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

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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 audiologic 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 article, the broader fatigue literature is reviewed to identify and describe core constructs, consequences, and methods for assessing fatigue and related constructs. Finally, the current knowledge linking hearing loss and fatigue is described and may be summarized as follows: Hearing impairment may increase 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; and amplification may minimize decrements in cognitive processing speed during sustained effortful listening. 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.

**Key words:** Cognition, Effort, Energy, Fatigue, Hearing loss, Listening effort, Mood, Sleepiness, Vigor, Weariness.

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## **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, and 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 (Tiesinga et al. 1996; Chaudhuri & Behan 2000; O'Connor 2004). 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 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: Behavior

For more than 100 years, and with mixed results, researchers have defined and examined fatigue as a performance decrement (Ackerman 2011). The athlete is very familiar with fatiguerelated 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 & Behan 2000). Fatigue-related performance decrements are also associated with various disease processes (e.g., rheumatoid arthritis and Parkinson's disease; Schwid et al. 2002; Garber & Friedman 2003). 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 & DeLuca 2010; Hornsby 2013).

## (SUBJECTIVE) FATIGUE DIMENSIONS AND RELATED CONSTRUCTS

Researchers continue to debate whether subjective fatigue is best described as a unidimensional or multidimensional

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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 (Piper et al. 1998; Stein 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 & 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 (-0.73 < r < -0.38) between the two moods (Lee et al. 1991; McNair & Heuchert 2010). Despite the negative association, factor analyses suggest they are independent constructs, not bipolar 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 & 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 et al. 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 et al. (2009) found that mentally fatigued cyclists (those that completed a mentally demanding cognitive task for 90 min before cycling) became physically fatigued (unable to maintain a certain rpm) faster than a control group of cyclists that watched a neutral documentary for 90 min before 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 & 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 Versus 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 & 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 (Krupp et al. 1989; Hann et al. 1998).

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 article, 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 to 30 min (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.

## 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 (O'Connor 2006; Lieberman 2007). 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 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 & 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 unidimensional or multidimensional 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 workrelated fatigue (van Veldhoven & Broersen 2003). Some work considers need for recovery scales as a proxy for work-related fatigue (Sluiter et al. 2003). In contrast, other study suggests that while often related, fatigue and need for recovery from work are independent constructs (Jansen et al. 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 et al. 2003; Lim & 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 (van der Linden et al. 2003; DeLuca 2005; Hornsby 2013; Hornsby et al. 2014).

There are two common approaches for measuring fatiguerelated 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 & 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 & 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 article. 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 & Calderon-Moultrie 2016, this issue, pp. 111S–117S), 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 study, 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 et al. 1992). However, the sensitivity of this measure for detecting more transient fatigue due to sustained mental demands is unclear (Marcora et al. 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 & Tharpe 2002; Bess et al. 2016), cancer survivors (Bower et al. 2005), and stress-related fatigue (Olsson et al. 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 axis. In nonfatigued individuals, cortisol levels vary in a systematic circadian (24 hr) 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; Wüst et al. 2000). In addition, changes in cortisol levels in response to stressful events may vary in fatigued and nonfatigued 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 noninvasive biomarker for effort and stress (Granger et al. 2007; Nater & Rohleder 2009). Several studies have reported associations between sAA and plasma norepinephrine levels, a surrogate marker of sympathetic nervous system activity, under different conditions of stress (Rohleder et al. 2004; Kuebler et al. 2014). Recent research also suggests a linkage between norepinephrine levels, modulated by the locus coeruleus, and fatigue-related task engagement/disengagement (Hopstaken et al. 2015b). 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 sleeprelated fatigue as opposed to cognitive or emotional fatigue.

#### Physiologic and Electrophysiologic Techniques

Several investigators have found components of the electroencephalogram to be sensitive to fatigue due to multiple factors, such as extended driving (Zhao et al. 2011; Craig et al. 2012), sustained cognitive tasks (Trejo et al. 2005; Lorist et al. 2009), and multiple sclerosis (Leocani et al. 2001). In addition to continuous monitoring of low-frequency brain activity (electroencephalogram), investigators have also used evoked response potentials to detect fatiguerelated changes in cognitive processing (Murata et al. 2005; Lorist et al. 2009. For example, Murata et al. found that the P300 evoked response potential was sensitive to fatigue-related changes in mental processing resulting from sustained mental work (performing mental arithmetic for 3 hr). 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 et al. 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 & 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 & Brisson 2014) and used to assess effects of hearing loss on cognitive load (e.g., Zekveld & Kramer 2014), has also recently been used to investigate mental fatigue. Hopstaken et al. (2015a, 2015b) 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 2-hr 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 min 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.

#### **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 & 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 to 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 selfcare, and more prone to depression than nonfatigued 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 (van der Linden et al. 2003; Bryant et al. 2004; Lim & Dinges 2008). For example, Lim and Dinges summarized literature in which the Psychomotor Vigilance Task (Dinges & Powell 1985) was used to examine the effects of sleep-related fatigue on vigilant attention and processing speed. The psychomotor vigilance task 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 et al. (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 to achieve a goal. Using classic tasks from the cognitive psychology literature, they assessed flexibility and planning abilities before and after 2hr of mentally demanding tasks. Compared with 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., Mitler 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 US alone. Lost production time at work is especially problematic among fatigued adults who also suffer from other chronic conditions.

## 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 (Hetu et al. 1988; Backenroth & Ahlner 2000; Copithorne 2006; Nachtegaal et al. 2009). As a field, we are just beginning to examine relationships between fatigue and hearing loss directly (Hornsby 2013; Bess & Hornsby 2014; 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. 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 coworkers 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 et al. (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 workrelated 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 study 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 et al. (2014) found children with hearing loss reported significantly more fatigue than agematched 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 (2016) 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% versus 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% versus 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-min period either unaided or when listening via hearing aids. Signal to noise ratios 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-min 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 study provides preliminary evidence that aided listening may reduce susceptibility to speech-processing induced fatiguerelated 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 & 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 signal to noise ratio (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 to 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 with 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 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.

A recent study by Bess et al. also investigated the effects of hearing loss on cortisol levels in children (6 to 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 axis that could put the children at increased risk for stress-related fatigue (Bess et al. 2016).

### 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 shortterm 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 Eckert et al. 2016, this issue, pp. 101S-110S).

Although systematic research is limited, cumulating evidence suggests that some 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 audiologic 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 study 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.

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#### REFERENCES

- Ackerman, P. L. (2011). 100 years without resting. In P. L. Ackerman (Ed.), Cognitive Fatigue: Multidisciplinary Perspectives on Current Research and Future Applications, Decade of Behavior/Science Conference (pp. 11–43). Washington, DC: American Psychological Association.
- Amato, M. P., Ponziani, G., Rossi, F., et al. (2001). Quality of life in multiple sclerosis: The impact of depression, fatigue and disability. *Mult Scler*, 7, 340–344.
- Arnold, L. M. (2008). Understanding fatigue in major depressive disorder and other medical disorders. *Psychosomatics*, 49, 185–190.
- Backenroth, G. A. M., & Ahlner, B. H. (2000). Quality of life of hearingimpaired persons who have participated in audiological rehabilitation counselling. *Int J Adv Counselling*, 22, 225–240.
- Barnes, C. M., & Van Dyne, L. (2009). I'm tired: Differential effects of physical and emotional fatigue on workload management strategies. *Human Relations*, 62, 59–92.
- Basner, M., & Dinges, D. F. (2011). Maximizing sensitivity of the psychomotor vigilance test (PVT) to sleep loss. *Sleep*, 34, 581–591.
- Bess, F. H., & Hornsby, B. W. (2014). Commentary: listening can be exhausting-fatigue in children and adults with hearing loss. *Ear Hear*, 35, 592–599.
- Bess, F. H., Gustafson, S. J., Corbett, B.A., Lambert, et al. (2015). Salivary cortisol profiles of children with hearing loss. *Ear Hear*. 2015 Dec 17. [Epub ahead of print].
- Boksem, M. A., Meijman, T. F., Lorist, M. M. (2005). Effects of mental fatigue on attention: An ERP study. *Brain Res Cogn Brain Res*, 25, 107–116.
- Bower, J. E., Ganz, P. A., Aziz, N. (2005). Altered cortisol response to psychologic stress in breast cancer survivors with persistent fatigue. *Psycho*som Med, 67, 277–280.
- Bryant, D., Chiaravalloti, N. D., DeLuca, J. (2004). Objective measurement of cognitive fatigue in multiple sclerosis. [peer reviewed]. *Rehabil Psychol*, 49, 114–122.
- Caffier, P. P., Erdmann, U., Ullsperger, P. (2003). Experimental evaluation of eye-blink parameters as a drowsiness measure. *Eur J Appl Physiol*, 89, 319–325.
- Cella, D., Riley, W., Stone, A., et al.; PROMIS Cooperative Group. (2010). The patient-reported outcomes measurement information system (PROMIS) developed and tested its first wave of adult self-reported health outcome item banks: 2005-2008. *J Clin Epidemiol*, 63, 1179–1194.
- Chalder, T., Berelowitz, G., Pawlikowska, T., et al. (1993). Development of a fatigue scale. *J Psychosom Res*, *37*, 147–153.
- Chaudhuri, A., & Behan, P. O. (2000). Fatigue and basal ganglia. J Neurol Sci, 179(S1–S2), 34–42.
- Copithorne, D. (2006). The fatigue factor: How I learned to love power naps, meditation, and other tricks to cope with hearing-loss exhaustion.[healthy hearing web site]. August 21, 2006. 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., et al. (2012). Regional brain wave activity changes associated with fatigue. *Psychophysiology*, 49, 574–582.
- Curt, G. A., Breitbart, W., Cella, D., et al. (2000). Impact of cancer-related fatigue on the lives of patients: New findings from the Fatigue Coalition. *Oncologist*, *5*, 353–360.
- DeLuca, J. (2005). Fatigue, cognition, and mental effort. In J. DeLuca (Ed.), Fatigue as a Window to the Brain (pp. 37–58). Cambridge, MA: MIT Press.
- Dinges, D., & Powell, J. (1985). Microcomputer analyses of performance on a portable, simple visual RT task during sustained operations. *Behavior Research Methods*, 17, 652–655.
- Dittner, A. J., Wessely, S. C., Brown, R. G. (2004). The assessment of fatigue: A practical guide for clinicians and researchers. J Psychosom Res, 56, 157–170.
- Eckert, M. A., Teubner-Rhodes, S., Vaden, K. (2016). Is listening in noise worth it? The neurobiology of speech recognition in challenging listening conditions. *Ear Hear*, 37, 101S–110S.
- Eggert, T., Sauter, C., Popp, R., et al.; "Vigilance" of the German Society for Sleep Research and Sleep Medicine (DGSM). (2012). The pupillographic sleepinesstest in adults: Effect of age, gender, and time of day on pupillometric variables. *Am J Hum Biol*, 24, 820–828.
- Evans, E. J., & Wickstrom, B. (1999). Subjective fatigue and self-care in individuals with chronic illness. *Medsurg Nurs*, 8, 363–369.
- Flechtner, H., & Bottomley, A. (2003). Fatigue and quality of life: Lessons from the real world. *Oncologist*, 8(Suppl 1), 5–9.

- Garber, C. E., & Friedman, J. H. (2003). Effects of fatigue on physical activity and function in patients with Parkinson's disease. *Neurology*, 60, 1119–1124.
- Gold, A. E., MacLeod, K. M., Deary, I. J., et al. (1995). Hypoglycemiainduced cognitive dysfunction in diabetes mellitus: Effect of hypoglycemia unawareness. *Physiol Behav*, 58, 501–511.
- Granger, D. A., Kivlighan, K. T., el-Sheikh, M., et al. (2007). Salivary alpha-amylase in biobehavioral research: Recent developments and applications. *Ann NY Acad Sci*, 1098, 122–144.
- Green, H. J. (1997). Mechanisms of muscle fatigue in intense exercise. *J Sports Sci*, 15, 247–256.
- Hann, D. M., Jacobsen, P. B., Azzarello, L. M., et al. (1998). Measurement of fatigue in cancer patients: Development and validation of the fatigue symptom inventory. *Qual Life Res*, 7, 301–310.
- Hetu, R., Riverin, L., Lalande, N., et al. (1988). Qualitative analysis of the handicap associated with occupational hearing loss. *Br J Audiol*, 22, 251–264.
- Hicks, C. B., & Tharpe, A. M. (2002). Listening effort and fatigue in school-age children with and without hearing loss. J Speech Lang Hear Res, 45, 573–584.
- Hopstaken, J. F., van der Linden, D., Bakker, A. B., et al. (2015a). A multifaceted investigation of the link between mental fatigue and task disengagement. *Psychophysiology*, 52, 305–315.
- Hopstaken, J. F., van der Linden, D., Bakker, A. B., et al. (2015b). The window of my eyes: Task disengagement and mental fatigue covary with pupil dynamics. *Biol Psychol*, 110, 100–106.
- Hornsby, B. (2012, August). Tired of listening: Subjective and objective measures of hearing related fatigue. Paper presented at the International Hearing Aid Conference (IHCON), Lake Tahoe, CA.
- Hornsby, B. W. (2013). The effects of hearing aid use on listening effort and mental fatigue associated with sustained speech processing demands. *Ear Hear*, 34, 523–534.
- Hornsby, B., & Kipp, A. M. (2016). Subjective ratings of fatigue and vigor in adults with hearing loss are driven by perceived hearing difficulties not degree of hearing loss. *Ear Hear*, *37*, e1–e10.
- Hornsby, B. W., Werfel, K., Camarata, S., et al. (2014). Subjective fatigue in children with hearing loss: Some preliminary findings. *Am J Audiol*, 23, 129–134.
- Jansen, N. W., Kant, I. J., van den Brandt, P. A. (2002). Need for recovery in the working population: Description and associations with fatigue and psychological distress. *Int J Behav Med*, 9, 322–340.
- Kato, Y., Endo, H., Kizuka, T. (2009). Mental fatigue and impaired response processes: Event-related brain potentials in a Go/NoGo task. *Int J Psychophysiol*, 72, 204–211.
- Kramer, S. E., Kapteyn, T. S., Houtgast, T. (2006). Occupational performance: Comparing normally-hearing and hearing-impaired employees using the Amsterdam Checklist for Hearing and Work. *Int J Audiol*, 45, 503–512.
- Krupp, L. B., LaRocca, N. G., Muir-Nash, J., et al. (1989). The fatigue severity scale. Application to patients with multiple sclerosis and systemic lupus erythematosus. *Arch Neurol*, 46, 1121–1123.
- Kuebler, U., von Känel, R., Heimgartner, N., et al. (2014). Norepinephrine infusion with and without alpha-adrenergic blockade by phentolamine increases salivary alpha amylase in healthy men. *Psychoneuroendocrinology*, 49, 290–298.
- Lal, S. K., & Craig, A. (2001). A critical review of the psychophysiology of driver fatigue. *Biol Psychol*, 55, 173–194.
- Leavitt, V. M., & DeLuca, J. (2010). Central fatigue: Issues related to cognition, mood and behavior, and psychiatric diagnoses. PM R, 2, 332–337.
- LeDuc, P. A., Greig, J. L., Dumond, S. L. (2005). Involuntary eye responses as measures of fatigue in US Army Apache aviators. *Aviat Space Environ Med*, 76(7 Suppl), C86–C91.
- Lee, K. A., Hicks, G., Nino-Murcia, G. (1991). Validity and reliability of a scale to assess fatigue. *Psychiatry Res*, 36, 291–298.
- Leocani, L., Colombo, B., Magnani, G., et al. (2001). Fatigue in multiple sclerosis is associated with abnormal cortical activation to voluntary movement: EEG evidence. *Neuroimage*, 13, 1186–1192.
- Lieberman, H. R. (2007). Cognitive methods for assessing mental energy. *Nutr Neurosci*, 10, 229–242.
- Lim, J., & Dinges, D. F. (2008). Sleep deprivation and vigilant attention. Ann NYAcad Sci, 1129, 305–322.
- Lim, J., Wu, W. C., Wang, J., et al. (2010). Imaging brain fatigue from sustained mental workload: An ASL perfusion study of the time-on-task effect. *Neuroimage*, 49, 3426–3435.
- Lorist, M. M., Bezdan, E., ten Caat, M., et al. (2009). The influence of mental fatigue and motivation on neural network dynamics: An EEG coherence study. *Brain Res*, 1270, 95–106.

- Lowenstein, O., Feinberg, R., Loewenfeld, I. E. (1963). Pupillary movements during acute and chronic fatigue a new test for the objective evaluation of tiredness. *Invest Ophthalmol Vis Sci*, 2, 138–157.
- Mackersie, C. L., & Calderon-Moultrie, N. (2016). Autonomic nervous system reactivity during speech repetition tasks: Heart-rate variability and skin conductance. *Ear Hear*, 37, 118S–125S.
- Mackworth, N. (1948). The breakdown of vigilance during prolonged visual search. *Q J Exp Psychol*, *1*, 6–21.
- Marcora, S. M., Staiano, W., Manning, V. (2009). Mental fatigue impairs physical performance in humans. *J Appl Physiol (1985)*, 106, 857–864.
- McGarrigle, R., Munro, K. J., Dawes, P., et al. (2014). Listening effort and fatigue: What exactly are we measuring? A British Society of Audiology Cognition in Hearing Special Interest Group "white paper." *Int J Audiol*, *53*, 433–440.
- McNair, D., Lorr, M., Droppleman, L. (1971). Profile of Mood States. San Diego, CA: Educational and Industrial Testing Service. Retrieved from http://www.mhs.com/product.aspx?gr=cli&id=overview&prod=poms.
- McNair, D. M., & Heuchert, J. W. P. (2010). Profile of Mood States: Technical Update. Toronto: Multi-Health Systems Inc.
- Melamud, L., Golan, D., Luboshitzky, R., et al. (2012). Melatonin dysregulation, sleep disturbances and fatigue in multiple sclerosis. J Neurol Sci, 314, 37–40.
- Michielsen, H. J., De Vries, J., Van Heck, G. L., et al. (2004). Examination of the dimensionality of fatigue: The construction of the fatigue assessment scale (FAS). *Eur J Psychol Assess*, 20, 39.
- Mitler, M. M., Carskadon, M. A., Czeisler, C. A., et al. (1988). Catastrophes, sleep, and public policy: Consensus report. *Sleep*, 11, 100–109.
- Murata, A., Uetake, A., & Takasawa, Y. (2005). Evaluation of mental fatigue using feature parameter extracted from event-related potential. *Int J Ind Ergonom*, 35, 761–770.
- Nachtegaal, J., Festen, J. M., Kramer, S. E. (2012). Hearing ability in working life and its relationship with sick leave and self-reported work productivity. *Ear Hear*, 33, 94–103.
- Nachtegaal, J., Kuik, D. J., Anema, J. R., et al. (2009). Hearing status, need for recovery after work, and psychosocial work characteristics: Results from an internet-based national survey on hearing. *Int J Audiol*, 48, 684–691.
- Nater, U. M., & Rohleder, N. (2009). Salivary alpha-amylase as a noninvasive biomarker for the sympathetic nervous system: Current state of research. *Psychoneuroendocrinology*, 34, 486–496.
- Newsholme, E. A., Blomstrand, E., Ekblom, B. (1992). Physical and mental fatigue: Metabolic mechanisms and importance of plasma amino acids. *Br Med Bull*, 48, 477–495.
- Nozaki, S., Tanaka, M., Mizuno, K., et al. (2009). Mental and physical fatigue-related biochemical alterations. *Nutrition*, 25, 51–57.
- Nyenhuis, D. L., Yamamoto, C., Luchetta, T., et al. (1999). Adult and geriatric normative data and validation of the profile of mood states. J Clin Psychol, 55, 79–86.
- O'Connor, P. J. (2004). Evaluation of four highly cited energy and fatigue mood measures. *J Psychosom Res*, *57*, 435–441.
- O'Connor, P. J. (2006). Mental energy: Assessing the mood dimension. Nutr Rev, 64(7 Pt 2), S7–S9.
- Olsson, E. M., Roth, W. T., Melin, L. (2010). Psychophysiological characteristics of women suffering from stress-related fatigue. *Stress Health*, 26, 113–126.
- Piper, B. F., Dibble, S. L., Dodd, M. J., et al. (1998). The revised Piper Fatigue Scale: Psychometric evaluation in women with breast cancer. *Oncol Nurs Forum*, 25, 677–684.
- Ricci, J. A., Chee, E., Lorandeau, A. L., et al. (2007). Fatigue in the U.S. workforce: Prevalence and implications for lost productive work time. *J Occup Environ Med*, 49, 1–10.
- Richter, M. (2016). The moderating effect of success importance on the relationship between listening demand and listening effort. *Ear Hear*, 37, 1118–117S.
- Roberts, A. D., Wessely, S., Chalder, T., et al. (2004). Salivary cortisol response to awakening in chronic fatigue syndrome. *Br J Psychiatry*, 184, 136–141.
- Robinson-Smith, G., Johnston, M. V., Allen, J. (2000). Self-care self-efficacy, quality of life, and depression after stroke. *Arch Phys Med Rehabil*, 81, 460–464.
- Rohleder, N., Nater, U. M., Wolf, J. M., et al. (2004). Psychosocial stressinduced activation of salivary alpha-amylase: An indicator of sympathetic activity? *Ann NY Acad Sci*, 1032, 258–263.
- Ryan, R. M., & Frederick, C. (1997). On energy, personality, and health: Subjective vitality as a dynamic reflection of well-being. J Pers, 65, 529–565.

- Schmidt-Reinwald, A., Pruessner, J. C., Hellhammer, D. H., et al. (1999). The cortisol response to awakening in relation to different challenge tests and a 12-hour cortisol rhythm. *Life Sci*, 64, 1653–1660.
- Schwid, S. R., Covington, M., Segal, B. M., et al. (2002). Fatigue in multiple sclerosis: Current understanding and future directions. J Rehabil Res Dev, 39, 211–224.
- Segerstrom, S. C., & Nes, L. S. (2007). Heart rate variability reflects selfregulatory strength, effort, and fatigue. *Psychol Sci*, 18, 275–281.
- Shigihara, Y., Tanaka, M., Ishii, A., et al. (2013). Two different types of mental fatigue produce different styles of task performance. *Neurol Psychiat Brain Res*, 19, 5–11.
- Shirom, A. (2011). Vigor as a positive affect at work: Conceptualizing vigor, its relations with related constructs, and its antecedents and consequences. *Rev Gen Psychol*, 15, 50.
- Sirois, S., & Brisson, J. (2014). Pupillometry. Wiley Interdiscip Rev Cogn Sci, 5, 679–692.
- Sluiter, J. K., de Croon, E. M., Meijman, T. F., et al. (2003). Need for recovery from work related fatigue and its role in the development and prediction of subjective health complaints. *Occup Environ Med*, 60(Suppl 1), i62–i70.
- Smets, E. M., Garssen, B., Bonke, B., et al. (1995). The multidimensional fatigue inventory (MFI) psychometric qualities of an instrument to assess fatigue. J Psychosom Res, 39, 315–325.
- Stein, K. D., Martin, S. C., Hann, D. M., et al. (1998). A multidimensional measure of fatigue for use with cancer patients. *Cancer Pract*, 6, 143–152.
- Stein, K. D., Jacobsen, P. B., Blanchard, C. M., et al. (2004). Further validation of the multidimensional fatigue symptom inventory-short form. *J Pain Symptom Manage*, 27, 14–23.
- Stern, J. A., Boyer, D., & Schroeder, D. (1994). Blink rate: A possible measure of fatigue. *Hum Factors*, 36, 285–297.
- Strasser, F., Müller-Käser, I., Dietrich, D. (2009). Evaluating cognitive, emotional, and physical fatigue domains in daily practice by single-item questions in patients with advanced cancer: A cross-sectional pragmatic study. J Pain Symptom Manage, 38, 505–514.
- Teichner, W. H. (1974). The detection of a simple visual signal as a function of time of watch. *Hum Factors*, *16*, 339–353.
- Thayer, R. E. (1986). Activation-deactivation adjective check list: Current overview and structural analysis. *Psychol Rep*, 58, 607–614.
- Tiesinga, L. J., Dassen, T. W., Halfens, R. J. (1996). Fatigue: A summary of the definitions, dimensions, and indicators. *Nurs Diagn*, 7, 51–62.
- Tran, Y., Wijesuriya, N., Tarvainen, M., et al. (2009). The relationship between spectral changes in heart rate variability and fatigue. J Psychophysiol, 23, 143–151.
- Trejo, L. J., Kochavi, R., Kubitz, K., et al. (2005). Measures and models for predicting cognitive fatigue. Paper presented at the Defense and Security.
- van der Linden, D., Frese, M., Meijman, T. F. (2003). Mental fatigue and the control of cognitive processes: Effects on perseveration and planning. *Acta Psychol (Amst)*, 113, 45–65.
- van Heukelom, R., Prins, J., Smits, M., et al. (2006). Influence of melatonin on fatigue severity in patients with chronic fatigue syndrome and late melatonin secretion. *Eur J Neuro*, 13, 55–60.
- van Veldhoven, M., & Broersen, S. (2003). Measurement quality and validity of the "need for recovery scale." Occup Environ Med, 60(Suppl 1), i3–i9.
- Ware, J. E. Jr., & Sherbourne, C. D. (1992). The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. *Med Care*, 30, 473–483.
- Whitehead, L. (2009). The measurement of fatigue in chronic illness: A systematic review of unidimensional and multidimensional fatigue measures. J Pain Symptom Manage, 37, 107–128.
- Williamson, A., Lombardi, D. A., Folkard, S., et al. (2011). The link between fatigue and safety. Accid Anal Prev, 43, 498–515.
- Wüst, S., Federenko, I., Hellhammer, D. H., et al. (2000). Genetic factors, perceived chronic stress, and the free cortisol response to awakening. *Psychoneuroendocrinology*, 25, 707–720.
- Yamaguchi, M., Deguchi, M., Wakasugi, J., et al. (2006). Hand-held monitor of sympathetic nervous system using salivary amylase activity and its validation by driver fatigue assessment. *Biosens Bioelectron*, 21, 1007–1014.
- Zekveld, A. A., & Kramer, S. E. (2014). Cognitive processing load across a wide range of listening conditions: Insights from pupillometry. *Psychophysiology*, 51, 277–284.
- Zhao, C., Zheng, C., Zhao, M., et al. (2011). Multivariate autoregressive models and kernel learning algorithms for classifying driving mental fatigue based on electroencephalographic. *Expert Sys Appl*, 38, 1859–1865.