We thank Dr. Agrawal and colleagues for providing a synopsis of the sleep and medical issues facing patients with traumatic brain injury (TBI), as were discussed in three companion articles on the topic published in the June 15, 2007, issue of this journal. Although these articles represent progress in our understanding of the intersection between TBI and sleep, they also serve as a potent reminder of how little is actually known on this topic. The Verma and Castriotta studies implement objective measures of sleep, but their populations are highly selected (rehabilitation centers or sleep clinics) and are therefore not representative of sleep dysfunction following TBI in the general population. Indeed, epidemiologic studies in highly selected populations often provide inflated prevalence estimates. Our study was population based, assessing consecutive subjects with a broad spectrum of TBI presenting to a level I trauma center, but we lacked objective measures of sleep and limited our analysis to hypersomnia. Other studies on the subject suffer from similar shortcomings. Therefore, a clear understanding of the scope of the problem remains outside our grasp. We still await a definitive population-based prospective cohort study of TBI and sleep with both objective and subjective measures to delineate the true incidence and prevalence of sleep disturbance in these patients.

Despite the lack of reliable prevalence estimates, current evidence points to substantial sleep disturbance following TBI. As a result, exciting research avenues abound. It’s likely that susceptibility to sleep disturbance following TBI is variable, influenced by gene-environment interactions. The APOE allele has been demonstrated to influence overall and rehabilitation outcome, coma recovery, risk of posttraumatic seizures, and cognitive and behavioral functions following TBI. The impact of APOE or other polymorphic alleles on TBI-induced sleep disturbance is unknown. Genome-wide association studies of TBI patients with similar injury severity with and without objective sleep disturbance are needed to provide a better understanding of the genetic underpinnings of variable susceptibility. In the future, this type of research has the potential to identify patients with TBI who are at greatest risk for developing sleep disturbance, providing opportunities for prevention through neuroprotection, if and when this becomes available. At the very least, symptomatic intervention could be undertaken earlier in efforts to increase patient participation in rehabilitation.

Beyond genomics, there’s also a need to research the impact of current treatment modalities on patients with TBI-related sleep disturbance. A pilot study of cognitive behavioral therapy for post-TBI insomnia in 11 subjects demonstrated encouraging results, with significant increases in sleep efficiency and reductions in Insomnia Severity Index scores. Regarding stimulants, a small study of 30 patients with TBI demonstrated no change in observational sleep-wake distribution, including total sleep time, in those receiving methylphenidate. These studies, although a good start, point to the need for larger, randomized, placebo-controlled trials investigating the impact of the treatment of TBI-associated sleep disorders on measures of rehabilitation outcome. Only in this manner can we confirm the clinical importance of identifying these patients following injury.

In appreciation of this research challenge, the U.S. Department of Defense recently accepted proposals for their Congressionally Directed Medical Research Program in the area of TBI (http://cdmrp.army.mil/funding/ptstdbirp.htm). These Concept Awards aim to, “spark new ideas, innovative technologies, and ground-breaking concepts that will drive the field of TBI research forward.” Proposal specifications overlap with many areas salient to post-TBI sleep disturbance, including the development of standardized diagnostic criteria and clinical management procedures and research into both the short- and long-term treatment of associated conditions. As sleep specialists and researchers, we can only hope that proposals addressing the sleep-related ramifications of TBI will be represented among the applications submitted for these Awards.

REFERENCES