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Limitations on visual information processing in the sleep-deprived brain and their underlying mechanisms

Michael WL Chee

Sleep deprivation (SD) which has become more prevalent globally, impairs various aspects of cognition. Slowing of visual processing, loss of selective attention, distractor inhibition, visual short-term memory and reduced peripheral processing capacity are associated with diminished engagement of fronto-parietal regions mediating top-down control of attention as well as selectively reduced visual extrastriate cortex activation. The onset of 'local sleep' following sustained wakefulness could account for these, as well as time-on-task effects. Concurrently, alterations in cortical-cortical as well as thalamo-cortical connectivity can disrupt the flow of sensory information from the periphery to association cortex responsible for higher order cognition. Our ability to process visual stimuli is compromised when sleep deprived, even during the periods when we are apparently responsive.

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Introduction

Voluntary sleep loss arising from lifestyle choices is prevalent [1] despite it producing an unpleasant mental fog, fatigue and sleepiness that elevate the likelihood of accidents [2], cognitive errors [3••] and emotional dysregulation [4]. Understanding the neural mechanisms underlying behavioral changes in the sleep-deprived state may be of benefit in reducing their negative impact. A good place to begin is to examine a faculty that is very consistently affected by this state – degradation of vigilance after a night of total sleep deprivation (SD) [5]. While highly valued high-order cognitive functions like executive function and memory can also be diminished when we are sleep-deprived, their degradation is likely to be subordinate to deficits in the basic ability to stay awake and perceive the external world [3••,6,7].

To the casual observer, a sleep-deprived person appears tired but otherwise able to function until they momentarily falter when briefly falling asleep. 'Wake-state instability' [8] is an influential concept which posits that the sleep-deprived brain toggles from between 'awake' and 'asleep' in a matter of seconds [9]. This aptly describes the seemingly preserved ability to respond at times while being profoundly impaired at others. Less obvious, and an important theme in this review, is evidence for degraded ability to process sensory stimuli when sleep-deprived, even during the periods when we are apparently responsive. A mechanism that can reconcile the seemingly disparate accounts of both intermittently and continuously degraded behavior in sleep deprivation is 'local sleep' (elaborated on later) which ultimately results in reduced attentional capacity.

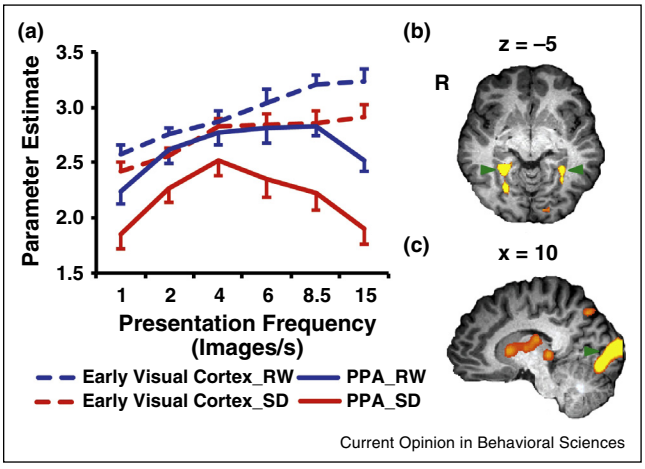
Degraded attention, insofar as it refers to 1) reduced capacity to process the stream of information our senses are continually presented with, and 2) an impaired ability to channel these limited resources to specific goals, is a useful framework for studying the neurobehavioral changes accompanying sleep deprivation (SD). As attention serves to enhance sensory processing [10], decreased functionality of fronto-parietal areas that exert top-down effects on sensory cortex can be expected to contribute to poorer perceptual performance. This review will focus on aspects of attention and/or visual processing that are altered by overnight total sleep deprivation.

Slower processing of rapidly presented pictures

The human visual system processes information with amazing rapidity, enabling us to identify a single flashed object appearing for as briefly as 20 ms. Examining neural responses to Rapid Serial Visual Presentation (RSVP) of pictures is an intuitive method to identify areas that evidence temporal limits in visual processing. Being able to process serially presented images briefly separated in time is of interest given the relevance of this faculty in tasks performed by sleep-deprived persons such as threat detection or rapid radiologic diagnosis.

The hierarchical organization of visual cortex is such that higher visual areas take time to integrate information relayed from early visual areas (Einhauser et al., 2007, Todd et al., 2011). As such, while a faster stream of novel pictures (e.g. 4 frames/s) increases sensory stimulation and

Figure 1



(A) Temporal response profiles across state in Parahippocampal Place Area (PPA). Parameter estimates are in arbitrary units. Group activation map showing the PPA. **(B)** Temporal response profiles across state in the early visual cortex. **(C)** Group activation map showing early visual cortex, thresholded at $p < 0.000005$, uncorrected. Note that the *y*-axis scale has been cropped to optimally display relevant activation magnitude values in the PPA and early visual cortex. (Adapted from Kong et al. [13•]).

can elicit more activation in higher visual areas, further increasing presentation rate (e.g. 15 frames/s) will result in failure to adequately process complex information, giving rise to an inverted u-shaped temporal response profile. Using this approach, the parahippocampal place area (PPA) and fusiform face areas (FFA) whose response profiles peak at the slower rates relative to earlier visual areas have been identified as bottlenecks for visual processing [11,12]. Lowered rate of visual processing in SD is evidenced by a slower peak rate in the temporal response profile in the PPA compared to in the well rested state [13•]. The PPA and FFA lie in extrastriate visual cortex and are relatively more sensitive to the degradation of top-down control of attention encountered during SD. In contrast, early visual areas where processing is not limited at the presentation frequencies tested and which are less sensitive to attentional modulation, demonstrate a monotonic increase in activation with presentation rate irrespective of state (Figure 1). Hence, visual areas that serve as potential bottlenecks for visual processing in the sleep-deprived state can been identified.

Impaired selection

Selectivity for object pictures can be measured by examining the difference in PPA responses to attended and unattended house pictures. This index of selectivity is lowered in sleep-deprived persons, when picture stimuli are temporally unpredictable [14]. However, when face and house stimuli appear in a temporally predictable manner, SD results in reduced PPA activation but without an accompanying change in selectivity [15]. This relative improvement in behavioral performance when stimuli are temporally predictable is consistent with similar effects found with vigilance in the well rested state [16].

Reduced spatial selective attention in SD also occurs in the preparatory period preceding stimulus onset and manifests in retinotopically specific visual cortex [17]. The latter indicates that effects of SD manifest in brain areas specifically engaged in the task and are not evident when these areas are not specifically probed. Deficits in attention evidenced by reduced fronto-parietal activation in association with degraded performance are also evident in visual tracking tasks that evaluate deployment of selective attention over a longer period than that spanned by a brief experimental trial [18,19•]. These point to a temporally more extensive loss of top-down control of attention than apparent from tests of psychomotor vigilance.

Reduced processing of peripheral information

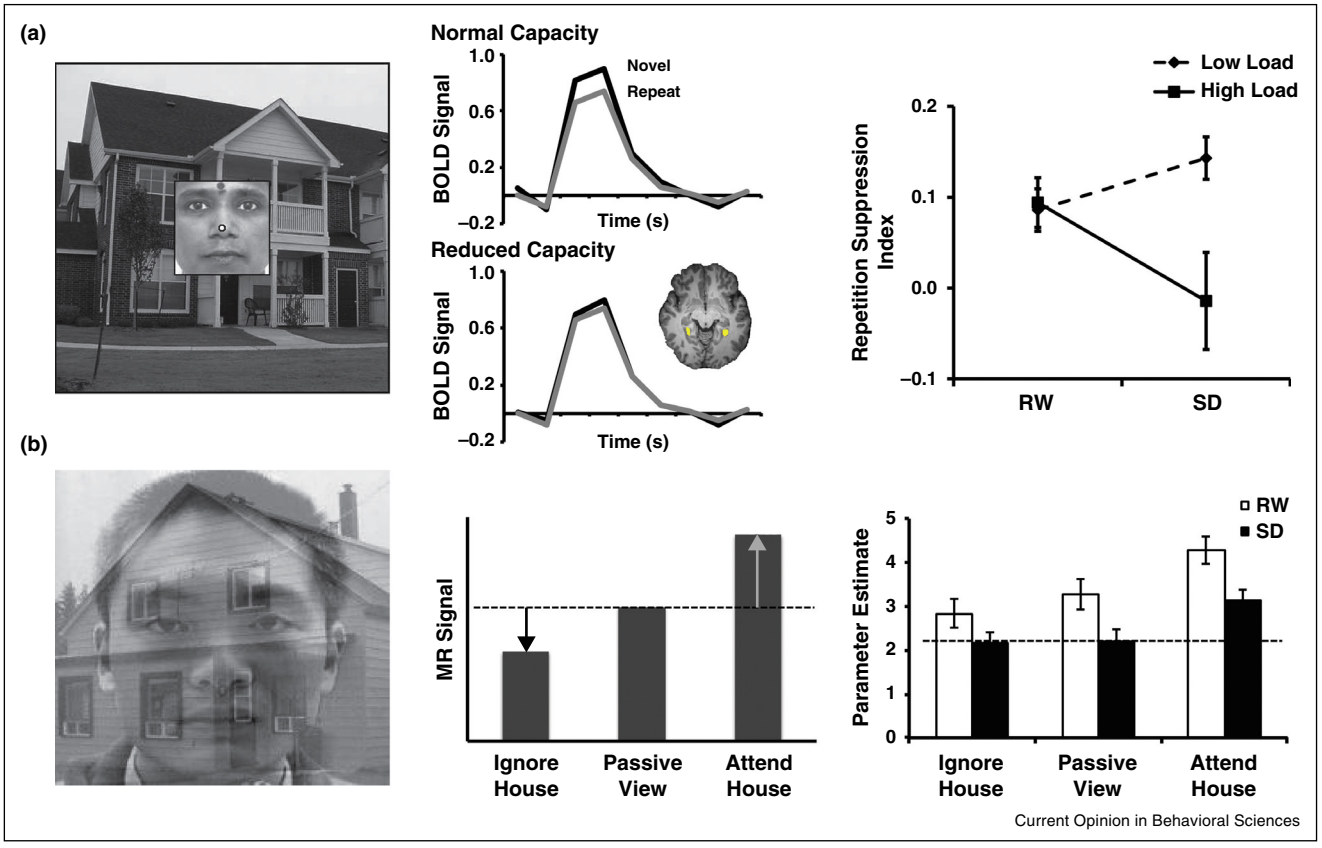
The Perceptual Load Theory of attention [20] proposes that focusing attention on a task-relevant stimulus will restrict the processing of task-irrelevant distractors according to the availability of residual perceptual processing capacity. Conversely, if a task-relevant stimulus places low demands on the perceptual system, spare capacity becomes available to process unattended distractors [21–23]. Experiments exploiting this framework typically involve a central target and peripheral distractors, a scenario akin to keeping focused on the traffic warden at a crossing while still being able to detect a child who strays onto the opposite side of the road.

The amount of processing appropriated to unattended distractors can be inferred from the magnitude of fMRI repetition suppression associated with distractor repetition [24]. The availability of resources for processing unattended stimuli can be manipulated by varying the perceptual clarity of the central target. Consistent with a state related reduction in peripheral processing capacity, sleep deprivation attenuated repetition suppression to peripheral pictures when central perceptual load was high but not when perceptual load was low [25]. This contrasts with the situation with rested participants where sufficient capacity is available such that perceptual load has no significant effect on repetition suppression (Figure 2A).

Impaired inhibition of distractors

Selective attention can be dissociated into enhancement of task-relevant information, and suppression of distractions/task-irrelevant information [26,27]. By keeping sensory input constant and manipulating the object of attention using ambiguous, overlapping face and house pictures [28], target facilitation and distractor suppression can be dissociated [29•]. In addition to the robust finding

Figure 2



(A) *Sleep deprivation and reduced perceptual processing capacity*. A series of scene–face composite pictures were shown. Faces were either undistorted (low-load condition) or degraded (high-load condition). Surrounding each face were either alternately repeated or novel background scenes. Activation in the PPA corresponding to repeated or non-repeated house pictures depicting repetition suppression when perceptual processing capacity is normal or compromised. Repetition suppression was reduced under conditions of high perceptual load during SD (Adapted from Kong et al. [25].) **(B)** *Sleep deprivation results in attenuated suppression of distractors*. The schematic shows an example of an ambiguous face/house whose activation in PPA was compared across three conditions: attend face, ignore house (AFIH), and attend house, ignore face (AHIF). Passive viewing of ambiguous pictures served as the control condition (CTRL). The middle schematic shows expected patterns of target enhancement and distractor suppression in the rested state. The last panel shows that enhancement of attended houses was relatively preserved but suppression of distractor houses was impaired during SD. RW = Rested wakefulness, SD = Sleep deprivation (from Kong et al. [29•]).

that PPA activation is reduced by SD, there is a selective deficit in suppression of PPA activation to ignored houses, sparing enhancement of PPA activation to attended houses [29•] (Figure 2B). This observation parallels studies of cognitive aging that highlight similar deficits in distractor suppression [30–32]. Suppressing distraction and keeping to task goals can be thought of as an executive function with *perceptual* consequences, for example, in the case of deficient filtering of target memoranda during tests of visual short-term memory [33] or with increased head turns toward peripheral distracting events during SD [34].

Impaired visual short-term memory

The ability to maintain a sensory representation for several seconds is crucial for enabling goal-directed behavior and is a core feature of attention [35]. This function is served by a capacity-limited visual short-term memory (VSTM). Most individuals are only able to store about four visual items at a time [36]. If short-term memoranda fail to be maintained over brief delays, critical items that we need queued for this manipulation task will be unavailable, thus degrading higher order cognitive functions which require access to such memoranda. Visual short-term memory capacity was reduced after a night of total sleep deprivation in two studies [37,38] but not in a third [33] where the circadian contribution to performance degradation could have been smaller. Interestingly, during sleep deprivation, cortical activation in the intraparietal sulcus that participates in short-term storage is lowered irrespective of memory load [37,38]. This suggests that fewer functional circuits (see later) are available for recruitment during SD.

Beyond the measurement of 'capacity', the qualitative aspects of short-term memory representations also matter [39]. Having participants maintain the location and color of three stimuli over a delay and then to report the color of the item at the cued location was used to assay memory precision. SD did not impair the precision of representations held in VSTM. However extending the retrieval delay to 10 s from 1 s reduced capacity [40].

The maintenance of short-term visual representations is thought to depend on recurrent reverberatory activity within cortical regions involved in sensory perception [41] and fronto-parietal regions involved in maintaining attention [42]. The probability that such representations fail with delay increases as the fronto-parietal [43••] and extrastriate areas [44] that support VSTM undergo random dropouts in neuronal firing during SD.

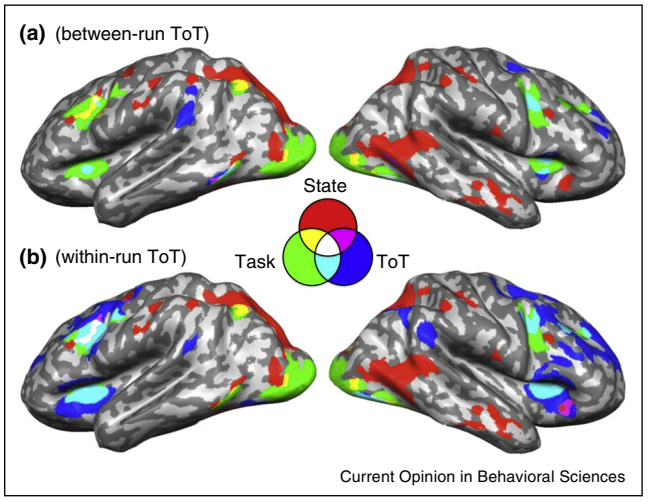
Intensified time-on-task effects

Behavioral studies of vigilant attention show that SD and time-on-task (ToT) interact to decrease performance [45,46,47•]. This interaction suggests that similar processing stages and, perhaps, similar brain regions may underlie such declines. Indeed, frontal and parietal regions show activation declines in a broad array of SD [18,37,48] and ToT studies [19•,49–51]. With sleep restriction, ToT effects and those arising from transient tracking errors can be differentiated [19•]. A direct comparison of the neural correlates of SD and ToT effects has also shown that these both involve a partially overlapping subset of task-activated regions (Figure 3), including frontal-parietal attention regions and ventral visual cortex [52•].

A possible explanation is that attentional circuits become fatigued with repeated use [47•,53]. This use-dependency account suggests that either prolonged wake or sustained task engagement exhausts the neural circuits supporting attention [54•]. Resource theories of the time on task effect are consistent with this account, as they argue that sustained attention requires effort and therefore drain cognitive resources [45,55]. These same resources are limited during SD [25,29•], leading to more severe ToT effects. Interestingly, even a brief ~1-min break between experimental runs is sufficient to return stimulus detection to almost baseline levels *for that state* [7].

While SD and ToT can both impair participant motivation, and lead to poorer performance [49,56] experimental participants typically evidence continued effort through an increase in false alarms as the target detection rates drop. Such results suggest a shift in detection ability, rather than complete failure to engage with the task [8,57]. This is consistent with the broader thesis that in addition to obvious 'wake-state instability', information processing in sleep-deprived persons is 'tonically' impaired as well (Figure 4).

Figure 3



Overlap of BOLD activation associated with task, state, and time-on-task. **(A)** Overlaps for between-run time-on-task. **(B)** Overlaps for within-run time-on-task. Note the three-way overlapping of activation in the middle frontal gyrus and ventral visual cortex (From Asplund et al. [52•]).

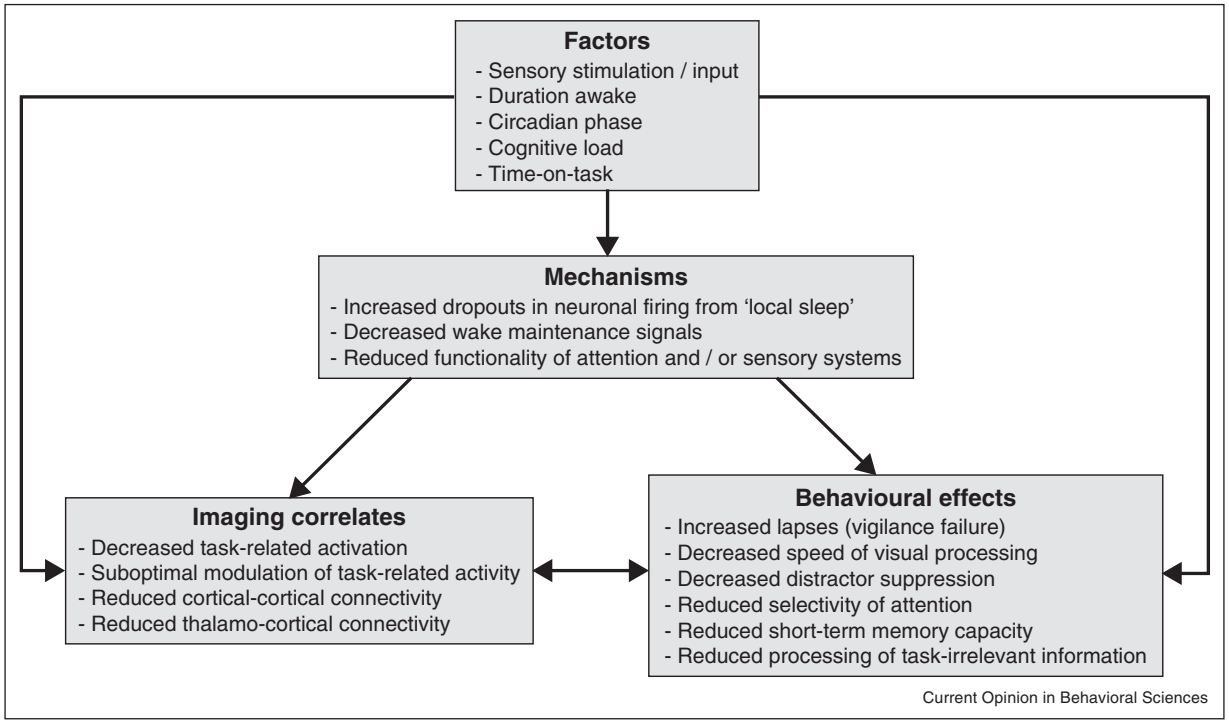
Changes in resting-state connectivity

Changes in resting state functional connectivity occur in sleep-deprived persons [58•,59] alongside alterations to how the default mode network (DMN) or parts of it are engaged during tasks [13•,37,60,61]. Changes in resting state connectivity provide another major systems level explanation for degraded behavioral performance in SD. Examining resting state networks, in theory, affords the identification of brain areas affected by SD but which are not revealed with task-related fMRI because the task used does not engage them.

Reduced connectivity within the DMN and reduced anti-correlation between the DMN and 'task-positive' networks like the dorsal attention network has been robustly reproduced [58•,59,62,63]. Changes in resting state connectivity in the sleep-deprived state appear to be consistent with those occurring along the descent from wakefulness to light sleep [64•,65] and can be distinguished from those associated with deeper stages of NREM sleep [65,66].

Increased daytime sleepiness in young adults and cognitively intact older adults appears to be correlated with reduced DMN connectivity [67]. However, changes in DMN connectivity appear less clearly correlated with reduced performance in SD compared to state shifts in task-related activation [57].

Figure 4



Schematic showing the inter-relationships between relevant environmental or endogenous factors affecting arousal, putative mechanisms that influence cognitive processing capability, neuroimaging features and neurobehavioral manifestations of sleep deprivation.

Reduced thalamo-cortical connectivity is an important change occurring in the transition from wake to sleep [65,68], as well as in sleep-deprived persons [69]. This disconnection of association cortex from afferent sensory inputs could contribute to the reduced perceptual sensitivity described in a number of studies reviewed here. However, it remains to be confirmed whether an increased 'small-worldness' in connectivity where short-range connectivity is enhanced and long-range connectivity is reduced, is an adaptive change [70] or merely an epiphenomenon.

Pattern analysis on a large number of participants suggests that N1 (very light sleep) frequently intrudes into resting state studies on 'awake' participants [71••]. This might contribute to inter-individual differences in behavioral performance even in seemingly well-rested and alert persons.

Reduced functional circuits in SD: the 'local sleep' hypothesis

Might there be a common mechanism that could underlie this diverse set of neurobehavioral observations? We could begin by noting that sleep deprivation consistently lowers task-related activation of the intraparietal sulcus and the lateral occipital parts of extrastriate cortex. The extent of this decrement correlates with decline in psychomotor vigilance [48] and its relief by cholinergic augmentation [38,72] corresponds with benefit on behavioral performance. A functional relationship between intervention and neuroimaging change was also found when rTMS was applied to the right lateral occipital region [73•].

Thus, there appears to be a reduction in the number of functional cortical circuits available to process visual information during SD. A 'functional circuit', refers to the assembly of neurons activated during the performance of a particular task. It could include neurons in close proximity, for example, those in visual cortex, as well as clusters connected by long-range fibers, such as those in frontal and parietal areas mediating attention.

Sustained wakefulness results in an increase in homeostatic sleep pressure resulting in 'local sleep' where circumscribed patches of cerebral cortex demonstrate physiological features of sleep in drowsy but still responsive animals [44,74]. Goal directed behavior like reaching, is more likely to fail during periods when clusters of frontal and parietal neurons show transient reductions in multi-unit activity [43••].

In human volunteers, correct responses elicit lower BOLD signal changes in the sleep-deprived state than

in the rested state. This suggests that in the rested state, there may be some redundancy in circuit activation allowing for random failures without compromising behavioral performance. When sleep-deprived, this reserve is reduced, leading to occasional behavioral lapses.

This 'local sleep' account of neurobehavioral degradation in SD is attractive in that it is relevant in both top-down or bottom-up sensory system failure accounts of degraded performance as well as time-on-task effects. However, at the present time, it is unclear whether 'local sleep' triggers altered connectivity or, if brainstem, hypothalamic and basal forebrain structures are the originators of lower cortical connectivity and reduced cortical activation [9,75]. Newer methods to evaluate 'dynamic functional connectivity' [76••] over temporal windows spanning seconds instead of minutes using both fMRI and EEG promise to shed light on this open question.

Conclusions

Deficits in visual perception or visual processing capacity are central to explaining neurobehavioral changes in sleep deprivation. Reduced engagement of fronto-parietal regions that mediate top-down control of attention has been demonstrated in multiple experiments evaluating different facets of attention and visual processing capacity. Independently of, or consequent to this, visual extrastriate cortex activation is markedly reduced. The onset of 'local sleep' at random intervals in these heavily engaged brain areas following sustained wakefulness could account for the observed reduction in task-related activation. Concurrently, several changes in cortical-cortical as well as thalamo-cortical connectivity can disrupt the normal passage of sensory information to association cortex. Over minutes, these physiological changes can be reliably distinguished from rested wakefulness. However, from trial-to-trial, on a temporal scale of seconds, they appear more stochastic, having the characteristics of 'wake-state' instability. Additional exploration of the sleep-deprived state will continue to contribute novel insights into impaired brain function.

Conflict of interest

Nothing declared.

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