Self-perceived fatigue and its impact on functional decline and mortality

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Congress in Geriatric Rehabilitation
Vrije Universiteit Brussels
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Fatigue

- A common complaint in older adults
- One of the most frequent reasons for encounter in GP
- Often a symptom of underlying illness
- Prevalent in certain medical treatments
- However, for many older persons it is not possible to identify a psychological or physiological explanation
- Fatigue is thus a complaint which is poorly understood
Definition of fatigue
Fatigue is an ambiguous concept, which especially relates to the reaction to physical and psychological work loads, but the concept may also include many different experiences and states of mind, e.g. the experience of exhaustion, impaired energy and vitality and need for sleep.

Fatigue is the normal physiological reaction in an organism, a part of the body or an organ, which has reached the limits of its capacity after heavy strain.

Measures of fatigue

- Global measures

- More complex multidimensional measures of fatigue

- More complex unidimensional measures of fatigue in relation to daily activities
Rationale for studying fatigue in daily activities in the Danish aging studies

Measuring fatigue in daily activities makes it possible to discriminate different levels of functional ability in well-functioning older adults.

Fatigue may be an early sign of later disability and thus an early sign of the aging process.

Gives possibilities for identification of older adults at risk of functional decline and thus for intervention.

Fatigue measured as Tiredness in daily activities

**Mob-T**
- Transfer
- Get outdoors
- Walk indoors
- Walk outdoors in nice weather
- Walk outdoors in poor weather
- Walk on stairs

**Lower Limb-T**
- Use toilet
- Wash lower body
- Dress lower body
- Take shoes/stockings on/off
- Cut toenails

Proportion of 70, 75-, 80-, and 85-year old men and women with good functional ability

Source: Avlund 2004

Odds ratios (95% CI) for onset of disability at five year follow-up by fatigue at age 75

<table>
<thead>
<tr>
<th></th>
<th>Mobility disability (n = 510)</th>
<th>Disability in ADL (n = 429)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tired in 2-4 activities</td>
<td>3.2 (1.4-7.6)</td>
<td>2.1 (1.0-4.2)</td>
</tr>
<tr>
<td>Tired in 1 activity</td>
<td>1.7 (0.8-3.8)</td>
<td>2.0 (1.0-3.9)</td>
</tr>
<tr>
<td>Not tired</td>
<td>1.0</td>
<td>1.0</td>
</tr>
</tbody>
</table>

Adjusted by sex, chronic diseases, cognitive function, self-rated health, depressive symptoms, housing tenure, social relations, physical activity

Source: Avlund et al. J Clin Epidemiol 2002
Will the results be the same with a shorter follow-up period?

Odd ratios (95% CI) for onset of mobility disability at 1½ year follow-up by fatigue

<table>
<thead>
<tr>
<th></th>
<th>Men (n = 648)</th>
<th>Women (n = 748)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tired in 1-6 activities</td>
<td>2.2(1.0-5.3)</td>
<td>3.5(1.9-6.5)</td>
</tr>
<tr>
<td>Not tired</td>
<td>1.0</td>
<td>1.0</td>
</tr>
</tbody>
</table>

Adjusted by ADL-disability, home help, falls, use of medication, social relations, psychological function, sense of coherence, control over own life and physical activity

Source: Avlund, Vass, Hendriksen. Age Ageing 2003
Will the results be the same with a longer follow-up period? And in a younger age-group?

Proportions of tired and not tired 70-year old men and women with functional decline during the next 15 years.

- **Women**
- **Men**
Odds ratios (95%) for onset of disability and mortality at 5-, 10- and 15- year follow-up by fatigue at age 70
(Adjusted by sex, number of diseases, VO₂ max)

<table>
<thead>
<tr>
<th></th>
<th>5-year follow-up</th>
<th>10-year follow-up</th>
<th>15-year follow-up</th>
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</thead>
<tbody>
<tr>
<td><strong>Onset of disability</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(n = 564)</td>
<td>9.09 (4.71-17.54)</td>
<td>1.87 (1.17-2.99)</td>
<td>1.84 (0.93-3.64)</td>
</tr>
<tr>
<td><strong>Mortality</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(n = 705)</td>
<td>1.83 (1.17-2.85)</td>
<td>2.16 (1.52-3.05)</td>
<td>2.31 (1.64-3.24)</td>
</tr>
</tbody>
</table>


Fig. 1 - Survival curves among 70-year-olds with and without fatigue during 21 year follow-up.

Source: Avlund 2010
Is fatigue also related to onset of walking limitations?

Onset of walking limitation at 5-year follow-up

Measured by a 10 meter laboratory test using a stop watch

Onset of walking limitations was defined as onset into the slowest quartile of maximal walking speed: > 1.33 m/sec.
Odds ratios (95% CI) for onset of walking limitations at 5-year follow-up by fatigue (n = 319)

<table>
<thead>
<tr>
<th></th>
<th>Crude</th>
<th>Adjusted*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tired</td>
<td>3.97(2.16-7.29)</td>
<td>2.78(1.43-5.41)</td>
</tr>
<tr>
<td>Not tired</td>
<td>1.0</td>
<td>1.0</td>
</tr>
</tbody>
</table>

* Adjusted by sex, walking speed and chronic diseases at baseline

Source: Avlund, Sakari-Rantala, Rantanen et al. J Am Geriatr Soc. 2004

Fatigue in daily activities predictive of

- Onset of disability after 1½, 3, 5, 10, and 15 years
  (Avlund et al. 1995-2008)
- Onset of functional limitations
  (Avlund et al. 2004)
- Mortality
  (Avlund et al. 1998; 2003; Schultz-Larsen et al. 2007)
- Use of health and social services
  (Avlund et al. 2001)
- Change and stability in physical activity
  (Poulsen et al. 2007)
Fatigue in daily activities

Both in young, young old and old-old

Among persons in different geographic localities in Denmark, Sweden, Finland, and Germany

Sources: Avlund et al. 1995-2008; Schultz-Larsen et al. 1992-2007; Poulson et al. 2006

Factors related to fatigue in non-disabled older adults

Social position
Pathology
Comorbidity
Specific diseases
Use of medication

Impairments
Muscle strength
Pain
Cognitive performance
VO2 Max

Walking limitations

Psychological factors
Depressive mood

Fatigue in daily activities

Sources: Schultz-Larsen 1992; Avlund et al. 1994a; 1997; 2003c; 2006; 2007a
Explanatory factors?

The associations between fatigues and onset of disability were attenuated but stayed strong and significant when adjusted by

- Socio-economic variables
- Pathology
  - i.e. comorbidity, specific diseases, medication
- Impairments
  - i.e. FEV1, VO2 Max,
  - Walking limitations

But what about muscle strength, cognitive performance, depression?

Sources: e.g. Avlund et al. 2002; Avlund et al. 2006; Schultz-Larsen et al. 2007

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Example: Odds ratios (95% CI) for onset of walking limitations at 5-year follow-up by fatigue (n = 319), adjusted by muscle strength

<table>
<thead>
<tr>
<th></th>
<th>Crude</th>
<th>Adjusted&lt;sup&gt;2&lt;/sup&gt;</th>
<th>Adjusted&lt;sup&gt;3&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fatigue</td>
<td>3.97(2.16-7.29)</td>
<td>3.07(1.59-5.93)</td>
<td>2.70(1.36-5.35)</td>
</tr>
<tr>
<td>Knee strength&lt;sup&gt;1&lt;/sup&gt;</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>weak</td>
<td>6.39(3.02-13.5)</td>
<td>2.55(0.94-6.91)</td>
<td></td>
</tr>
<tr>
<td>medium</td>
<td>1.81(0.86-3.82)</td>
<td>1.02(0.41-2.54)</td>
<td></td>
</tr>
</tbody>
</table>

1. Adjusted by weight
2. Adjusted by sex and baseline walking speed
3. Further adjusted by knee strength
Example: Odds ratios (95% CI) for onset of walking limitations at 5-year follow-up by fatigue (n = 319), adjusted by cognitive performance

<table>
<thead>
<tr>
<th></th>
<th>Crude</th>
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<th>Adjusted&lt;sup&gt;2&lt;/sup&gt;</th>
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</thead>
<tbody>
<tr>
<td>Fatigue</td>
<td>3.97(2.16-7.29)</td>
<td>3.07(1.59-5.93)</td>
<td>2.98(1.53-5.80)</td>
</tr>
<tr>
<td>Word fluency</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>weak</td>
<td>1.99(1.01-3.91)</td>
<td>1.41(0.66-3.03)</td>
<td></td>
</tr>
<tr>
<td>medium</td>
<td>1.61(0.82-3.14)</td>
<td>1.29(0.61-2.72)</td>
<td></td>
</tr>
</tbody>
</table>

1. Adjusted by sex and baseline walking speed
2. Further adjusted by word fluency

Example: Odds ratios (95% CI) for onset of walking limitations at 5-year follow-up by fatigue (n = 319), adjusted by depressive mood

<table>
<thead>
<tr>
<th></th>
<th>Crude</th>
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<th>Adjusted&lt;sup&gt;3&lt;/sup&gt;</th>
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</thead>
<tbody>
<tr>
<td>Fatigue</td>
<td>3.97(2.16-7.29)</td>
<td>3.07(1.59-5.93)</td>
<td>3.20(1.63-6.28)</td>
</tr>
<tr>
<td>Depr mood</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>often</td>
<td>2.46(1.27-4.76)</td>
<td>1.83(0.88-3.78)</td>
<td></td>
</tr>
<tr>
<td>sometimes</td>
<td>1.42(0.75-2.69)</td>
<td>1.22(0.59-2.49)</td>
<td></td>
</tr>
</tbody>
</table>

1. Measured by the CESD depressive mood-subscale
2. Adjusted by sex and baseline walking speed
3. Further adjusted by depressive mood
Conclusions

• Fatigue is influenced by multiple potential modifiable factors
• None of these factors explain the associations between fatigue and the various outcomes
• Fatigue may be thus be regarded as a subjective measure of frailty
• Fatigue may be used to identify non-disabled individuals at high risk of functional decline

New research questions

Is the association between fatigue and functional decline explained by

• Biological factors (e.g. low grade inflammation, mitochondrial function, telomer length, immune function)?
• Other physiological factors (e.g. muscle fatigue)
• Social, psychological, physiological and health factors throughout the life course, e.g. factors in childhood, adolescence, young adulthood, midlife?
• Psychological factors (other measures, concepts)?
• Sleep problems?
• Pain?
• Medication?
• Health behaviour?
New research questions

Are other measures of fatigue related to functional decline?

Is fatigue related to other early indicators of aging (e.g. biological indicators)?

Is fatigue in midlife related to functional decline in old age?

Does it have effect with specific intervention on fatigue?

Copenhagen Aging and Midlife Biobank (CAMB)

General purpose:

To establish a midlife biobank with focus on biological, cognitive and social variables - in order to study aging processes over the entire life course

www.camb.dk
The Copenhagen Aging and Midlife Biobank (CAMB) – to be established 2009-2011

Pregnancy/Birth ⇔ Childhood/adulthood ⇔ Midlife

The Danish Longitudinal Study on Work, Unemployment and Health (born 1949, 1959)
Age 40/50 ⇔ 45/55

The Metropolit Study (born 1953)
Age 0 › 12 > 18 > 51

The Copenhagen Perinatal Cohort (born 1959-61)
Age 0 › 1 - 6 > 20 ⇔ 34 ⇔ 45

Copenhagen Aging and Midlife Biobank (CAMB)
Follow-up study 2009 – 11 including blood samples, questionnaire, physical and mental tests

20,000 will be invited, we expect/hope for 7,000 participants

The data collection takes place at the National Research Center for the Working Environment in Copenhagen

Data collection started up 20 April 2009

By 29 May 2010: 3,000 participants
Perspectives - CAMB

• CAMB provides an outstanding possibility to study the influences of factors early in life (childhood and adolescence) on early aging in midlife

• CAMB will form the basis for numerous future studies on the importance of biological, cognitive and environmental factors in midlife for premature aging in later life

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Funded by the Velux Foundation

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Funded by the Nordea Foundation

UNIVERSITY OF COPENHAGEN

Aging Clinical and Experimental Research

REVIEW ARTICLES

Fatigue in older adults: an early indicator of the aging process?**

Kirsten Avlund†,‡,§,∥

†Department of Social Medicine, Institute of Public Health, University of Copenhagen, ‡Research Centre for Prevention and Health, Copenhagen County, §Danish Aging Research Centre, University of Aarhus, Odense and Copenhagen, ∥Center for Healthy Aging, University of Copenhagen, Denmark

ABSTRACT. The aim of this paper is to give an overview of research on fatigue in older adults, with a focus on fatigue as an early indicator of the aging process. Fatigue is a strong predictor of functional limitations, disability, mortality, and other adverse outcomes in young-old and old-old populations, between men and women, and in different geographic localities. Several biological, physiological and social explanations are proposed. Fatigue may be seen not only as a self-reported indicator of frailty, defined as a physiologic state of increased vulnerability to stresses, which results from decreased physiologic reserves and even dysregulation of multiple physiologic systems, but also this state may be accelerated because of the cumulative impact of social, mental and biological factors throughout life. (Aging Clin Exp Res 2016; 22: 200–11) ©2010 Institute of Gerontology