



# HHS Public Access

Author manuscript

*Ear Hear.* Author manuscript; available in PMC 2017 July 01.

Published in final edited form as:

*Ear Hear.* 2016 ; 37(Suppl 1): 136S–144S. doi:10.1097/AUD.0000000000000289.

## A Taxonomy of Fatigue Concepts and Their Relation to Hearing Loss

Benjamin W.Y. Hornsby<sup>1</sup>, Graham Naylor<sup>2</sup>, and Fred H. Bess<sup>1</sup>

<sup>1</sup>Department of Hearing & Speech Sciences, Vanderbilt Bill Wilkerson Center, Vanderbilt University School of Medicine, Nashville, TN, USA

<sup>2</sup>MRC/CSO Institute of Hearing Research, Scottish Section, Glasgow, UK

### Abstract

Fatigue is common in individuals with a variety of chronic health conditions and can have significant negative effects on quality of life. Although limited in scope, recent work suggests persons with hearing loss may be at increased risk for fatigue, in part due to effortful listening that is exacerbated by their hearing impairment. However, the mechanisms responsible for hearing loss-related fatigue, and the efficacy of audiological interventions for reducing fatigue, remain unclear. To improve our understanding of hearing loss-related fatigue, as a field it is important to develop a common conceptual understanding of this construct. In this paper the broader fatigue literature is reviewed to identify and describe core constructs, consequences and methods for assessing fatigue and related constructs. Finally, our current knowledge linking hearing loss and fatigue is described and may be summarised as follows:

- Hearing impairment increases the risk of subjective fatigue and vigor deficits.
- Adults with hearing loss require more time to recover from fatigue after work, and have more work absences.
- Sustained, effortful, listening can be fatiguing.
- Optimal methods for eliciting and measuring fatigue in persons with hearing loss remain unclear and may vary with listening condition.
- Amplification may minimize decrements in cognitive processing speed during sustained effortful listening.

---

Address correspondence to Benjamin W. Y. Hornsby, Vanderbilt Bill Wilkerson Center, Room 8310 Medical Center East, South Tower, 1215 21st Ave. South, Nashville, TN 37232-8242 USA. ben.hornsby@vanderbilt.edu.

Financial Disclosures/Conflict of Interest: The first author's work on this project was supported, in part, by a grant from Oticon A/S. The second author was an employee of Oticon A/S at the time this work was carried out. The third author has no financial relationships relevant to this article to disclose.

This work was supported, in part, by a grant to the first author from Oticon A/S, by the National Institute on Deafness and Communication Disorders (NIDCD) of the National Institutes of Health under award number R21DC012865 (Hornsby-PI) and by the Institute of Education Sciences (IES), U.S. Department of Education, through Grant R324A110266 to Vanderbilt University (Bess-PI). Any opinions expressed are those of the authors and do not necessarily represent the views of the National Institutes of Health, the Institute of Education Sciences, or the U.S. Department of Education.

Future research is needed to develop reliable measurement methods to quantify hearing loss-related fatigue; explore factors responsible for modulating fatigue in people with hearing loss; and identify and evaluate potential interventions for reducing hearing loss-related fatigue.

## Keywords

cognition; fatigue; energy; vigor; mood; hearing loss; sleepiness; weariness; effort; listening effort

---

## I. DEFINING FATIGUE

Fatigue is a complex construct that has been defined many ways. In fact, a standardized definition does not exist. Definitions found in the literature vary, in part, based on the discipline of the person describing the construct (e.g., layperson, physiologist, cognitive psychologist, physician) and the focus of their study (e.g., muscle fatigue in athletes, cognitive fatigue in multiple sclerosis). Fatigue has also routinely been defined as a symptom, indicative of physical or mental disease (e.g., multiple sclerosis, depression) or a consequence of the treatment of diseases (e.g., chemotherapy). This range of definitions complicates comparisons across studies and the generalization of research findings and highlights the need for explicit definitions in published literature. This section describes two common and distinct ways of conceptualizing and defining fatigue.

### Subjective fatigue: Feelings

Probably the most intuitive way to define fatigue is as a subjective experience or mood state. Common terminology used to describe fatigue subjectively includes feelings of weariness, tiredness, a lack of vigor or energy, or decreased motivation to continue on a task (Chaudhuri and Behan, 2000; O'Connor, 2004; Tiesinga, Dassen, and Halfens, 1996). These percepts are best identified via subjective measurement (Whitehead, 2009). The onset, duration, and severity of the fatigue are also often described subjectively (Dittner et al., 2004). Subjective fatigue can result from a wide range of factors, including sustained physical or mental effort, emotional distress, sleep disturbance and physical or mental disease processes. Chaudhuri and Behan (2000) define “central” fatigue as a lack of motivation or desire (subjective traits) to continue a physical or mental task in the absence of neuromuscular processing deficits.

### Fatigue as a performance decrement: Behaviour

For over 100 years, and with mixed results, researchers have defined and examined fatigue as a performance decrement (Ackerman, 2011). The athlete is very familiar with fatigue-related performance decrements. While the underlying mechanisms are complex, this type of fatigue is often viewed on the cellular level in terms of depletion of energy stores in muscle tissue and has been extensively studied (e.g., Green, 1997). This type of fatigue has been referred to as “peripheral” fatigue, defined as difficulty initiating or maintaining some physical tasks due to limitations in peripheral processing abilities (i.e., at cellular, circulatory or neuromuscular level; Chaudhuri and Behan, 2000). Fatigue-related performance decrements are also associated with various disease processes (e.g., rheumatoid arthritis and Parkinson’s disease; Garber and Friedman, 2003; Schwid et al., 2002). In both normal and

pathologic cases, these decrements are often referred to as “physical fatigue” given the focus on physical performance decrements.

Although not a universal finding, fatigue-related decrements in cognitive processing abilities (e.g., attention, processing speed, memory) may be observed following periods of sustained and demanding mental work. Physical or cognitive fatigue-related performance decrements are sometimes referred to as objective measures of fatigue, to distinguish these measures from subjective reports. The term “cognitive fatigue” has also been used to refer specifically to fatigue-related performance decrements on cognitive tasks (Ackerman, 2011). It is not uncommon for performance decrements to be accompanied by changes in subjective fatigue. However, relationships between changes in subjective ratings and associated performance decrements are often absent or weak, suggesting that separate aspects of the fatigue experience are being assessed (Leavitt and DeLuca, 2010; Hornsby, 2013).

## II. (SUBJECTIVE) FATIGUE DIMENSIONS AND RELATED CONSTRUCTS

Researchers continue to debate whether subjective fatigue is best described as a unidimensional or multidimensional construct (Michielsen, et al., 2004). This section describes several common dimensions, or domains, used to characterize the fatigue experience. These dimensions have been identified largely through interviews and surveys and via factor analyses of questionnaire data during the development of instruments for quantifying fatigue (Stein et al., 1998; Piper et al., 1998). The focus here is primarily on the subjective experience, but in some cases fatigue dimensions are also described in terms of performance decrements.

### Energy/vigor/vitality

Like fatigue, the construct of “energy” has been defined and described in many ways. From a social perspective having “mental energy” is important for quality of life (O’Connor, 2006). From a physics perspective, energy is well defined as the capacity to do work. As a mood, the term energy has similar connotations. When we have energy we feel able to do physical or mental work (O’Connor, 2004). The terms vigor and vitality are also commonly used when describing energy as a mood state. For example, the Activation-Deactivation Adjective Checklist (AD-ACL; Thayer, 1986), a common tool for assessing energy, uses the adjectives “active, energetic, vigorous, lively and full of pep” to quantify “Energy-Arousal”. These same adjectives are used on another standardized mood scale, the short form of the Profile of Mood States (POMS; McNair et al., 1971), to assess the construct of “vigor”. Likewise, the term “vitality”, defined as positive feelings of “aliveness” and energy, has similar connotations (Ryan and Frederick, 1997). Researchers actively debate whether the constructs of energy, vigor and vitality are the same construct or unique components of some other larger underlying construct (Shirom, 2011).

The subjective constructs of energy and fatigue are clearly related, with multiple studies showing a strong negative correlation ( $-0.38 < r < -0.73$ ) between the two moods (Lee et al., 1991; McNair and Heuchert, 2010). Despite the negative association, factor analyses suggest they are independent constructs, not bi-polar attributes of a single mood. That is, while individuals reporting high levels of fatigue also generally report low levels of energy/vigor,

substantial variability exists (e.g., Lee et al., 1991; McNair and Heuchert, 2010). For example, an athlete may feel both fatigued and invigorated following an especially challenging workout or competition. Or conversely, a student may feel mentally fatigued following a long and difficult examination, but also feel a strong desire for alternative mental or physical activity (e.g., go for a run or go out with friends).

### **General fatigue**

This subjective experience refers to a general sense of feeling tired, worn out, or sluggish. Or, in the energy domain, a feeling of low energy or motivation to complete a task. Although it might be considered a unidimensional construct, this term is included on several multidimensional fatigue scales (Smets et al., 1995; Stein et al., 1998). It captures a general feeling of fatigue regardless of the underlying factors or mechanisms (e.g., sleep loss, medications, disease, or sustained physical or mental work) responsible for the percept.

### **Physical/somatic fatigue**

Physical fatigue refers to a reduced ability (performance decrement) or desire (subjective) to physically perform tasks (Chalder et al., 1993). This is generally the result of sustained physical exertion or the consequence of a disease process. Subjectively, somatic symptoms are often used to quantify this type of fatigue (e.g., My legs feel weak). Clearly, subjective complaints of muscle weakness could also be, and frequently are, measured separately as 'objective' fatigue-related performance decrements.

### **Mental/cognitive fatigue**

In contrast to physical fatigue, mental fatigue refers to a reduced ability (performance decrement) or desire (subjective) to perform mental or cognitive processes or tasks (Chalder et al., 1993; van der Linden, Frese and Meijman, 2003). Subjective assessment of mental/cognitive fatigue is based on responses to surveys or questionnaires completed by the individual or their caregiver. For example, mental fatigue may be assessed subjectively by asking about perceived difficulties with concentration, attention, clear thinking, and memory (Chalder et al., 1993; Stein et al., 2004).

Alternatively, research suggests that a variety of simple and complex cognitive processing abilities, such as attention, processing speed, memory and decision-making, are degraded in individuals in a fatigued state (e.g., Ackerman, 2011). Thus, as mentioned above, some authors use the term "cognitive fatigue" to refer specifically to performance decrements in cognitive processing abilities, rather than referring to a subjective feeling or mood. We note the potential for confusion in this term, as it may be used to refer to a subjective fatigue, or an objective consequence of fatigue. This is noteworthy because both types may be expected to manifest themselves in relation to hearing impairment.

Despite obvious differences, the distinction between the domains of mental and physical fatigue is not always clear. For example, in addition to well-known cellular mechanisms, physical fatigue is also modulated by central cognitive processes. Marcora and colleagues (2009) found that mentally fatigued cyclists (those that completed a mentally demanding cognitive task for 90 minutes prior to cycling) became physically fatigued (unable to

maintain a certain rpm) faster than a control group of cyclists that watched a neutral documentary for 90 minutes prior to cycling. This association between mental and physical fatigue highlights the complexity of fatigue as a construct.

### **Emotional/affective fatigue**

Emotional or affective fatigue is included as a domain on several multidimensional fatigue scales (e.g., Piper et al., 1998; Stein et al., 1998; 2004). Like other fatigue domains, emotional fatigue may be described as the reduced ability or desire to perform physical or mental tasks; however, this reduced ability/desire is the result of emotional or psychological demands on the individual. Barnes and Van Dyne (2009) suggest emotional fatigue is the consequence of emotional demands of others and results in feeling “overwhelmed, drained, and used up”. Emotional fatigue has been studied in relation to workplace strategies and issues (e.g., Barnes and Van Dyne, 2009) and is an important consequence of cancer and cancer-related treatments (Curt et al., 2000). Similar to other fatigue domains, emotional fatigue is often correlated with depression (e.g., Strasser et al., 2009).

### **Fatigue duration: Transient vs. long-term**

It makes sense to differentiate between a more long-term fatigued state (e.g., feelings of fatigue that are constant or recurrent and not necessarily due to specific, transient, events or situations) resulting from some chronic health or environmental condition, and more short-term, transient, fatigue due to the mental or physical demands of a given situation. Acute or transient fatigue is common and a normal consequence of sustained and demanding physical or mental work. In the healthy population, this type of fatigue tends to resolve quickly with breaks or rest and has a minimal impact on quality of life. However, for some individuals, the transient fatigue is more frequent and severe and can be brought about by the completion of routine activities during the day. This type of fatigue can have significant negative effects on quality of life (Evans and Wickstrom, 1999; Robinson-Smith et al., 2000). To examine the time course for long-term fatigue, it is important to consider the frequency, severity, and persistence of the fatigue. These characteristics vary based on the underlying cause of the fatigue and vigor deficits and are assessed directly in several fatigue scales (Hann et al., 1998; Krupp et al., 1989).

In terms of more transient fatigue, the vast majority of research in this area has focused on the time course of muscle fatigue following sustained physical activity. Most relevant to this paper, however, is the development of fatigue due to sustained mental/cognitive processing demands. A variety of factors are known to influence the development of subjective and behavioral fatigue in response to sustained mental work, including task and subject-specific factors, such as, the time-on-task, mental workload, the mental effort allocated to the task, task importance, and motivation (e.g., Ackerman, 2011). Depending on the combination of subject and task characteristics, fatigue may develop rapidly, slowly, or not at all during the measurement process. Some studies have shown evidence of subjective fatigue and performance decrements in as little as 20–30 minutes (Mackworth, 1948; Teichner, 1974). In contrast, a video game enthusiast might happily apply extreme mental effort toward successful completion of the game for several hours with little or no complaints of fatigue or decrements in performance.

### III. MEASURING FATIGUE AND ENERGY

Fatigued individuals often describe their condition as “having no energy”. In fact, those who are unable to complete daily activities or are overwhelmed by such activities, frequently attribute this condition to a state of “low energy or lack of energy”. To most of us, mental energy is considered important for accomplishing daily tasks and for quality of life—it is viewed as a multidimensional concept that includes such constructs as mood, cognition, motivation, sleepiness and quality of life (Lieberman, 2007; O’Connor, 2006). To be sure, the scientific literature on mental energy is limited. There is no consensus on the definition of mental energy, and the relationship between feelings of energy and fatigue are not well understood. Some researchers view energy and fatigue as opposites of the same construct whereas others view these two entities as separate constructs (Lieberman, 2007). Despite the ambiguity of the relationships between fatigue and energy several approaches have been developed to assess these constructs. A review of the more common assessment approaches appears below.

#### Subjective assessment of fatigue and energy deficits

Subjective assessment is a common approach for measuring fatigue and low energy, and a wide range of instruments is available for use. Some instruments assess fatigue/energy as part of a more global assessment of health or mood. For example, the Profile of Mood States (POMS; McNair et al., 1971) assesses an individual’s overall mood by examining several mood states, such as tension, depression, anger, confusion, as well as fatigue and vigor (McNair et al., 1971). There are seven items used to assess fatigue (e.g., Worn out, Listless) and eight items used to assess vigor (e.g., Lively, Energetic). Respondents circle a number between 0 (Not at all) and 4 (Extremely) that best describes how they have been feeling during the past week, including the day of completing the POMS. The Medical Outcomes Study Short Form (SF-36; Ware and Sherbourne, 1992) is another widely used generic instrument that assesses vitality/energy as part of an individual’s overall health. Likewise, the Patient-Reported Outcomes Measurement Information System (PROMIS) is used to assess components, including fatigue, of physical, mental and social health, as well as providing an estimate of global health (e.g., Cella et al., 2010). These measures are well validated and have normative data for both the general healthy population and individuals with various chronic diseases.

Other instruments have been designed specifically to assess the constructs of fatigue and/or energy. Recent reviews by Dittner et al (2004) and Whitehead (2009) identified over 40 instruments designed specifically to measure fatigue and energy deficits in various clinical populations. While many scales are available there is no consensus on a “gold standard” measure of subjective fatigue. Clearly, the lack of consensus on even a definition of fatigue limits our ability to standardize measures. In addition, the diversity of measures is driven, in part, by the diverse needs of the clinicians and researchers administering the tools. Instruments vary in terms of their construction format, number of test items, and whether they treat fatigue/energy as a uni-dimensional or multi-dimensional construct. The specific aspects of fatigue that are assessed also vary across instruments. Important characteristics

include the duration of the fatigue, its frequency of occurrence, and the magnitude or intensity of the experience.

In addition to the characteristics of the fatigue, some instruments also assess the functional impact of the fatigue on daily activities and quality of life. The Revised Piper Fatigue Scale (Piper et al., 1998) is an example of a measure that assesses duration of fatigue (minutes to months) as well as its severity and behavioral impact on daily activities (e.g., at work/school, socializing). Likewise, subjective “need for recovery” scales have been used to measure the need to recuperate from work-related fatigue (van Veldhoven and Broersen, 2003). Some work considers need for recovery scales as a proxy for work-related fatigue (Sluiter, et al., 2003). In contrast, other work suggests that while often related, fatigue and need for recovery from work are independent constructs (Jansen, Kant, and Brandt, 2002).

### **Assessing fatigue/energy via behavioral performance decrements**

Monitoring task performance over time is another approach that has been used for many years to study both physical and mental fatigue. Researchers have examined fatigue effects on diverse cognitive tasks (e.g., attention, memory, learning, mental planning, executive control; van der Linden, Frese and Meijman, 2003; Lim and Dinges, 2008; Shigihara et al., 2013). Performance on any cognitive task could potentially be used as a metric for detecting fatigue effects; however, tasks requiring sustained cognitive effort have been shown to be particularly effective for demonstrating cognitive performance decrements (DeLuca, 2005; Lieberman, 2007). Fatigue-related deficits in cognitive processing may be exacerbated in impaired populations, such as multiple sclerosis, traumatic brain injury and (potentially) hearing impairment. These same individuals may also experience fatigue even in situations where the mental demands appear limited, such as completion of routine daily activities (DeLuca, 2005; van der Linden, Frese and Meijman, 2003; Hornsby, 2013; Hornsby et al., 2014).

There are two common approaches for measuring fatigue-related decrements in cognitive processing (Ackerman, 2011). One “indirect” approach is to assess cognitive ability before and after a prolonged period of time during which mental effort may vary (e.g., before and after a work day or classroom session). A variation on this “real world” approach is to create a situation where mental effort must be sustained for a period of time, essentially creating a standardized “fatiguing task”, and again measure cognitive abilities before and after the completion of the task. This approach loses some face validity, but may decrease variability by forcing all participants to complete exactly the same tasks.

An alternative, more “direct”, approach is to utilize a mentally challenging task which allows one to monitor cognitive performance directly, and continuously, over an extended time period. Vigilance tasks are a classic example of this approach. In general, vigilance tasks require participants to maintain attention for and respond to simple, infrequent, target events (e.g., a light flash or tone) while ignoring irrelevant stimuli. Fatigue is inferred when response speed slows, accuracy decreases and/or false alarms increase (Lieberman, 2007; Basner and Dinges, 2011).

Fatigue-related changes in cognitive processing are most readily observed in individuals suffering from more severe and long-term fatigue (e.g., extended sleep loss/poor sleep; extended shift work or long distance monotonous driving). In more acute or transient situations, observing fatigue-related decrements in cognitive processing has proven more challenging. Factors such as motivation, applied effort, task workload and consequences of errors, can influence the development and magnitude of performance decrements on a given task (Ackerman, 2011). Complicating things further, learning effects can be a significant confound when using a performance decrement as a marker for fatigue. Specifically, performance on many tasks is expected to improve over time due to practice and learning effects. These learning effects may minimize, or mask altogether, any fatigue-related performance decrements for an individual despite subjective ratings suggesting fatigue. Individual variations in these opposing processes may also explain, in part, the limited correlations observed between subjective ratings of fatigue and fatigue-related performance decrements. It may also explain the limited effectiveness of some (not all) more complex cognitive tasks for detecting fatigue via performance decrements. Specifically, performance on cognitively complex tasks may be more impacted by practice and learning effects than more simple tasks, such as vigilance tasks (Dinges and Powell, 1985; Lieberman, 2007).

### **Biologic and physiologic methods for assessing fatigue and energy deficits**

Not surprisingly, physical and physiologic changes often accompany the subjective and behavioral consequences of fatigue. Researchers have used these changes to provide more objective metrics of fatigue. This section briefly touches on some of the more common approaches including biologic markers, as well as physiologic and electrophysiologic techniques. A thorough discussion of approaches, however, is beyond the scope of this paper. Here the focus is on fatigue-related changes associated with sustained mental or psychological demands as opposed to sustained physical demands. Also, although there may be overlap between the physical and physiologic markers associated with fatigue and those associated with effort (e.g., listening effort- see Mackersie, this issue; Richter, this issue), here the focus is on fatigue.

**Biologic markers**—There has been much work examining the biologic mechanisms of fatigue associated with chronic health conditions (e.g., cancer and multiple sclerosis). Despite this work, our understanding of the biologic mechanisms of fatigue, particularly mental fatigue, is limited. Plasma glucose level is a well-known metabolic factor associated with variations in physical and mental energy, effort and fatigue due to sustained exercise or disease (e.g., Gold et al., 1995; Newsholme, Blomstrand and Eckblom, 1992). However, the sensitivity of this measure for detecting more transient fatigue due to sustained mental demands is unclear (Marcora, Staiano and Manning, 2009).

Cortisol is a biologic marker that has been used in the study of fatigue in a wide range of populations including hearing loss (Hicks and Tharpe, 2002), cancer survivors (Bower, Ganz and Aziz, 2005) and stress-related fatigue (Olsson, Roth and Melin, 2010). Cortisol levels are not a direct marker of fatigue; rather these levels are sensitive to an individual's stress levels and energy expenditure, which are often associated with fatigue. Cortisol can be measured multiple ways including via saliva, hair and urine. Cortisol is an important part of



the body's response to stress and is regulated by the hypothalamic-pituitary-adrenal (HPA) axis. In non-fatigued individuals, cortisol levels vary in a systematic circadian (24 hour) cycle. A normal, rapid, increase in cortisol levels upon awakening is referred to as the Cortisol Awakening Response (CAR) and in a fatigued state this pattern may be disrupted (Roberts et al., 2004). Disruptions in the "typical" CAR have been associated with perceived stress, including the stress associated with preparing for the upcoming day, and stress associated with a variety of chronic health problems (Schmidt-Reinwald et al., 1999; Wust, Federenko, Hellhammer, & Kirschbaum, 2000). In addition, changes in cortisol levels in response to stressful events may vary in fatigued and non-fatigued individuals, with fatigued individuals typically showing smaller variations in cortisol level (e.g., Bower et al, 2005).

Salivary alpha-amylase (sAA) is another saliva parameter that has been used as a non-invasive biomarker for effort and stress (Granger et al., 2007; Nater et al., 2009). Several studies have reported associations between sAA and plasma norepinephrine levels, a surrogate marker of sympathetic nervous system (SNS) activity, under different conditions of stress (Kuebler et al., 2014; Rohleder et al., 2004). Recent research also suggests a linkage between norepinephrine levels, modulated by the locus coeruleus, and fatigue-related task engagement/disengagement (Hopstaken et al., 2015). Unfortunately, research examining the relationships between sAA levels and fatigue is limited and results are mixed (Yamaguchi et al., 2006; Nozaki et al., 2009). Thus the utility of sAA as a biomarker for fatigue in individuals with hearing loss remains unclear. Finally, melatonin is another hormone that has been examined in fatigue research. Normal melatonin production and release follows a circadian pattern and disrupted patterns have been observed in persons with chronic health issues and recurrent fatigue (e.g., van Heukelom et al., 2006; Melamud, et al., 2012). However, because melatonin levels impact sleep patterns, research has focused primarily on sleep-related fatigue as opposed to cognitive or emotional fatigue.

**Physiologic and Electrophysiologic techniques**—Several investigators have found components of the Electroencephalogram (EEG) to be sensitive to fatigue due to multiple factors, such as extended driving (Craig et al., 2012; Zhao, et al., 2011), sustained cognitive tasks (Lorist et al., 2009; Trejo et al., 2005), and multiple sclerosis (Leocani et al., 2001). In addition to continuous monitoring of low-frequency brain activity (EEG), investigators have also used Evoked Response Potentials (ERPs) to detect fatigue-related changes in cognitive processing (Lorist et al., 2009; Murata et al., 2005). For example, Murata et al. (2005) found the P300 ERP was sensitive to fatigue-related changes in mental processing resulting from sustained mental work (performing mental arithmetic for 3 hours). Several other electrophysiologic measures thought to assess various aspects of cognitive processing have been used to examine mental fatigue with varying degrees of success, including the N1, P2, N2b, P3, Error Related Negativity, and Lateralized readiness potential (e.g., Boksem, Meijman, & Lorist, 2005; Kato et al., 2009).

The spontaneous eye blink has been used extensively to assess sleepiness and drowsiness (Caffier et al., 2003), especially associated with long-duration driving-related fatigue (Stern et al., 1994; Lal and Craig, 2001; Tran et al., 2009). Prolonged eye closures, and an increase in duration of eye closures have been observed in fatigued state. Fixed changes in pupil diameter have also been observed in a fatigued state (e.g., LeDuc et al., 2005). Oscillations

in pupil diameter, referred to as “fatigue waves” have also been used as an objective measure of sleep-related fatigue effects (Lowenstein et al., 1963; Eggert, et al., 2012). Although pupillographic methods have been used extensively and found sensitive to fatigue effects, the vast majority of work has focused on fatigue related to sleep or monotony. The utility of this metric for detecting fatigue due to other factors is unclear.

Measurement of pupil diameter, commonly used in the cognitive psychology literature (Sirois and Brisson, 2014) and used to assess effects of hearing loss on cognitive load (e.g., Zekveld et al., 2014), has also recently been used to investigate mental fatigue. Hopstaken et al (2014, 2015) suggest variations in pupil diameter are indicative of task engagement, a process which may be reduced in a fatigued state. They had participants work continuously on demanding cognitive tasks (visual n-back tasks) for a two hour period and found baseline pupil diameter decreased with time-on-task. Results were consistent with subjective ratings of task engagement and fatigue which decreased and increased respectively, with time-on-task.

Variability of heart rate provides a measure of parasympathetic control over the heart. The heart rate may increase or decrease in response to a variety of factors including physical and mental effort, distress, and anxiety that are potentially associated with fatigue. Tran et al (2009) investigated relationships between fatigue and heart rate variability (HRV) in healthy adults. They measured heart rate and HRV before starting a monotonous, simulated driving task and 5 minutes after starting the task. Participants were monitored visually during the task and the task was terminated at the first signs of fatigue (increased head nodding and increased eye closure duration during blinks). Heart rate and HRV were again measured immediately after ending the task. An association between low-frequency HRV and fatigue was observed. Likewise, Segerstrom and Nes (2007) found self-regulatory effort and fatigue, based on participants’ persistence to solve an unsolvable mental task, were associated with increases in HRV.

#### **IV. CONSEQUENCES OF FATIGUE/LOW ENERGY**

As expected, the consequences of fatigue and energy deficits vary widely depending on the duration and severity of the problem. For individuals experiencing recurrent or long-term, severe fatigue the negative consequences can be significant.

##### **Quality of life**

Fatigue, particularly due to chronic health issues, can have significant physical, social and psychological consequences. Amato et al (2001) found subjective fatigue was a significant predictor of quality of life in adults with multiple sclerosis. Likewise, oncology patients with severe and recurrent fatigue report a wide range of fatigue-related mental and emotional problems that negatively affect their quality of life, including difficulties concentrating, loss of motivation, feelings of loneliness and irritability (Curt et al., 2000; Flechtner and Bottomley, 2003). Multiple studies have found strong associations between fatigue and depression (e.g., Arnold, 2008). Curt et al (2000) found that cancer survivors experiencing fatigue “at least a few times a month” reported that fatigue-related issues kept them from normal daily activities, such as being social with friends and taking care of family needs.

Finally, Evans and Wickstrom (1999) found that fatigue was common among adults with chronic illness and strongly correlated with their self-care abilities which are also strongly correlated with quality of life (Robinson-Smith et al., 2000).

Fatigue severity during an active disease state also modulates the effects of fatigue on quality of life following treatment. Flechtner and Bottomley (2003) found that individuals being treated for cancer who scored high on a fatigue scale during their cancer treatments were more likely to report poorer quality of life following recovery from treatment than those who reported lower fatigue during their treatments. These differences in quality of life were present even 6–7 years following treatment ending. In summary, adults with recurrent, longstanding fatigue tend to be less active, more socially isolated, less able to monitor their own self-care, and more prone to depression than non-fatigued adults.

### **Cognitive processing**

Individuals experiencing mental fatigue often subjectively report difficulties maintaining attention or thinking quickly, clearly and efficiently. Cognitive abilities, such as working memory, attention, executive control, and processing speed, have been monitored to detect mental fatigue (Bryant et al., 2004; van der Linden, et al., 2003; Lim and Dinges, 2008). For example, Lim and Dinges (2008) summarized literature in which the Psychomotor Vigilance Task (PVT; Dinges and Powell, 1985) was used to examine the effects of sleep-related fatigue on vigilant attention and processing speed. The PVT is a simple visual reaction time task that measures sustained attention and is highly sensitive to factors affecting mental fatigue. Converging evidence from multiple studies suggests that fatigue results in a generalized slowing in processing speed and a decreased ability to maintain attention (Lieberman, 2007; Lim et al. 2010).

Likewise, van der Linden, Frese and Meijman (2003) examined the effects of mental fatigue on executive control in normal adults. They defined executive control as the ability to regulate and control thought and motor processes in order to achieve a goal. Using classic tasks from the cognitive psychology literature, they assessed flexibility and planning abilities before and after two hours of mentally demanding tasks. Compared to a control group, fatigued individuals showed evidence of fatigue-induced impairment of executive control.

### **Workplace productivity/safety issues**

Fatigue-related decrements in cognitive function can have important consequences. For example, fatigued adults in the workplace are less productive, more likely to miss work and have extended work absences, and are more prone to errors and accidents than those not suffering from fatigue (Ricci et al., 2007; Williamson, et al., 2011). From a safety perspective, fatigue-related decrements in attention, processing speed and distractibility have been implicated in specific industrial accidents with major public health and environmental consequences, such as the near meltdown of the Three Mile Island Nuclear reactor (e.g., Mittle et al., 1988). Even in the absence of severe accidents, fatigue-related loss of work productivity is a significant economic issue. Ricci et al (2007) suggests productivity decreases associated with fatigue costs businesses over 100 billion dollars annually in the

U.S. alone. Lost production time at work is especially problematic among fatigued adults who also suffer from other chronic conditions.

## V. FATIGUE CONCEPTS- Relation to hearing loss

### Subjective fatigue - relation to hearing loss

Much of what we know about relationships between fatigue and hearing loss is subjective, coming from anecdotal reports or indirectly from related qualitative research (Backenroth and Ahlner, 2000; Copithorne, 2006; Hetu et al., 1988; Nachtegaal et al., 2009). As a field, we are just beginning to examine relationships between fatigue and hearing loss directly (Bess and Hornsby, 2014; Hornsby, 2013; McGarrigle, et al., 2014). The limited available evidence suggests that hearing loss, like many other chronic health conditions, increases risk for subjective fatigue and vigor deficits in adults and children (Hetu, et al., 1988; Hornsby et al., 2014). For example, Hetu et al. (1988) interviewed metal plant workers to identify perceived difficulties and consequences associated with their hearing loss. As expected, common reports included difficulty understanding speech and reduced awareness of environmental sounds. To compensate for these difficulties, individuals reported a need for increased attention, concentration and effort at work. This, in turn, led to reports of increased stress, tension and fatigue. The fatigue experienced by some workers was such that they were “too tired for normal activities” (Hetu et al 1988, p. 255).

A similar finding was reported by Kramer et al. (2006). In this study, working adults with hearing loss reported their work duties required more effort in hearing to complete than did their normally hearing co-workers doing the same/similar jobs. Furthermore, an analysis of rates of sick leave revealed that persons with hearing loss were approximately four times more likely than workers without hearing loss to miss work due to complaints of “mental distress” (defined as sick leave due to “fatigue, strain or burnout”).

Nachtegaal and colleagues (2009, 2012) examined associations between hearing difficulties, work productivity (including taking sick leave), and need for recovery. Their results suggested that as hearing difficulties increased, self-rated work productivity decreased. In addition, individuals with greater hearing difficulties were also more likely to report being less able to complete all required work duties and needed more time to fully recover from their work-related stress. The increased need for recovery following work also appeared to increase the risk of extended (>5 days) sick leave. Findings such as these suggest that the additional effort in hearing expended throughout the day by persons with hearing loss may be a significant factor affecting quality of life and work experience.

Although limited in scope, recent work using validated fatigue scales also supports the idea that children and adults with hearing loss are at increased risk for fatigue. For example, preliminary data from Hornsby and colleagues (2014) found children with hearing loss reported significantly more fatigue than age-matched children without hearing loss. Although the sample size was small (n=10), the magnitude of deficit experienced by the children with hearing loss was substantial and larger than that reported by children with other chronic health conditions, such as cancer, rheumatoid arthritis, diabetes, and obesity.

Likewise, Hornsby and Kipp (2015) found that adults with hearing loss seeking help for their hearing difficulties reported significantly less vigor than age-matched normative data (Nyenhuis et al., 1999). In addition, they found that adults with hearing difficulties were much more likely (32% vs. 7%) to experience severe vigor deficits (scores >1.5 standard deviations below normative means). Differences between groups on the fatigue subscale of the POMS were also significant, but smaller (15% vs. 7%). While it is intuitive that hearing loss-related fatigue would be driven by listening experiences, the relative contribution of listening difficulties versus other factors (e.g., age, motivation, comorbid conditions, etc...) remains unclear. Additional work is clearly needed to characterize the subjective issues of adults with hearing loss in relation to fatigue and vigor deficits.

### **Behavioral assessments of fatigue - relation to hearing loss**

Research on fatigue-related performance decrements (i.e. behavioral assessment of fatigue) is difficult to carry out, requiring trial-and-error to arrive at experimental conditions and parameters which reliably elicit the phenomena intended for study. Thus it is not surprising that work with persons with hearing loss in this area is limited. Hornsby (2013) examined the effects of hearing aid use on subjective fatigue and fatigue-related performance decrements. In that study, participants completed a cognitively demanding speech-in-noise dual-task over a 50-minute period either unaided or when listening via hearing aids. Signal-to-noise ratios (SNRs) were individually chosen to result in aided understanding of ~75% correct. Subjective ratings obtained immediately before and after completing the speech dual-task revealed large increases in fatigue and a reduced ability to maintain focus and attention following the 50-minute task, regardless of listening condition (i.e., with or without hearing aids). In addition, several performance measures derived from the dual-task (word recognition, word recall, visual reaction times) were monitored over the course of the task. When listening with hearing aids, word recognition, word recall and processing speed (visual reaction times) remained stable over time. Likewise, when listening unaided, word recognition and word recall were poorer than when aided, but they also remained stable over time. In contrast, response speed to the visual signal slowed significantly over time (a fatigue-related performance decrement) when listening without hearing aids. This work provides preliminary evidence that aided listening may reduce susceptibility to speech-processing induced fatigue-related performance decrements in cognitive processing speed. Despite the behavioral evidence of fatigue (performance decrement) when listening unaided but not aided, subjective reports were not sensitive to unaided-aided differences. This finding is not unique, as discrepancies between subjective and objective measures of fatigue are not uncommon (Leavitt and DeLuca, 2010).

In addition, substantial individual variability was observed across participants in this study. Some participants had only minimal, or no, changes in subjective ratings. Likewise, changes in processing speed (visual reaction times) over time varied widely with some participants slowing substantially while others changed only minimally. However, a series of correlation analyses did not reveal any associations between these changes and multiple variables (e.g., PTA, age, word recognition, etc). Thus, the reason for the wide variability remains unknown. It is also worth noting that in a separate experiment (Hornsby, 2012), using the same speech dual-task paradigm, but at a poorer SNR (individually chosen to result in aided

understanding of ~50% correct), no fatigue-related performance decrements were noted in either (unaided/aided) condition. However, subjective differences were observed, with unaided listening leading to larger increases in fatigue than when aided. The reason for the divergent outcomes is not clear and serves to highlight the potential impact of experimental parameters on the development and expression of fatigue.

### **Biologic and physiologic assessments of fatigue - relation to hearing loss**

Hicks and Tharpe (2002) measured cortisol levels in children (5–11 years old) with and without hearing loss (n=10/group) at the beginning (~9:00 a.m.) and end (~2:00 p.m.) of the school day and predicted a blunted response in the children with hearing loss compared to their normative controls. In fact, no significant differences in cortisol levels were observed between groups in this study. However, the limited number of samples obtained during the day did not allow for assessment of the cortisol awakening response (CAR), a potentially important marker of fatigue, and provided only a gross measure of the diurnal cortisol patterns between groups. Moreover, the sample size may have been too small to detect between-group differences.

Recent work by Bess et al., (2015, in review) also investigated the effects of hearing loss on cortisol levels in children (6–12 years old). Participants included 32 children with normal hearing and 28 children with mild-moderate hearing loss. In this study, salivary cortisol was measured on two separate days and at six time points across the waking hours. Results revealed that the CAR in children with hearing loss was elevated upon awakening and blunted in terms of the normal initial increase upon awakening (i.e., the CAR was reduced). This pattern is consistent with the hypothesis that children with hearing loss experience continual and higher stress during the day than their normal hearing peers, hence elevated cortisol at wakening. The blunted response upon awakening also suggests a dysregulation of the hypothalamic-pituitary-adrenal (HPA) axis that could put the children at increased risk for stress-related fatigue.

## **VI. CONCLUSIONS**

Despite its ubiquity and significant negative effects on quality of life, fatigue has proven to be a complex phenomenon that is difficult to define and quantify. The principal forms of defining fatigue are subjectively or, alternatively, as a performance decrement. Subjective fatigue may be multidimensional in nature, with common dimensions including physical, mental/cognitive, and emotional fatigue and the related constructs of energy/vigor/vitality. It is also useful to distinguish between transient or acute fatigue due to short-term cognitive or physical load (which dissipates upon the cessation of the task), and sustained or long-term fatigue, such as that due to a disease condition, which is more persistent. Fatigue can be measured via self-report (subjectively), as a performance decrement on sustained tasks, or via various involuntary biological and physiological markers. Different approaches are probably measuring different aspects of fatigue and energy, as relations between them are often weak (see Mackersie and Eckert et al, this issue).

Although systematic research is limited, cumulating evidence suggests that adults and children with hearing loss may be at increased risk for fatigue and energy deficits. This is

most clear with respect to subjective ratings of longer-term fatigue. Effects of hearing impairment on acute fatigue due to sustained mental demands have also been observed, but measurement paradigms are currently not well developed. Importantly, some initial work suggests that audiological interventions, such as hearing aids, may reduce susceptibility to fatigue. However, there are significant gaps in our understanding of the relationship between hearing loss and fatigue, and robust evidence that interventions such as hearing aids reduce the incidence of long-term fatigue is still lacking.

Future work should seek to identify or develop measurement methods (subjective, physiologic and behavioral) for detecting, quantifying and monitoring hearing-related fatigue in adults and children. These types of measures are required to better understand the fatigue experience of persons with hearing loss and to systematically investigate underlying mechanisms and factors responsible for susceptibility to hearing-related fatigue. Once developed, these measures could be used to investigate factors that may modulate fatigue as well as the efficacy of potential interventions designed to reduce fatigue, in persons with hearing loss.

## Acknowledgments

This work was supported, in part, by a grant to the first author from Oticon A/S, by the National Institute on Deafness and Communication Disorders (NIDCD) of the National Institutes of Health under award number R21DC012865 (Hornsby-PI) and the Institute of Education Sciences (IES), U.S. Department of Education, through Grant R324A110266 to Vanderbilt University (Bess- PI). The content expressed are those of the authors and do not necessarily represent the views of the National Institutes of Health, the Institute of Education Sciences, or the U.S. Department of Education.

## References

- Ackerman, PL. 100 years without resting. In: Ackerman, PL., editor. *Cognitive Fatigue: Multidisciplinary Perspectives on Current Research and Future Applications*, Decade of Behavior/ Science Conference. Washington, DC: American Psychological Association; 2011. p. 11-43.
- Amato MP, Ponziani G, Rossi F, Liedl CL, Stefanile C, Rossi L. Quality of life in multiple sclerosis: the impact of depression, fatigue and disability. *Mult Scler*. 2001; 7(5):340-344. [PubMed: 11724451]
- Backenroth GAM, Ahlner BH. Quality of life of hearing-impaired persons who have participated in audiological rehabilitation counselling. *International Journal for the Advancement of Counselling*. 2000; 22(3):225-240.
- Barnes CM, Van Dyne L. I'm tired': Differential effects of physical and emotional fatigue on workload management strategies. *Human Relations*. 2009; 62(1):59-92.
- Basner M, Dinges DF. Maximizing sensitivity of the psychomotor vigilance test (PVT) to sleep loss. *Sleep*. 2011; 34(5):581-591. [PubMed: 21532951]
- Bess FH, Hornsby BWY. Commentary: listening can be exhausting--fatigue in children and adults with hearing loss. *Ear Hear*. 2014; 35(6):592-599. [PubMed: 25255399]
- Bess FH, Gustafson SJ, Corbett BA, Lambert WE, Camarata SM, Hornsby BWY. Salivary Cortisol Profiles of Children with Hearing Loss. *Ear Hear*. 2015 in review.
- Boksem MA, Meijman TF, Lorist MM. Effects of mental fatigue on attention: an ERP study. *Cognitive Brain Research*. 2005; 25(1):107-116. [PubMed: 15913965]
- Bower JE, Ganz PA, Aziz N. Altered cortisol response to psychologic stress in breast cancer survivors with persistent fatigue. *Psychosomatic Medicine*. 2005; 67(2):277-280. [PubMed: 15784794]
- Bryant D, Chiaravalloti ND, DeLuca J. Objective Measurement of Cognitive Fatigue in Multiple Sclerosis. [Peer Reviewed]. *Rehabilitation Psychology*. 2004; 49(2):114-122.

- Caffier PP, Erdmann U, Ullsperger P. Experimental evaluation of eye-blink parameters as a drowsiness measure. *European Journal of Applied Physiology*. 2003; 89(3–4):319–325. [PubMed: 12736840]
- Cella D, Riley W, Stone A, Rothrock N, Reeve B, Yount S, ... Choi S. The Patient-Reported Outcomes Measurement Information System (PROMIS) developed and tested its first wave of adult self-reported health outcome item banks: 2005–2008. *Journal of clinical epidemiology*. 2010; 63(11): 1179–1194. [PubMed: 20685078]
- Chalder T, Berelowitz G, Pawlikowska T, Watts L, Wessely S, Wright D, Wallace EP. Development of a fatigue scale. *J Psychosom Res*. 1993; 37(2):147–153. [PubMed: 8463991]
- Chaudhuri A, Behan PO. Fatigue and basal ganglia. *J Neurol Sci*. 2000; 179(S 1–2):34–42. [PubMed: 11054483]
- Copithorne, D. The Fatigue Factor: How I Learned to Love Power Naps, Meditation, and Other Tricks to Cope With Hearing-Loss Exhaustion. *Healthy Hearing Web site*. 2006 Aug 21. Retrieved May 6, 2014 from <http://www.healthyhearing.com/content/articles/Hearing-loss/Treatments/7844-The-fatigue-factor-how>
- Craig A, Tran Y, Wijesuriya N, Nguyen H. Regional brain wave activity changes associated with fatigue. *Psychophysiology*. 2012; 49(4):574–582. [PubMed: 22324302]
- Curt GA, Breitbart W, Cella D, Groopman JE, Horning SJ, Itri LM, ... Portenoy RK. Impact of cancer-related fatigue on the lives of patients: new findings from the Fatigue Coalition. *The Oncologist*. 2000; 5(5):353–360. [PubMed: 11040270]
- DeLuca, J. Fatigue, Cognition, and Mental Effort. In: DeLuca, J., editor. *Fatigue as a window to the brain*. Cambridge, Mass: MIT Press; 2005. p. 37–58.
- Dinges D, Powell J. Microcomputer analyses of performance on a portable, simple visual RT task during sustained operations. *Behavior Research Methods*. 1985; 17(6):652–655.
- Dittner AJ, Wessely SC, Brown RG. The assessment of fatigue: a practical guide for clinicians and researchers. *J Psychosom Res*. 2004; 56(2):157–170. [PubMed: 15016573]
- Eggert T, Sauter C, Popp R, Zeitlhofer J, Danker-Hopfe H. The pupillographic sleepiness test in adults: Effect of age, gender, and time of day on pupillometric variables. *American Journal of Human Biology*. 2012; 24(6):820–828. [PubMed: 23012225]
- Evans EJ, Wickstrom B. Subjective fatigue and self-care in individuals with chronic illness. *Medsurg Nurs*. 1999; 8(6):363–369. [PubMed: 11000775]
- Flechtner H, Bottomley A. Fatigue and quality of life: lessons from the real world. *Oncologist*. 2003; 8(Suppl 1):5–9. [PubMed: 12626781]
- Garber CE, Friedman JH. Effects of fatigue on physical activity and function in patients with Parkinson's disease. *Neurology*. 2003; 60(7):1119–1124. [PubMed: 12682317]
- Gold AE, MacLeod KM, Deary IJ, Frier BM. Hypoglycemia-induced cognitive dysfunction in diabetes mellitus: effect of hypoglycemia unawareness. *Physiology & behavior*. 1995; 58(3):501–511. [PubMed: 8587958]
- Granger DA, Kivlighan KT, el-Sheikh M, Gordis EB, Stroud LR. Salivary alpha-amylase in biobehavioral research: recent developments and applications. *Annals of the New York Academy of Sciences*. 2007; 1098:122–144. [PubMed: 17332070]
- Hann D, Jacobsen P, Azzarello L, Martin S, Curran S, Fields K, ... Lyman G. Measurement of fatigue in cancer patients: development and validation of the Fatigue Symptom Inventory. *Quality of Life research*. 1998; 7(4):301–310. [PubMed: 9610214]
- Hetu R, Riverin L, Lalande N, et al. Qualitative analysis of the handicap associated with occupational hearing loss. *Br J Audiol*. 1988; 22(4):251–64. [PubMed: 3242715]
- Hicks CB, Tharpe AM. Listening effort and fatigue in school-age children with and without hearing loss. *J Speech Lang Hear Res*. 2002; 45(3):573–584. [PubMed: 12069009]
- Hopstaken JF, van der Linden D, Bakker AB, Kompier MA. A multifaceted investigation of the link between mental fatigue and task disengagement. *Psychophysiology*. 2014
- Hopstaken JF, van der Linden D, Bakker AB, Kompier MA. The window of my eyes: Task disengagement and mental fatigue covary with pupil dynamics. *Biological psychology*. 2015; 110:100–106. [PubMed: 26196899]
- Hornsby, B. Tired of Listening: Subjective and Objective Measures of Hearing Related Fatigue. Paper presented at the International Hearing Aid Conference (IHCON); Lake Tahoe, CA. 2012 Aug.



- Hornsby BWY. The Effects of Hearing Aid Use on Listening Effort and Mental Fatigue Associated With Sustained Speech Processing Demands. *Ear and Hearing*. 2013; 34:523–534. [PubMed: 23426091]
- Hornsby B, Kipp AM. Subjective Ratings of Fatigue and Vigor in Adults with Hearing Loss Are Driven by Perceived Hearing Difficulties Not Degree of Hearing Loss. *Ear and Hearing*. 2015; Advance online publication. doi: 10.1097/AUD.0000000000000203
- Hornsby BWY, Werfel K, Camarata S, Bess FH. Subjective Fatigue in Children With Hearing Loss: Some Preliminary Findings. *American Journal of Audiology*. 2014; 23(1):129–134. [PubMed: 23824428]
- Jansen NW, Kant I, van den Brandt PA. Need for recovery in the working population: description and associations with fatigue and psychological distress. *International journal of behavioral medicine*. 2002; 9(4):322–340. [PubMed: 12512472]
- Kato Y, Endo H, Kizuka T. Mental fatigue and impaired response processes: event-related brain potentials in a Go/NoGo task. *International Journal of Psychophysiology*. 2009; 72(2):204–211. [PubMed: 19135100]
- Kramer SE, Kapteyn TS, Houtgast T. Occupational performance: comparing normally-hearing and hearing-impaired employees using the Amsterdam Checklist for Hearing and Work. *Int J Audiol*. 2006; 45(9):503–512. [PubMed: 17005493]
- Krupp LB, LaRocca NG, Muir-Nash J, Steinberg AD. The fatigue severity scale. Application to patients with multiple sclerosis and systemic lupus erythematosus. *Arch Neurol*. 1989; 46(10):1121–1123. [PubMed: 2803071]
- Kuebler U, von Kanel R, Heimgartner N, Zuccarella-Hackl C, Stirnimann G, Ehlert U, Wirtz PH. Norepinephrine infusion with and without alpha-adrenergic blockade by phentolamine increases salivary alpha amylase in healthy men. *Psychoneuroendocrinology*. 2014; 49:290–298. [PubMed: 25128931]
- Lal SK, Craig A. A critical review of the psychophysiology of driver fatigue. *Biological psychology*. 2001; 55(3):173–194. [PubMed: 11240213]
- Leavitt VM, DeLuca J. Central fatigue: issues related to cognition, mood and behavior, and psychiatric diagnoses. *PM R*. 2010; 2(5):332–337. [PubMed: 20656614]
- LeDuc PA, Greig JL, Dumond SL. Involuntary eye responses as measures of fatigue in US Army Apache aviators. *Aviation, space, and environmental medicine*. 2005; 76(Supplement 1):C86–C91.
- Lee KA, Hicks G, Nino-Murcia G. Validity and reliability of a scale to assess fatigue. *Psychiatry Res*. 1991; 36(3):291–298. [PubMed: 2062970]
- Lim J, Dinges DF. Sleep deprivation and vigilant attention. *Ann N Y Acad Sci*. 2008; 1129:305–322. [PubMed: 18591490]
- Lim J, Wu WC, Wang J, Detre JA, Dinges DF, Rao H. Imaging brain fatigue from sustained mental workload: an ASL perfusion study of the time-on-task effect. *Neuroimage*. 2010; 49(4):3426–3435. [PubMed: 19925871]
- Lieberman HR. Cognitive methods for assessing mental energy. *Nutr Neurosci*. 2007; 10(5–6):229–242. [PubMed: 18284031]
- Lorist MM, Bezdan E, ten Caat M, Span MM, Roerdink JBTM, Maurits NM. The influence of mental fatigue and motivation on neural network dynamics; an EEG coherence study. *Brain Research*. 2009; 1270(0):95–106. [PubMed: 19306850]
- Mackworth N. The breakdown of vigilance during prolonged visual search. *Quarterly Journal of Experimental Psychology*. 1948; 1(1):6–21.
- Marcora SM, Staiano W, Manning V. Mental fatigue impairs physical performance in humans. *Journal of Applied Physiology*. 2009; 106(3):857–864. [PubMed: 19131473]
- McGarrigle R, Munro KJ, Dawes P, Stewart AJ, Moore DR, Barry JG, Amitay S. Listening effort and fatigue: What exactly are we measuring? A British Society of Audiology Cognition in Hearing Special Interest Group ‘white paper’. *International Journal of Audiology*. 2014; 53(7):433–445. [PubMed: 24673660]
- McNair, D.; Lorr, M.; Droppleman, L. Profile of mood states. San Diego, Calif: Educational and Industrial Testing Service; 1971. <http://www.mhs.com/product.aspx?gr=cli&id=overview&prod=poms>

- Michielsen HJ, De Vries J, Van Heck GL, Van de Vijver FJ, Sijtsma K. Examination of the Dimensionality of Fatigue: The Construction of the Fatigue Assessment Scale (FAS). *European Journal of Psychological Assessment*. 2004; 20(1):39.
- McNair, DM.; Heuchert, JWP. Profile of mood states: Technical update. Toronto: Multi-Health Systems Inc; 2010.
- Mitler MM, Carskadon MA, Czeisler CA, Dement WC, Dinges DF, Graeber RC. Catastrophes, sleep, and public policy: consensus report. *Sleep*. 1988; 11(1):100. [PubMed: 3283909]
- Nachtegaal J, Kuik DJ, Anema JR, et al. Hearing status, need for recovery after work, and psychosocial work characteristics: Results from an internet-based national survey on hearing. *Int J Audiol*. 2009; 48(10):684–691. [PubMed: 19863354]
- Nachtegaal J, Festen JM, Kramer SE. Hearing ability in working life and its relationship with sick leave and self-reported work productivity. *Ear Hear*. 2012; 33(1):94–103. [PubMed: 21826005]
- Nater UM, Rohleder N. Salivary alpha-amylase as a non-invasive biomarker for the sympathetic nervous system: current state of research. *Psychoneuroendocrinology*. 2009; 34(4):486–496. [PubMed: 19249160]
- Newsholme E, Blomstrand E, Ekblom B. Physical and mental fatigue: metabolic mechanisms and importance of plasma amino acids. *British medical bulletin*. 1992; 48(3):477–495. [PubMed: 1360309]
- Nozaki S, Tanaka M, Mizuno K, Ataka S, Mizuma H, Tahara T, ... Watanabe Y. Mental and physical fatigue-related biochemical alterations. *Nutrition*. 2009; 25(1):51–57. [PubMed: 18834718]
- Nyenhuis DL, Yamamoto C, Luchetta T, Terrien A, Parmentier A. Adult and geriatric normative data and validation of the profile of mood states. *J Clin Psychol*. 1999; 55(1):79–86. [PubMed: 10100834]
- O'Connor P. Evaluation of four highly cited energy and fatigue mood measures. *Journal of Psychosomatic Research*. 2004; 57(5):435–441. [PubMed: 15581646]
- O'Connor PJ. Mental Energy: Assessing the Mood Dimension. *Nutrition Reviews*. 2006; 64:S7–S9. [PubMed: 16910215]
- Olsson EM, Roth WT, Melin L. Psychophysiological characteristics of women suffering from stress-related fatigue. *Stress and Health*. 2010; 26(2):113–126.
- Lowenstein O, Feinberg R, Loewenfeld IE. Pupillary Movements During Acute and Chronic Fatigue A New Test for the Objective Evaluation of Tiredness. *Investigative Ophthalmology & Visual Science*. 1963; 2(2):138–157.
- Piper BF, Dibble SL, Dodd MJ, Weiss MC, Slaughter RE, Paul SM. The revised Piper Fatigue Scale: psychometric evaluation in women with breast cancer. *Oncol Nurs Forum*. 1998; 25(4):677–684. [PubMed: 9599351]
- Ricci JA, Chee E, Lorandean AL, Berger J. Fatigue in the U.S. workforce: prevalence and implications for lost productive work time. *J Occup Environ Med*. 2007; 49(1):1–10. [PubMed: 17215708]
- Roberts AD, Wessely S, Chalder T, Papadopoulos A, Cleare AJ. Salivary cortisol response to awakening in chronic fatigue syndrome. *The British Journal of Psychiatry*. 2004; 184(2):136–141. [PubMed: 14754825]
- Robinson-Smith G, Johnston MV, Allen J. Self-care self-efficacy, quality of life, and depression after stroke. [Research Support, Non-U.S. Gov't]. *Arch Phys Med Rehabil*. 2000; 81(4):460–464. [PubMed: 10768536]
- Rohleder N, Nater UM, Wolf JM, Ehlert U, Kirschbaum C. Psychosocial stress-induced activation of salivary alpha-amylase: an indicator of sympathetic activity? *Annals of the New York Academy of Sciences*. 2004; 1032:258–263. [PubMed: 15677423]
- Ryan RM, Frederick C. On energy, personality, and health: Subjective vitality as a dynamic reflection of well-being. *Journal of personality*. 1997; 65(3):529–565. [PubMed: 9327588]
- Schmidt-Reinwald A, Pruessner JC, Hellhammer DH, Federenko I, Rohleder N, Schurmeyer TH, Kirschbaum C. The cortisol response to awakening in relation to different challenge tests and a 12-hour cortisol rhythm. *Life Sciences*. 1999; 64(18):1653–1660. [PubMed: 10328525]
- Schwid SR, Covington M, Segal BM, Goodman AD. Fatigue in multiple sclerosis: current understanding and future directions. *Journal of rehabilitation research and development*. 2002; 39(2):211–224. [PubMed: 12051465]

- Segerstrom SC, Nes LS. Heart rate variability reflects self-regulatory strength, effort, and fatigue. *Psychological science*. 2007; 18(3):275–281. [PubMed: 17444926]
- Shigihara Y, Tanaka M, Ishii A, Tajima S, Kanai E, Funakura M, Watanabe Y. Two different types of mental fatigue produce different styles of task performance. *Neurology, Psychiatry and Brain Research*. 2013; 19(1):5–11.
- Shirom A. Vigor as a positive affect at work: Conceptualizing vigor, its relations with related constructs, and its antecedents and consequences. *Review of General Psychology*. 2011; 15(1):50.
- Sirois S, Brisson J. Pupillometry. *Wiley Interdisciplinary Reviews: Cognitive Science*. 2014; 5(6):679–692. [PubMed: 26308873]
- Sluiter J, De Croon E, Meijman T, Frings-Dresen M. Need for recovery from work related fatigue and its role in the development and prediction of subjective health complaints. *Occupational and environmental medicine*. 2003; 60(suppl 1):i62–i70. [PubMed: 12782749]
- Smets EM, Garssen B, Bonke B, De Haes JC. The Multidimensional Fatigue Inventory (MFI) psychometric qualities of an instrument to assess fatigue. *J Psychosom Res*. 1995; 39(3):315–325. [PubMed: 7636775]
- Stein KD, Martin SC, Hann DM, Jacobsen PB. A Multidimensional Measure of Fatigue for Use with Cancer Patients. *Cancer Practice*. 1998; 6(3):143–152. [PubMed: 9652245]
- Stein KD, Jacobsen PB, Blanchard CM, Thors C. Further validation of the multidimensional fatigue symptom inventory-short form. *J Pain Symptom Manage*. 2004; 27(1):14–23. [PubMed: 14711465]
- Strasser F, Müller-Käser I, Dietrich D. Evaluating cognitive, emotional, and physical fatigue domains in daily practice by single-item questions in patients with advanced cancer: a cross-sectional pragmatic study. *Journal of Pain and Symptom Management*. 2009; 38(4):505–514. [PubMed: 19822275]
- Teichner WH. The detection of a simple visual signal as a function of time of watch. *Hum Factors*. 1974; 16(4):339–353. [PubMed: 4435787]
- Thayer RE. Activation-deactivation adjective check list: Current overview and structural analysis. *Psychological reports*. 1986; 58(2):607–614.
- Tiesinga LJ, Dassen TW, Halfens RJ. Fatigue: a summary of the definitions, dimensions, and indicators. *Nurs Diagn*. 1996; 7(2):51–62. [PubMed: 8716946]
- Tran Y, Wijesuriya N, Tarvainen M, Karjalainen P, Craig A. The relationship between spectral changes in heart rate variability and fatigue. *Journal of Psychophysiology*. 2009; 23(3):143–151.
- Trejo, LJ.; Kochavi, R.; Kubitz, K.; Montgomery, LD.; Rosipal, R.; Matthews, B. Measures and models for predicting cognitive fatigue. Paper presented at the Defense and Security; 2005.
- van der Linden D, Frese M, Meijman TF. Mental fatigue and the control of cognitive processes: effects on perseveration and planning. *Acta Psychol (Amst)*. 2003; 113(1):45–65. [PubMed: 12679043]
- van Veldhoven M, Broersen S. Measurement quality and validity of the “need for recovery scale”. *Occupational and environmental medicine*. 2003; 60(suppl 1):i3–i9. [PubMed: 12782740]
- Ware JE Jr, Sherbourne CD. The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. *Med Care*. 1992; 30(6):473–483. [PubMed: 1593914]
- Whitehead L. The measurement of fatigue in chronic illness: a systematic review of unidimensional and multidimensional fatigue measures. *J Pain Symptom Manage*. 2009; 37(1):107–128. [PubMed: 19111779]
- Williamson A, Lombardi DA, Folkard S, Stutts J, Courtney TK, Connor JL. The link between fatigue and safety. *Accident Analysis & Prevention*. 2011; 43(2):498–515. [PubMed: 21130213]
- Wust S, Federenko I, Hellhammer DH, Kirschbaum C. Genetic factors, perceived chronic stress, and the free cortisol response to awakening. *Psychoneuroendocrinology*. 2000; 25(7):707–720. [PubMed: 10938450]
- Yamaguchi M, Deguchi M, Wakasugi J, Ono S, Takai N, Higashi T, Mizuno Y. Hand-held monitor of sympathetic nervous system using salivary amylase activity and its validation by driver fatigue assessment. *Biosensors and Bioelectronics*. 2006; 21(7):1007–1014. [PubMed: 15871919]
- Zekveld AA, Kramer SE. Cognitive processing load across a wide range of listening conditions: Insights from pupillometry. *Psychophysiology*. 2014; 51(3):277–284. [PubMed: 24506437]

Zhao C, Zheng C, Zhao M, Tu Y, Liu J. Multivariate autoregressive models and kernel learning algorithms for classifying driving mental fatigue based on electroencephalographic. *Expert Systems with Applications*. 2011; 38(3):1859–1865.

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript