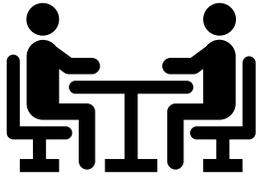
  - FAS
  - FSS
  - M-FIS
  - MFI-20
  - DMFS

Ranked order graph voting:

- Defined characteristics of a 'good' measure

Survey

- Rank characteristics: order of importance

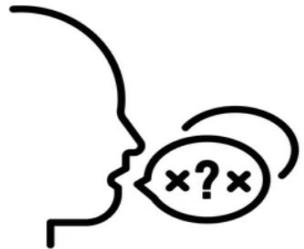- Rank 6 outcome measures on performance for each key characteristics

Fatigue versus other conditions? ?

Recommendation

? **Is fatigue a problem?**

Could there be a mood disorder?

Is sleep a problem?

Pain, low BP, other chronic conditions?

Physical activity, diet, alcohol?

Medication side-effects?

New memory issues?

Communication disability?

Stroke Fatigue Clinical Assessment Tool (SF-CAT)

Ask your patient/client if they:	
Assess whether fatigue is an issue	
Feel tired all the time or get tired quickly since your stroke? Need additional help and support for this?	Y: screen for the potential causes and precipitating factors (below), use FSS-7 for quantitative assessment
Consider mood disorders	
Feel sad or depressed? Feel anxious or stressed?	Y: screen for depression (e.g. PHQ9) Y: screen for anxiety (e.g. GAD7)
Consider sleep quality	
Have difficulty falling or staying asleep? Wake up frequently, or wake feeling unrefreshed? Fall asleep unintentionally during the day?	Y: screen for insomnia, depression, and/or anxiety Y: screen for sleep apnea/other sleep disorders (e.g. GSAQ)
Consider new/uncontrolled conditions	
Have any new pain that bothers you? Have hypotension? Have chronic conditions (diabetes, hypothyroidism, anemia, etc.) that are not optimally controlled?	Y: assess pain Y: address/refer Y: address/refer
Consider physical/nutrition status	
Exercise regularly? Keep active? Regularly miss meals?	N: address/refer Y: address/refer
Consider role of medication	
Get side effects from your medications (e.g. beta blockers, benzodiazepines, polypharmacy)?	Y: address/refer
Drink alcohol?	Y: how much and how often? address/refer
Consider new/undiagnosed cognitive impairment	
Have new problems remembering things or concentrating?	Y: screen for cognitive impairment (e.g. MoCA)
Consider speech and/or language disorder	
Do you often feel fatigued after talking or listening to others talk?	Y: Screen (e.g. sections 9 and 10 NIH Stroke Scale) refer as appropriate

Recommendations

The challenge:

- We don't know what causes fatigue

- Identification of 12 potential causes

- Prioritisation and ranking of potential causes

- Evidence searches and synthesis

Priority areas for research:

Inflammation & immune dysregulation

Dopamine pathways
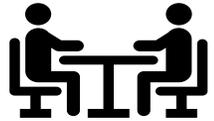
Neural network dysfunction

Precise delineation of lesions

Recommendations

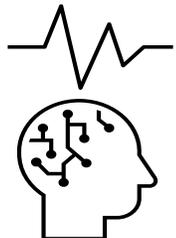**Promising interventions** for research:

Psychoeducational approaches

Dopamine re-uptake inhibitors

Exercise &/or exercise memetics

Neuromodulation therapies

Future clinical trials should:

- Be based on a theoretical mechanism

- Use the FSS-7 as primary outcome

- Include people with aphasia

- Be codesigned with lived experience

- Follow the SRRR Trial Development & Control Intervention Design frameworks

Clinical Guidelines Consensus level evidence

NATIONAL CLINICAL GUIDELINE FOR STROKE
for the United Kingdom and Ireland

https://www.strokeguideline.org/

- Standardized fatigue **assessment** (early & 6-month)

  - Fatigue Severity Scale

    Fatigue assessment scale, modified Fatigue Impact Scale

  - Ax for factors that could precipitate / exacerbate fatigue

Australia & New Zealand Living Guidelines for Stroke Management
https://informme.org.au/guidelines/living-clinical-guidelines-for-stroke-management

Stroke FOUNDATION

- Provide accessible **information and education**

  - Early reassurance, peer support, include support crew

- **Management – multifactorial** approaches

  - Acceptance & adjustment

  - Diary & scheduling

  - Pacing activities, rest

  - Compensation / adaptation of tasks

AHA Scientific Statement

Poststroke Fatigue: Emerging Evidence and Approaches to Management
A Scientific Statement for Healthcare Professionals
From the American Heart Association

Guidelines

International Journal of Stroke WSO

Canadian Stroke Best Practice Recommendations: Mood, Cognition and Fatigue following Stroke, 6th edition update 2019

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From recommendations to action

At least 20 ongoing trials targeting post-stroke fatigue

- Development and testing of new comprehensive assessment – Oslo, Norway

- Revision and testing of assessments appropriate for people with aphasia - New York, USA

- Education programs – Nottingham, UK and Newcastle, Australia

- Medications – Newcastle, Australia and Toronto, Canada

- Exercise – Umea, Sweden; Toronto, Canada; Aalborg, Denmark

- Non-invasive brain stimulation – Leeds, UK and New York, USA