The impact of sleep apnea on fatigue

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The obstructive sleep apnea syndrome (OSAS) is a common medical condition. The condition is characterized by sleep-disordered breathing, with arousals from apneas and hypopneas leading to sleep fragmentation and ensuing fatigue. Night sweats and morning headaches are among the accompanying symptoms, with daytime sleepiness being the most predominant. Given the prevalence of fatigue in OSAS patients and its negative consequences on daily functioning and quality of life, its identification in these individuals is of great importance. This is of particular relevance in those for whom fatigue persists despite treatment of OSAS, as this can indicate that the OSAS is not the main or only cause. It is therefore vital to have a good understanding of the overlap between fatigue and related constructs, such as sleepiness and depression, and to use a valid and reliable instrument that is not confounded by these constructs and OSAS severity with which to identify patients at high risk of fatigue. Knowledge of the prevalence of fatigue in patients with OSAS and its determinants is important for secondary prevention in order to identify patients at risk of adverse secondary outcomes such as clinical depression, impaired quality of life, loss of productivity at work, and an increased risk of motor vehicle accidents. Int J Sleep Wakefulness 2007;1(2):

The obstructive sleep apnea syndrome (OSAS) is a common medical condition, with an estimated prevalence of 2–4% in middle-aged men and 1–2% in women, although prevalence rates vary between studies [1,2]. However, given that the definition of OSAS is continually evolving, these prevalence rates may neither be robust nor reflect the actual number of patients with OSAS. In addition, OSAS is generally under-diagnosed and under-treated, and it is estimated that up to 5% of the adult population in Western countries has undiagnosed OSAS [1]. This figure was confirmed in a recent analysis of data from the Sleep in America 2005 Poll undertaken by the National Sleep Foundation, which showed that one in four individuals from a representative sample of US adults would be considered high-risk candidates for a diagnosis of OSAS [3].

Hence, the prevalence and incidence of OSAS are likely to increase in the future as a result of the increasing elderly population and the rise in obesity that is expected to take on epidemic proportions. Risk factors for the development of OSAS include increasing age at least up to 65 years, obesity, male sex (with a 2:1 ratio), and craniofacial and upper-airway abnormalities [1,4]. Genetics, smoking, menopause, and nasal congestion are possible risk factors, but further studies are warranted to confirm their potential role in OSAS [1,4].

OSAS is characterized by sleep-disordered breathing, with arousals from apneas and hypopneas leading to sleep fragmentation and ensuing fatigue [1]. Associated symptoms comprise sweating during the night and morning headaches, with daytime sleepiness being the most predominant symptom. In addition, OSAS may lead to adverse secondary outcomes including:

• Clinical depression [5].
• Impaired quality of life [1].
• Loss in work productivity [6].
• Increased risk of car accidents [7].

Moreover, OSAS has been associated with the following more serious health outcomes:

• Hypertension [8].
• Glucose intolerance [9].
• Cardiovascular disease and mortality [10,11].

It is important to pay specific attention to fatigue in relation to OSAS as it may be an invalidating symptom that can be reduced with an adequate intervention. However, if OSAS is
not the only or major cause of the fatigue reported by patients, this complaint will still have a major impact on patients' lives even after adequate treatment for the OSAS. Therefore, the focus of the current article is to evaluate the impact of OSAS on fatigue, to identify the overlap between fatigue and related constructs such as sleepiness and depression, and to provide recommendations as to how fatigue can best be assessed in patients with OSAS in clinical practice.

Fatigue, sleepiness, and related symptoms
Daytime sleepiness is a cardinal feature of OSAS that is often used interchangeably with fatigue because patients frequently complain of symptoms of both conditions. Although sleepiness, which reflects a physiological need for sleep, can be objectively quantified with tests, measurements of fatigue are more elusive and rely almost exclusively on self-report [12]. It is possible that this is the reason why fatigue in OSAS tends to have been assessed as a sub-component of quality of life rather than in its own right [13,14]. Given that fatigue is also included within the diagnostic criteria for major depression, as listed in the Diagnostic and Statistical Manual of Mental Disorders IV – text revision, this only adds to its complexity. A final problem is OSAS severity, which may serve as a confounder in this puzzle.

Some attempts have been made to disentangle this complexity and tease out the relative influence of sleepiness, mood, and presence of OSAS on fatigue. Indeed, some studies suggest that depression rather than severity of OSAS may explain fatigue in sufferers [12,15]. In addition, fatigue and sleepiness seem to be two independent constructs [16], indicating that the level of fatigue cannot be inferred by measures of sleepiness but should be assessed in its own right. A number of complaints, such as somnolence, are inherent to OSAS. When OSAS is treated, syndrome specific complaints will also disappear. However, fatigue can have multiple causes, with OSAS being only one of them. For clinical practice, knowledge of the prevalence of fatigue in patients with OSAS and its determinants is important for secondary prevention in order to identify those patients at risk of adverse secondary outcomes, such as clinical depression [5], impaired quality of life [1], loss of productivity at work [6], and increased risk of motor vehicle accidents [7]. For this purpose, it is particularly important to have a valid and reliable scale with which to assess fatigue in the context of OSAS that is not confounded by disease severity and symptoms of depression.

Dimensionality of fatigue
Initially, fatigue was seen as a unidimensional construct [17], but the current perception is that fatigue is a multidimensional construct [18–20], divided into physical and mental components [21]. However, there is no consensus about this distinction, and support for the multidimensionality concept has been derived predominantly from statistical criteria that often overestimate the number of dimensions or assume multidimensionality in testing several models [22].

Some researchers have questioned the putative superiority of a multidimensional structure of fatigue [22–27]. Michielsen and colleagues examined the dimensionality of four existing fatigue measures and found strong support for the unidimensionality of the questionnaires used [22]. Unidimensionality of fatigue measures was not only found among healthy persons [22,27], but also in patients with sarcoidosis [25], breast cancer [28], and chronic pain [26]. This suggests that fatigue can be assessed adequately in terms of general fatigue.

Measuring of fatigue
Friedberg and Jason [13], and Alberts et al. [14] reviewed several questionnaires available for measuring fatigue in subjects with chronic fatigue syndrome [13] and in several populations with different diseases and the general population [14]. The majority have been developed for specific patient groups or ill persons in general, with the Fatigue Scale being one of the few developed for use in both hospital and community populations [21]. Generally, multidimensional fatigue scales are seen as more comprehensive and hence more adequate for providing a complete description of the patient's fatigue experience [14]. They are able to take into consideration that persons with the same overall score may differ substantially in their experience [20]. However, a disadvantage of multidimensional scales is the length of time they take to complete. Fatigue is frequently measured using subscales of broader measures; the Energy and Fatigue facet of the World Health Organization Quality of Life assessment instrument (WHOQOL-100) is a good example of this [29]. Recently, Dittner, Wessely, and Brown described 30 existing fatigue questionnaires [30]. This included information on the psychometric properties of the questionnaires and illustrations of their use. They provided recommendations for the selection of a fatigue scale for clinicians and researchers.

The Fatigue Assessment Scale
The Fatigue Assessment Scale (FAS), a short, valid, reliable, and easy to administer unidimensional fatigue questionnaire, was developed a few years ago [22,24]. The initial item pool from which it was developed comprised 40 items taken from four commonly used fatigue questionnaires:

- The Fatigue Scale [20].
- The Checklist Individual Strength [31].
• The Emotional Exhaustion subscale of the Maslach Burnout Inventory [32].
• The Energy and Fatigue scale of the WHOQOL-100 [29].

Several steps, described by Michielsen and colleagues, resulted in the final 10-item FAS, which can be used to quantify chronic fatigue [22,24]. First, items from the four fatigue questionnaires were removed that (i) could only be completed by specific groups (e.g. workers), (ii) were asking two questions at the same time, or (iii) were not obvious fatigue items. Second, a semantical procedure that was also used by the WHOQOL Group [33] was followed to reduce the 40-item pool. This procedure entailed a content analysis of the questions to identify semantically equivalent questions. Third, any questions that were substandard to the construct fatigue were deleted. Questions were then carefully grouped into categories asking about a similar type of fatigue. Judgements of semantical equivalence and categories were carried out by consensual agreement of two researchers. After the semantical analysis, the item per semantical group with the highest factor loading on the one-factor solution of the 40 items was chosen. In addition, an extra item concerning mental exhaustion was included. The reason for adding this item was to ensure that the most often represented domains of fatigue, mental and physical fatigue, were assessed in the same manner [21].

In the test phase, the FAS demonstrated good reliability and content validity [22]. Two subsequent studies among healthy persons showed the scale has a high internal consistency. Factor analysis and correlations confirmed the convergent and divergent validities. Indeed, using a higher-order factor analysis, the FAS had the highest factor loading on a one-factor solution when five fatigue questionnaires were included in the analysis [22,27]. Moreover, factor analysis revealed that fatigue, depression, and emotional stability are three separate constructs [22]. The authors examined whether the questionnaire should be scored differently for men and women and found that gender bias did not play a role in scoring of the FAS [22]. Studies among patients with sarcoidosis [25,34] and breast cancer [28] provided similar findings.

The psychometric properties of FAS were recently examined in 94 patients with OSAS (apnea–hypopnoea index [AHI] 35±26 events/h) from the Antwerp University Hospital (Antwerp, Belgium), and a gender (77 males), age (51 years), and body mass index (29.3) matched control group with non-apneic snoring or mild OSAS (AHI ≤15 events/h). The association between fatigue, as measured using the FAS, and sleepiness was examined [35]. Besides the FAS, patients completed the Epworth Sleepiness Scale [36], the Neuroticism–Extraversion–Openness Five-Factor Inventory [37], the Beck Depression Inventory [38], the Global Mood Scale [39], and the Short-Form Health Survey (SF-36) [40], a general health status scale, prior to diagnosis. Factor analysis showed the FAS to be a unidimensional scale that measures one concept in patients with OSAS and their controls. Moreover, the internal consistency of the FAS was good (Cronbach alpha coefficient 0.92). Patients with OSAS experienced more fatigue than the matched controls, but there were no differences regarding sleepiness. The correlation coefficient between fatigue and sleepiness was 0.54. Both fatigue and sleepiness correlated strongly with the SF-36 vitality scale (r = −0.84 and −0.95, respectively). Additionally, fatigue was strongly associated with neuroticism (0.54), depression (0.70), and negative affect (0.83; p < 0.001 for all) [35].

Conclusion

There is evidence to suggest that fatigue should be studied in its own right in patients with OSAS. The FAS, a brief, valid, and reliable instrument, which utility has recently been demonstrated in patients with OSAS [35], may be a helpful instrument in the continuing attempts to further disentangle the potential overlap between disease severity, sleepiness, depression, and fatigue in the context of OSAS. One advantage of the FAS in the context of this condition is that it is not confounded by somatic symptoms and is independent of depression. Additional properties of the FAS that should be examined in OSAS patients are test-retest reliability, sensitivity to change, and criterion validity. Future, large-scale prospective studies of patients, with fatigue are warranted in order to investigate the relative influence of OSAS severity, sleepiness, and depression on fatigue.

Disclosures

The authors have no relevant financial relationships to disclose.

References


