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COMMENTARY

Is there a link between mild sleep disordered breathing and psychiatric and psychosomatic disorders?

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The paper by Gold[1] in this issue of *Sleep Medicine Reviews* describes a theoretical model for a large group of disorders such as functional somatic syndromes, anxiety disorders, and substance abuse. The basic thesis is that mild sleep disordered breathing (SDB) is the most likely explanation of all these disorders of "uncertain etiology". Theoretical models are useful in science and medicine in particular. Theoretical models include novel ideas and usually challenge current wisdom and practice. Such models can be fertile to the field particularly if they promote "out of the box" thinking.

A basic premise of Gold's model is the belief that mild SDB, i.e., upper airway resistance syndrome (UARS) or snoring, is very common in most of these disorders and may be causally related to them. However, a careful review of the literature linking SDB to functional somatic syndromes and anxiety disorders does not support such a statement. Specifically, the vast majority of studies that the author cites are based on self-reported data,[2–9] lack a control group,[10–16] have a small sample size,[12,17–20] do not control for confounding factors or comorbid conditions,[10–16] report non-significant results,[17] or are case reports.[21,22] Also, the studies on the use of continuous positive airway pressure (CPAP) for treating mild SDB and the associated symptoms suffer from the same methodological limitations (case reports, small sample sizes, or absence of a control group).[12,16,20,22] Importantly, in most of the studies reviewed a selection bias may exist, as those patients with sleep problems from clinical populations were more likely to volunteer or to be referred by a physician to participate in the studies. Notably, no studies in general population random samples using polysomnography (PSG) that support the association of SDB with these functional disorders are cited.

From a clinical standpoint it is possible that for example some patients with chronic fatigue syndrome (CFS) may suffer from SDB and the diagnosis of CFS should not be made in the presence of diagnosable disorders.[23,24] Also, SDB should be ruled out if there is a prominent complaint of fatigue, e.g., Gulf war illness.[19,20] Furthermore, it is possible that in anxious persons, breathing difficulties at night may be associated with heightened over-reaction. It is also possible that a breathing-related arousal in a "light" sleeper may generate an anxiety reaction. But no data or clinical experience suggest that these events are the cause of chronic psychiatric disorders such as panic disorder, generalized anxiety disorder (GAD), social phobia, posttraumatic stress disorder (PTSD), or obsessive-compulsive disorder (OCD).

Dr. Gold claims that the link between SDB and psychiatric disorders is the activation of the hypothalamic-pituitary-adrenal (HPA) axis. Many studies until recently have failed to show an association between sleep apnea and HPA axis activation.[25] Our comprehensive assessment of the HPA axis in obese patients with sleep apnea that included 24 h frequent blood sampling reported two interesting findings: 1) in obese men HPA axis activity is decreased compared with that of matched non-obese controls, 2) sleep apnea is associated with a mild nighttime elevation of cortisol levels which is corrected after the use of CPAP for 3 months.[26] Furthermore, we reported that the exaggerated response of adrenocorticotropic hormone (ACTH) to corticotropin-releasing hormone (CRH) test suggest a hyposecretion of hypothalamic CRH in sleep apneics.[26] More recent studies by our group in non-obese apneics have shown a mild or no elevation of nighttime cortisol levels between apneics and controls.[27,28] Cumulatively, these findings suggest a very different profile of HPA axis activity in sleep apnea *versus* the majority of psychiatric syndromes reported by Gold.[29] We do not know of any studies on HPA axis in patients with mild SDB. However, there is no reason to believe that mild sleep apnea is associated with "great" activation of HPA axis, whereas moderate/severe sleep apnea is associated with an overall relative

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Abbreviation

ACTH	adrenocorticotropic hormone
CFS	chronic fatigue syndrome
CPAP	continuous positive airway pressure
CRH	corticotropin-releasing hormone
GAD	generalized anxiety disorder
HPA axis	hypothalamic-pituitary-adrenal axis
OCD	obsessive-compulsive disorder
PSG	polysomnography
PTSD	posttraumatic stress disorder
SDB	sleep disordered breathing
UARS	upper airway resistance syndrome

hypoactivity of the axis and only a mild elevation of cortisol levels at night.

Sleep apnea is known to affect blood pressure, sleepiness and fatigue, and neurocognitive function, and the effects are more clear in patients with severe apnea.[30–32] Patients with mild apnea do not show any benefit from the use of CPAP[33,34] and also, as correctly Dr. Gold points, cannot tolerate it. It is contradictory that the author recommends the use of CPAP for those for whom no benefit has been demonstrated and who are the least likely to adhere to its use.

The field of Psychiatry has made major advances both as far as the etiology and the treatment of anxiety and depressive disorders. Both biological and psychological interventions have been tested in hundreds of well-controlled studies and offer a big relief to many of these patients. To abandon these well-established approaches for treatments that may worsen their symptoms is potentially dangerous. This does not mean that individual patients who also on clinical grounds, i.e., male gender, middle-age, obesity, heavy snoring, are suspect of having SDB should not be tested and treated if indicated for this disorder.

Our major concern about Dr. Gold's model is not its theoretical speculation (there is no "right" or "wrong" as he says) but its diagnostic and therapeutic implications. He implies that millions of people with psychiatric or psychosomatic symptoms or people exposed to disasters or wars, e.g., September 11, Gulf oil spill, New Zealand earthquake, should be evaluated and treated for SDB since it is a major risk factor for these problems or any disorders arising from catastrophic events. Furthermore, Dr Gold suggests that anxiety, panic, OCD, social phobia, PTSD should be treated with CPAP. Such recommendations, if they were to be followed, can have serious adverse consequences. It will have a negative impact on the health of our patients, on our economy and, not least on the credibility of our field.

We are open to new ideas and approaches in our field. We have demonstrated that we are also willing to revise our ideas/views when new data arise. For example, in insomnia which for 40 years has been the center of controversy in regard to the utility of the sleep lab, we have shown recently, in a series of studies, that objective measures obtained in the sleep lab are clinically useful in determining the biological severity of the disorder.[35–39] This approach is different from the current prevailing view that "routine PSG" is not recommended[40] and that management of insomnia should be based only on subjective data. In this regard we believe that it will be useful if Dr. Gold and his colleagues pursue studies with rigorous methodology that will support or reject their model.

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