Sleep Research Highlight:
Mathematical Model of Sleep Loss

More than 25 years ago, basic principles of how sleep timing and duration are regulated in humans were captured in the seminal two-process model of sleep regulation.[1] The regulatory processes featured in this model are 1) a homeostatic process, which keeps track of time spent awake and time spent asleep, and 2) a circadian process, which keeps track of time of day. It has been shown that these processes predict waking neurobehavioral function under conditions of total sleep deprivation.[2] However, recent sleep dose-response studies[3,4] revealed that the two-process model does not accurately capture the cumulative performance impairments observed over days of chronic sleep restriction.[4] This suggests the existence of an additional process,[5] modulating the homeostatic process over the long term (days to weeks). An attempt was made to implement such a modulating process in the framework of the two-process model,[6] but the approach taken initially was not successful in simultaneously predicting performance during total sleep deprivation and across days of sleep restriction. McCauley and colleagues in the Sleep and Performance Research Center at Washington State University Spokane extended the effort, and discovered a modeling solution to this problem[7] that may have some far-reaching implications for understanding the effects of sleep loss on neurobehavioral functioning.

A set of differential equations for the homeostatic process was formulated, representing two underlying biological subprocesses interacting dynamically with each other (and with the circadian process) during wakefulness and during sleep. One subprocess is characterized by time constants in the order of hours, the other by time constants in the order of days, and their reciprocal interactions involve positive feedback.[7] The neurobiological underpinnings are not fully known, and many systems and substrates are likely to be involved. One hypothesis involves adenosinergic mechanisms: the subprocess with the shorter time constants would reflect changes in (extracellular) concentrations of adenosine, and the subprocess with the longer time constants would reflect up- and downregulation of adenosine receptors. Upregulation of adenosine receptors occurs in response to sleep loss, and in turn increases sensitivity to sleep loss.[8] It is precisely this kind of system that the model of McCauley and colleagues suggests causes the build-up of neurobehavioral impairment across days of sleep restriction. Such a mechanism implies that, besides trait vulnerability to sleep deprivation,[9] a person's sensitivity to sleep loss is determined by his/her sleep history—as was recently demonstrated experimentally.[10]

Analysis of the model's dynamics as a function of sleep dose yielded a surprising finding: the two interacting homeostatic subprocesses showed fundamentally different overall behavior under conditions of total sleep deprivation and severe sleep restriction (less than ~4 hours sleep per day) than under conditions of less or no sleep restriction.[7] This so-called "bifurcation" effect provided an integrated prediction framework for the ostensibly different neurobehavioral effects of total sleep deprivation vs. chronic sleep restriction as observed in the laboratory.[4] The bifurcation was confirmed by the data of the two major published dose-response studies of sustained sleep restriction[3,4]: for restriction to 8 hours or less, down to 4 hours, time in bed per day, performance deficits increased over days but eventually appeared to converge to an equilibrium state of stable, suboptimal performance; whereas for restriction to 3 or 0 hours time in bed per day performance deficits escalated rapidly and did not converge to an equilibrium state. See Fig. 1.
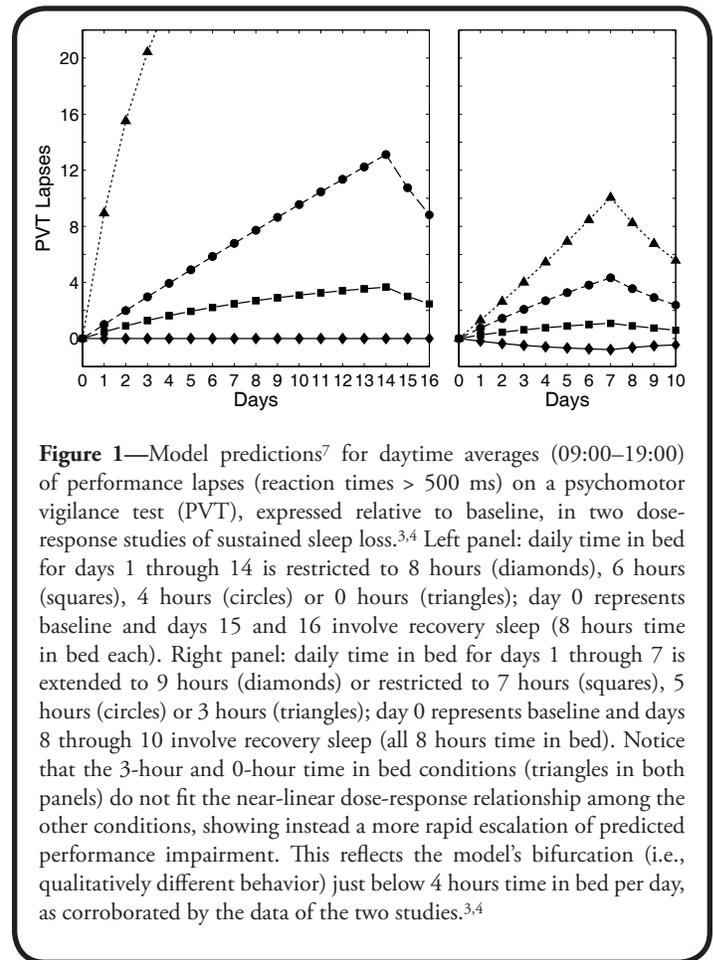

Figure 1—Model predictions[7] for daytime averages (09:00–19:00) of performance lapses (reaction times > 500 ms) on a psychomotor vigilance test (PVT), expressed relative to baseline, in two dose-response studies of sustained sleep loss.[3,4] Left panel: daily time in bed for days 1 through 14 is restricted to 8 hours (diamonds), 6 hours (squares), 4 hours (circles) or 0 hours (triangles); day 0 represents baseline and days 15 and 16 involve recovery sleep (8 hours time in bed each). Right panel: daily time in bed for days 1 through 7 is extended to 9 hours (diamonds) or restricted to 7 hours (squares), 5 hours (circles) or 3 hours (triangles); day 0 represents baseline and days 8 through 10 involve recovery sleep (all 8 hours time in bed). Notice that the 3-hour and 0-hour time in bed conditions (triangles in both panels) do not fit the near-linear dose-response relationship among the other conditions, showing instead a more rapid escalation of predicted performance impairment. This reflects the model's bifurcation (i.e., qualitatively different behavior) just below 4 hours time in bed per day, as corroborated by the data of the two studies.[3,4]

Assuming further validation efforts will be successful, the model of McCauley and colleagues makes a number of notable predictions. Simulations driven by the model show that one or two nights of recovery sleep should suffice for neurobehavioral recuperation after a period of acute total sleep deprivation,[11] but several more recovery nights may be needed to overcome the cumulative effects of sustained sleep restriction.[3] Moreover, although "sleeping in" to

overcome the effects of prior sleep loss would accelerate recuperation, this strategy is predicted to be neither necessary nor sufficient to restore performance to baseline levels.[12] The model also predicts that an extended recovery night after a period of chronic sleep loss should result in more performance improvement the greater the amount of prior sleep loss. However, if the pattern of sleep restriction is repeated after the recovery night, then the performance improvement will dissipate quickly—after just a few days it would seem as if the recovery night never took place. Preliminary data from a laboratory study at the University of Pennsylvania appear to support this prediction.[13] The hours of service implications in extended work environments could be profound, as is illustrated for a hypothetical medical residency program in Fig. 2.
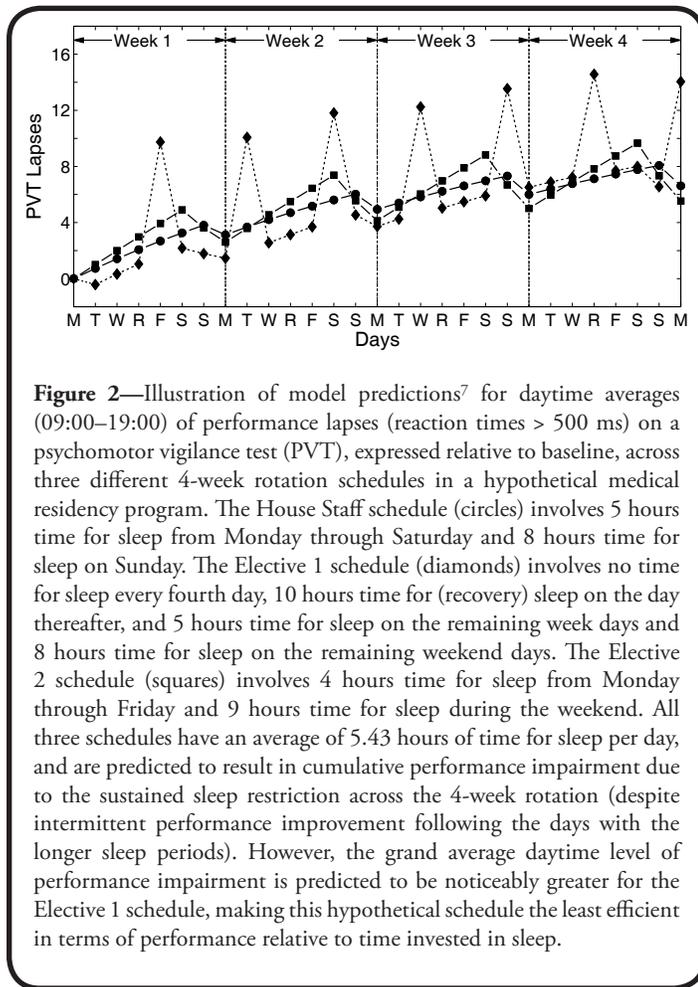

Figure 2—Illustration of model predictions[7] for daytime averages (09:00–19:00) of performance lapses (reaction times > 500 ms) on a psychomotor vigilance test (PVT), expressed relative to baseline, across three different 4-week rotation schedules in a hypothetical medical residency program. The House Staff schedule (circles) involves 5 hours time for sleep from Monday through Saturday and 8 hours time for sleep on Sunday. The Elective 1 schedule (diamonds) involves no time for sleep every fourth day, 10 hours time for (recovery) sleep on the day thereafter, and 5 hours time for sleep on the remaining week days and 8 hours time for sleep on the remaining weekend days. The Elective 2 schedule (squares) involves 4 hours time for sleep from Monday through Friday and 9 hours time for sleep during the weekend. All three schedules have an average of 5.43 hours of time for sleep per day, and are predicted to result in cumulative performance impairment due to the sustained sleep restriction across the 4-week rotation (despite intermittent performance improvement following the days with the longer sleep periods). However, the grand average daytime level of performance impairment is predicted to be noticeably greater for the Elective 1 schedule, making this hypothetical schedule the least efficient in terms of performance relative to time invested in sleep.

A schedule with sustained sleep restriction to, say, 4 hours time in bed daily produces considerable cumulative performance deficits, as shown in Fig. 1. Yet, if such a schedule is followed by one or more days with more modest sleep restriction, then the prediction is not that there will be more modest additional degradation of performance, but rather that some improvement will occur. Although subjective experience might support this prediction, it is counterintuitive from a cumulative "sleep debt" perspective.[14] Indeed, the new model does not substantiate a "sleep debt" account of the neurobehavioral consequences of sleep loss. Instead, the model dynamics imply that the effects of sleep restriction and sleep extension on performance should be interpreted in terms of physiologic balance shifts that depend on the prevailing ratio of total wake time to total sleep time. In this view, interestingly, the seemingly irresolvable question of "which components of sleep are most important for recuperation" is, at least in a practical sense, largely irrelevant.

References

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