Identification of a Biomarker of Sleep Deficiency—Are We Tilting Windmills?

The amount of time spent asleep by adults in the United States and other developing countries is decreasing. It is estimated that over 40 years ago, adults slept in excess of 8 hours per night, but now sleep barely 7 hours per night (1) During this time frame, there has been a corresponding increase in obesity and diabetes mellitus which in part has been attributed to a reduction in time sleeping (2). In addition, sleep deficiency and other sleep disorders have been implicated as risk factors for hypertension, cardiovascular disease and cancer (3-5). Consequently, billions of excess health care dollars are spent on medical conditions associated with sleep deficiency or sleep disorders (6,7). Their impact also include substantial costs resulting from lost productivity as well as increased absenteeism, presenteeism and motor vehicle or industrial accidents (6,7). Thus, sleep disorders and sleep deficiency are significant threats to public health and productivity in the United States and worldwide and no evidence of a decline is on the horizon. One barrier to reducing their impact is the difficulty in identifying on a societal and personal level the major consequence of sleep deficiency, sleepiness.

Despite the extraordinary progress made by sleep and circadian science in recent years, developing an accurate and easy to use biomarker for sleepiness and/or sleep deficiency has been elusive. Currently used objective assessments of sleepiness such as the multiple sleep latency test or the psychomotor vigilance test are either difficult to use outside the laboratory environment or do not evaluate all domains of sleep deficiency. Subjective assessments of sleepiness are unreliable because many individuals cannot recognize their impairment (8) and in some occupational scenarios (e.g., truck drivers, railroad engineers); there is personal incentive to deny its presence because of the fear of losing employment or income (9).

If developed, there would be several uses for a sleepiness or sleep deficiency biomarker. These include:

- Research: especially in field studies of the impact of sleep deficiency and/or sleepiness in both small and large size cohorts;
- Fitness for duty: in clinical and occupational settings (e.g., operating a motor vehicle, aircraft pilot) where objective assessment of sleepiness would be important in determining whether an individual could perform their job;
- Personal health: such testing might ultimately provide a means for an individual to determine his/her level of sleepiness and allow self adjustment of medication or positive airway pressure in the case of obstructive sleep apnea patients, analogous to currently used home glucose testing in persons with diabetes mellitus;

- Disease risk stratification: level of sleep deficiency might identify individuals with a greater likelihood of developing other medical conditions such as cardiovascular disease or diabetes.

In an attempt to "jumpstart" interest and research into developing a sleepiness or sleep deficiency biomarker, the Division of Sleep Medicine at Harvard Medical School hosted a conference on September 21-22, 2010 supported by the National Heart, Lung and Blood Institute and commercial entities entitled "Finding a Research Path for the Identification of Biomarkers of Sleepiness" (10). A number of prominent national and international speakers presented possible approaches to achieving this goal including behavioral, physiologic, genomic and proteomic solutions. This conference was followed by a panel discussion on this same topic at the annual Sleep 2011 international conference. Despite these high profile public discourses, there has been little progress in finding a sleepiness/sleep deficiency biomarker. A brief search of PubMed identified only one paper published since the conference directly relevant to this area (11).

Why has there been so little progress? I would propose the major reason is lack of a public "outcry". Despite high profile incidences such as the crash of Colgan Air Flight #3407 (12) and the grounding of the Exxon Valdez (13), and a report from the Institute of Medicine (6) the general public has not adopted sleep issues as a major public health concern. In contrast, cancer, heart disease, obesity and diabetes, all of which may in part be consequences of sleep deficiency or a sleep disorder, are higher in the public consciousness. As a result, it is unlikely that funding initiatives such as a RFA on research into sleepiness or sleep deficiency biomarkers from the National Institutes of Health will be forthcoming.

What can be done? It should be the mission of all of us who are involved in sleep research and clinical Sleep Medicine to promote to the public the importance of sleep deficiency and sleep disorders in adversely impacting public health. Until there is a ground swell of public support, I fear attempts to identify biomarkers for sleepiness or sleep deficiency may be similar to "tilting at windmills."

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