The Case for Trait Determinants of Arousal and Sleepiness

Comment on Bonnet M; Arand D. Performance and Cardiovascular Measures in Normal Adults with Extreme MSLT Scores and Subjective Sleepiness Levels. *SLEEP* 2005:28(6):685-693

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UNDERSTANDING CAUSES AND CONSEQUENCES OF DAYTIME SLEEPINESS IS OF INTEREST TO RESEARCHERS AND CLINICIANS IN THE SLEEP FIELD. Investigation of this topic has led to greater attention to measurement of daytime sleepiness and has also led to the concept of alertness as independent from sleepiness (instead of simply viewing alertness as the reciprocal of sleepiness). Many state variables have been shown to reliably affect various measures of daytime function. For example, quantity of prior sleep, quality of prior sleep (sleep fragmentation), and use of sedating medication have all been manipulated to produce state changes and reliable effects on subsequent levels of sleepiness. While it is commonly accepted that state variables have a profound impact on sleepiness, some research findings have not been readily explained by state variables. The theoretical possibility of trait components in the expression of sleepiness has been proposed to address these findings (eg, see references 4,5).

Prior research interpreted to support a trait component to sleepiness includes a study of 129 young asymptomatic sleepers that found about 1/3 of the sample had mean MSLT scores of less than 8 minutes. The assumption was that these subjects were long sleepers and therefore sleep-deprived, despite reporting adequate total sleep time at night. A subsequent study tested this hypothesis by performing sleep extension in groups of sleepy and alert subjects. Subjects spent 10 hours in bed for 6 consecutive nights. Although sleepiness on the MSLT increased most in the ‘sleepy’ group, these subjects never reached the baseline level of the ‘alert’ group. These findings can be used to support the view that there is a trait component to sleepiness such that some individuals are inherently able to fall asleep more readily than others, independent of fluctuations due to state variables.

Lavie et al has also argued in favor of a ‘trait’ basis to regulation of sleepiness, based on sleep observed during ultra-short sleep cycles. In this protocol, subjects are put on 20 minute cycles, with a 7 minute sleep period and 13 minute wake period. The ‘sleep propensity function,’ as measured by sleep latencies and total sleep time during this regimen, tend to be stable within individuals. That is, factors known to affect sleepiness such as time of day effects or accumulated sleep loss consistently affected some subjects more than others.

Most recently, Van Dongen et al investigated individual differences in neurobehavioral impairment associated with sleepiness. Normal sleepers underwent 36 hours of sleep deprivation following a week of prior sleep restriction, and again underwent 36 hours of sleep deprivation following a week of sleep extension. The pattern of results showed large inter-individual differences, with much smaller intra-individual differences. These results were interpreted to suggest that response to sleep loss has a trait component.

The study by Bonnet and Arand in this issue of *SLEEP* provides additional support for the view that daytime sleepiness is influenced by trait factors. They have identified subgroups of normal sleepers who are either alert or sleepy on an MSLT and found that subsequent MSLT scores were fairly stable. Additionally, these groups exhibited differences in cardiac autonomic activity. One caution is that it is uncertain if the differences in cardiac autonomic activity are due to increased cardiac sympathetic activation as attributed by the authors, or may also be due to decreased cardiac parasympathetic activity.

Cardiac autonomic activity can be estimated from the spectral analysis of cardiac beat to beat intervals. Pharmacological blockade studies have shown that the high frequency power component (HF) derived from this analysis specifically reflects cardiac parasympathetic activity (eg, see references 10,11). These same studies have shown that the low frequency power component (LF) is not a specific measure of cardiac sympathetic activity and instead reflects a mix of parasympathetic and sympathetic influences (see also review by Berntson et al). Thus “normalized” HF [HF/(LF+HF)] and “normalized” LF [LF/(LF+HF)] and LF/HF are neither specific markers of cardiac parasympathetic or sympathetic activity. Instead, they provide some insight into cardiac sympathovagal balance, but do not enable us to distinguish between an increase in cardiac sympathetic activity or decrease in cardiac parasympathetic activity (and vice versa).

This intriguing study by Bonnet and Arand is the first to correlate a measure of objective sleepiness (MSLT) with measures of cardiac sympathovagal balance. They report that on 2 of 3 days in the laboratory, mean MSLT correlated positively and significantly with mean LF/HF. Furthermore, LF/HF was significantly and consistently higher in the Alert group (MSLT > 10 minutes). These results suggest that variations in sleepiness, as indexed by the MSLT, can be associated with changes in cardiac sympathovagal balance. Other studies that have investigated the effects of sleep deprivation on measures of cardiac autonomic activity show that cardiac autonomic activity can be altered by increased sleepiness.

Holmes et al found that a night with no sleep decreased car-

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diac sympathetic activity (estimated with pre-ejection period, a pharmacologically validated measure) but did not significantly alter cardiac parasympathetic activity. Similarly, 2 studies that recorded muscle sympathetic nerve activity in the morning after a night of sleep deprivation also found that sympathetic activity decreased.\textsuperscript{14,15}

The results are less clear when it comes to partial sleep deprivation. Muenter et al\textsuperscript{16} reported no change in cardiac parasympathetic activity (assessed as the root mean square of R-R intervals) before and after only 4 nights of 4 hours of sleep per night, but had subjects breath in time to a metronome during the recording of the ECG. While paced breathing has been found to increase cardiac parasympathetic activity (eg, see reference 17) it is unclear how generalizable these results are. Muenter et al had no measure of cardiac sympathetic activity. Spiegel et al\textsuperscript{18} did report changes in cardiac sympathovagal balance (using the auto-correlation coefficient rRR) after 6 nights of only 4 hours of sleep per night as compared to 7 nights of 12 hours of sleep per night, suggesting a cumulative sleep debt either decreases cardiac parasympathetic activity or increases cardiac sympathetic activity.

In conclusion, this study by Bonnet and Arand provides further evidence in favor of trait components of sleepiness, as indexed by the MSLT, and possibly arousal, as indexed by cardiac sympathovagal balance. While this study has shown that there is an association between measures of sleepiness and arousal, additional research using more specific measures of cardiac autonomic activity is needed.

REFERENCES