

# Connecting the Dots: From Trait Vulnerability during Total Sleep Deprivation to Individual Differences in Cumulative Impairment during Sustained Sleep Restriction

Commentary on Rupp et al. Trait-like vulnerability to total and partial sleep loss. *SLEEP* 2012;35:1163-1172.

Hans P.A. Van Dongen, PhD

*Sleep and Performance Research Center, Washington State University, Spokane, WA*

Prominent discoveries in human sleep deprivation research since the turn of the millennium include (1) the cumulative, dose-response build-up of cognitive performance deficits across days of sustained sleep restriction<sup>1,2</sup>; and (2) the substantial, trait-like individual differences in vulnerability to cognitive impairment during acute total sleep deprivation (controlling for prior sleep history).<sup>3</sup> These findings have spurred further research in laboratories around the world, yielding increasingly detailed knowledge about the effects on cognitive performance caused by total sleep deprivation, sustained sleep restriction, nap sleep, displaced sleep, recovery sleep, prior sleep history, interactions with circadian rhythmicity, and individual differences therein. Some of these effects have also been captured in quantitative models of fatigue and performance.<sup>4,5</sup> Investigation of the temporal dynamics thereof has indicated that in schedules with sleep restriction to less than ~4 hours per day (which includes total sleep deprivation), performance deficits escalate progressively.<sup>5</sup> Such schedules appear to be fundamentally more challenging to sustain than schedules with sleep restriction to more than ~4 hours per day, which *also* cause cumulative deficits<sup>1,2,6</sup> but more gradually.<sup>5</sup>

Despite such progress in human sleep deprivation research, individual differences in responses to sleep loss have remained under-investigated and largely unexplained.<sup>7</sup> In this issue of *SLEEP*, Rupp and colleagues<sup>8</sup> contribute to filling this gap, by bridging between the findings of cumulative build-up of cognitive performance deficits across days of sustained sleep restriction and substantial individual differences in vulnerability to impairment during total sleep deprivation. In a within-subject research design,  $N = 19$  carefully screened healthy volunteers (ages 18–39, 8 females) were studied in two conditions: (a) 2 nights and days of total sleep deprivation (63 hours of continuous wakefulness), and (b) 7 days of sleep restriction to 3 hours time in bed (04:00–07:00) each night. The two conditions were administered in randomized, counterbalanced order; were separated by 2 to 4 weeks; and were each preceded by 7 days with 10 hours time in bed (laboratory controlled) to satiate the need for sleep prior to the experimental interventions.

During the sleep deprivation days and sleep restriction days of the two study conditions, subjects were continuously monitored, and cognitive performance was measured hourly. Cogni-

tive performance tasks included a psychomotor vigilance test (PVT), a 1-back working memory task, and a mathematical processing task. Also included were assessments of subjective sleepiness on the Stanford Sleepiness Scale (SSS), objective sleepiness as measured by sleep latency on a 20-minute Maintenance of Wakefulness Test (MWT), and a handful of Likert-type scales of mood intensity. Outcome data for use in analyses were determined by averaging daytime (08:00–20:00) measurements obtained during the last day of each study condition.

Rupp et al. thus compared individual differences in the effects of total sleep deprivation with individual differences in the cumulative effects of sustained sleep restriction. Group mean effects of condition (which were greatest here for the total sleep deprivation condition) and of order of conditions (e.g., due to learning curves) were accounted for in data analyses. For the remaining variance in the data, systematic between-subjects differences across the two study conditions were distinguished from within-subjects (error) variance through a variance components analysis.<sup>9</sup> Then, the intraclass correlation coefficient (ICC) was calculated, which is the percentage of variance explained by systematic between-subjects differences after accounting for the condition and order effects.

The results of the study were striking. Subjects showed sizable individual differences in responses to sleep loss,<sup>8</sup> comparable in magnitude to those observed previously.<sup>3</sup> Importantly, the individual differences were systematic across the two study conditions, with ICC values of 68% for the mathematical processing task, 88% for the 1-back working memory task, and 86% and 89% for two measures of performance on the ICC values were likewise high for some of the mood intensity outcomes, but less so for subjective and objective sleepiness. Secondary analyses with baseline assessments included as covariates corroborated these results and ruled out the possibility that the individual differences seen under conditions of sleep loss merely reflected preexisting individual differences in aptitude or response bias.

The study demonstrated that individual differences in impairment due to sleep loss are generalizable from acute total sleep deprivation to sustained sleep restriction, with subjects showing essentially the same degree of vulnerability under both conditions. Since vulnerability to performance impairment from total sleep deprivation had been shown to be trait-like,<sup>3</sup> it was inferred that vulnerability to performance impairment from sustained sleep restriction represents the same trait.<sup>8</sup> The authors did note that the sleep restriction condition in their study curtailed sleep to less than 4 hours daily, placing it in the same realm of escalating performance impairment as total sleep deprivation. Although it would be parsimonious to assume that the vulnerability trait

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Address correspondence to: Hans P.A. Van Dongen, PhD, Research Professor, Sleep and Performance Research Center, Washington State University Spokane, P.O. Box 1495, Spokane, WA 99210-1495, USA; Phone: (509) 358-7755; Fax: (509) 358-7810; E-mail: [hvd@wsu.edu](mailto:hvd@wsu.edu)

also extends to sleep schedules with sleep restriction to 4 hours per day or more, this remains to be demonstrated.

The findings documented by Rupp et al. have real-world implications. They make the trait characteristic of vulnerability to sleep loss relevant for conditions of severe sleep restriction, which are encountered in many around-the-clock, safety-sensitive operations including hospitals, emergency response, and the military. Mission success in such settings depends on optimal cognitive functioning of individuals and small teams, which is jeopardized by differential vulnerability to sleep loss found even among highly selected populations such as fighter pilots.<sup>10</sup> Pending confirmation in field studies, the findings by Rupp and colleagues<sup>8</sup> imply that an individual's level of vulnerability could be determined in advance of a critical mission during a relatively brief period of acute total sleep deprivation (e.g., during training), with the expectation that the individual's level of vulnerability will be equivalent during the mission proper. This is important also for models of fatigue and performance, which have been shown to be individualizable for performance prediction during acute total sleep deprivation,<sup>11,12</sup> but awaited confirmation that this would extend to schedules with sustained sleep restriction.

Not surprisingly, there is an ongoing, intense search for biomarkers and other predictors of vulnerability to sleep loss.<sup>13,14</sup> While prior work by Rupp et al.<sup>15</sup> has contributed to this search, the issue was not further addressed in their current paper.<sup>8</sup> However, a much overlooked feature of vulnerability to sleep loss, noticed also by Rupp and colleagues, is that the vulnerability ranking of individuals depends on what they are being asked to do.<sup>3,10,16</sup> That is, individual differences due to sleep loss in impairment on some performance tasks are not consistently related to what is observed for the same individuals on other performance tasks, such that subjects' ranking in terms of vulnerability varies from task to task. Although further studies and larger samples are needed to resolve the degree of overlap or orthogonality in cognitive responses to sleep loss, this multifaceted aspect of vulnerability to sleep loss challenges the idea that an individual can be straightforwardly characterized in this regard by means of a biomarker.

Attempts have been made to categorize individuals' multi-dimensional responses to sleep deprivation in terms of the cognitive domains represented by different performance tasks, such as sustained attention or cognitive throughput. There is evidence, however, that the effects of sleep deprivation on performance are not categorically shaped by cognitive domains, but rather by the distinct cognitive processes underlying performance on the task at hand.<sup>17</sup> For example, performance impairment on a classical working memory task, the Sternberg task, has been shown to be degraded by sleep deprivation overall, but not because of working memory impairment. Rather, deficits in one or more of the other cognitive processes involved in performing the task (e.g., stimulus encoding) appeared to be involved.<sup>18</sup>

These scientific developments call for a different perspective in trying to explain differential vulnerability to sleep deprivation and sleep restriction. Based on a theory about the brain organization of sleep,<sup>19</sup> it has been posited that sleep loss induces cognitive impairment by making groups of neurons involved in task performance become functionally unresponsive as a consequence of repetitive use, thereby intermittently interfering with information processing.<sup>20</sup> Functional neuroimaging

data have suggested that this phenomenon may result in locally diminished capacity for information throughput, which degrades neural circuit-specific information processing and thus task-specific performance. As such, the variability of individual differences in performance deficits across tasks may be due to differences in how much the tasks repetitively engage neural circuits for which the individuals are differentially vulnerable to use-dependent effects.<sup>21</sup>

These complexities of individual differences in vulnerability to sleep loss notwithstanding, the results of the work of Rupp et al.<sup>8</sup> point to broad similarities in the cognitive effects of sleep loss when comparing total sleep deprivation and partial sleep restriction. In contrast, the physiologic, metabolic, endocrine, and immune consequences of these two modes of sleep loss have been found to differ, with sustained sleep restriction inducing long-term changes in recovery potential<sup>15</sup> and potentially in health and well-being.<sup>22</sup> Despite different temporal dynamics, however, there is no evidence for a qualitative difference in the way sleep loss degrades cognitive functioning whether incurred through acute total sleep deprivation or through sustained sleep restriction.

#### CITATION

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#### DISCLOSURE STATEMENT

Dr. Van Dongen has indicated no financial conflicts of interest.

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