Recovery from Sleep Deprivation Occurs during Propofol Anesthesia

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Background: Some neurophysiologic similarities between sleep and anesthesia suggest that an anesthetized state may reverse effects of sleep deprivation. The effect of anesthesia on sleep homeostasis, however, is unknown. To test the hypothesis that recovery from sleep deprivation occurs during anesthesia, the authors followed 24 h of sleep deprivation in the rat with a 6-h period of either *ad libitum* sleep or propofol anesthesia, and compared subsequent sleep characteristics.

Methods: With animal care committee approval, electroencephalographic/electromyographic electrodes and intrajugular cannulae were implanted in 32 rats. After a 7-day recovery and 24-h baseline electroencephalographic/electromyographic recording period, rats were sleep deprived for 24 h by the disk-over-water method. Rats then underwent 6 h of either propofol anesthesia (n = 16) or *ad libitum* sleep with intralipid administration (n = 16), followed by electroencephalographic/electromyographic monitoring for 72 h.

Results: In control rats, increases above baseline in non-rapid eye movement sleep, rapid eye movement sleep, and non-rapid eye movement delta power persisted for 12 h after 24 h of sleep deprivation. Recovery from sleep deprivation in anesthetized rats was similar in timing to that of controls. No delayed rebound effects were observed in either group for 72 h after deprivation.

Conclusion: These data show that a recovery process similar to that occurring during naturally occurring sleep also takes place during anesthesia and suggest that sleep and anesthesia share common regulatory mechanisms. Such interactions between sleep and anesthesia may allow anesthesiologists to better understand a potentially important source of variability in anesthetic action and raise the possibility that anesthetics may facilitate sleep in environments where sleep deprivation is common.

SLEEP deprivation is common in patients in the intensive care unit¹ and can result in worsened agitation and respi-

ratory, immune, and endocrine system dysfunction.^{2–4} Although naturally occurring sleep readily reverses consequences of sleep deprivation,⁵ such sleep can be difficult to obtain in an intensive care environment. In sleep-deprived critically ill patients, behavioral similarities between levels of sedation approaching general anesthesia and naturally occurring sleep have raised the possibility that the anesthetized state may substitute for sleep and may thus allow recovery from sleep deprivation.^{6,7}

Although general anesthesia differs electroencephalographically from naturally occurring sleep, anesthetics may act partly by duplicating activities of brain regions important in initiating or maintaining sleep.⁸ Effects of anesthetics on regional neuronal activity suggest activation of endogenous sleep-promoting pathways.^{9,10} Sleep deprivation potentiates anesthetic-induced loss of righting reflex,¹¹ and anesthetic agents increase sleep when administered into brain regions known to regulate sleep.¹² In addition, the neurotransmitter adenosine increases sleep,¹³ enhances anesthetic potency,¹⁴ and delays recovery from halothane anesthesia.¹⁵ These observations imply that sleep and anesthesia are neurophysiologically related and suggest that anesthesia and sleep may have similar effects on the sleep-deprived state.

During recovery from sleep deprivation, increases in the intensity and amount of non-rapid eye movement (NREM) and rapid eye movement (REM) sleep are observed that are related to the extent of deprivation and represent a homeostatic recovery response.¹⁶ To test the hypothesis that recovery from sleep deprivation occurs during the anesthetized state, we followed a 24-h period of sleep deprivation in a rat model with 6 h of either propofol anesthesia or *ad libitum* sleep. We then compared NREM and REM sleep characteristics of rats given anesthesia to those of rats allowed to sleep *ad lib*. If recovery from sleep deprivation were to occur during anesthesia, the duration and degree of the recovery response after emergence should be similar to that observed in controls. If no recovery were to occur, however, the sleep-deprived state should continue throughout the anesthetic. A larger recovery response (manifested as increased NREM and REM intensity and duration) than in controls would then be expected on emergence from anesthesia.

Materials and Methods

This study was performed with approval from the animal care committee at our institution (Institutional

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Animal Care and Use Committee, University of Chicago, Chicago, Illinois) for the care and use of laboratory animals. Male Sprague-Dawley rats (Harlan Industries, Indianapolis, IN) weighing 250–300 g were anesthetized with intraperitoneal ketamine (70 mg/kg) and xylazine (6 mg/kg). A silastic PE-10 intravenous catheter (IITC, Woodland Hills, CA) was implanted into the internal jugular vein and tunneled to exit through the neck. During the same surgery, five stainless steel screws (Small Parts Inc., Miami Lakes, FL) were implanted through the skull to serve as dural electroencephalographic electrodes, and two electromyographic electrodes were implanted in the neck musculature. After the surgical procedure, rats recovered for 7 days in a temperature- (21°–24°C) and light-controlled room with *ad libitum* access to food and water. Lights were turned on at 6:00 AM and off at 6:00 PM, and the intravenous catheter was flushed every other day with 0.2 ml saline to maintain patency. Including the preoperative phase, rats were adapted to this light cycle for 10–14 days before initiating electrophysiologic monitoring.

After the 7-day recovery period, rats were acclimated to the disk-over-water sleep deprivation apparatus for 24 h in preparation for the deprivation protocol. In this paradigm, rats are placed on a 45-cm-diameter disk suspended horizontally over a pan of water with continuous computerized electroencephalographic/electromyographic monitoring. When sleep onset is detected, the computer rotates the disk at a rate of 3 revolutions/min, causing the rat to wake up and walk to avoid falling into the water. When the rat awakens, rotation stops. This method has been previously validated as able to produce near-total sleep deprivation without excessive physical exertion.¹⁷

During the initial 24-h acclimation period, rats were placed in the disk-over-water apparatus with a platform over the wheel to eliminate the water hazard and to allow *ad libitum* activity. After acclimation, electroencephalographic/electromyographic recordings were obtained for a 24-h period beginning and ending at 12:00 noon to establish baseline values. Immediately after the baseline period, the platform was removed and rats underwent a 24-h period of total sleep deprivation. Temperature and lighting conditions in the apparatus during baseline and deprivation were the same as for adaptation (21°–24°C and lights on from 6:00 AM to 6:00 PM).

When the sleep-deprivation period ended, the platform was replaced, and 16 rats were anesthetized with a continuous infusion of propofol (Zeneca Pharmaceuticals, Wilmington, DE) diluted to 5 mg/ml with 0.9% saline and administered *via* syringe pump (Baxter AS50; Baxter Healthcare Corp., Round Lake, IL). Sedation was begun at a propofol dose of 500 $\mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ and continued until the righting reflex was lost and the rat was able to tolerate clip-type pulse oximetry without moving. Sedation was then titrated downward at 5-min intervals to the lowest level required to maintain loss of

righting reflex and tolerance of pulse oximetry and to prevent spontaneous movement with gentle prodding. Rats were allowed to breathe spontaneously, rectal temperature was maintained higher than 36°C *via* heat lamp, and continuous pulse oximetry (Ohmeda Biox 3740; Ohmeda, Madison, WI) was used to verify oxygen saturation greater than 90%. Vital signs, infusion rates, and rat behavior were continuously monitored and recorded every 15 min. The infusion was continued for a total of 5.5 h (12:00 PM–5:30 PM). Control rats for which *ad libitum* sleep was allowed ($n = 16$) underwent the same protocol but received an infusion of 5% intralipid (Baxter Healthcare, Deerfield, IL) at 1 ml/h, a rate equal to the average ml/h rate for rats receiving propofol. At 5:30 PM, all infusions were discontinued, and the electroencephalogram/electromyogram was monitored continuously in both groups for 72 h to determine the time course and characteristics of NREM and REM recovery sleep.

Electroencephalographic and electromyographic data for all rats were recorded on a Grass model 78 polygraph (Grass-Telefactor, West Warwick, RI) with a paper speed of 10 mm/s and also relayed to a computer for digital recording and spectral analysis. Electroencephalographic and electromyographic data were divided into 30-s epochs and were scored as waking, NREM, or REM sleep using an automated scoring system previously validated against visual and behavioral methods.^{17,18} Portions of the electroencephalogram/electromyogram were also scored visually to verify the reliability of the automated system. Definitions of sleep stages have been presented in detail previously.¹⁸

In addition to sleep staging, spectral analysis was performed on the midline electroencephalogram. After amplification and filtering (0.5–18 Hz [3 dB points, 12 dB/oct]), the electroencephalogram was sampled at 64 Hz. Using a 4-s window with a Hanning window vector to minimize artifact at the borders of each window, six equally-spaced fast Fourier transforms were performed for each 30-s epoch to calculate the frequency distribution of electroencephalographic power. Low-frequency delta (2–4 Hz) power was extracted for each window, averaged over the epoch, and divided by bandwidth to obtain power density.

At the conclusion of all electroencephalographic/electromyographic recording, all rats were killed by intraperitoneal injection of 300 mg/kg pentobarbital.

Statistical Analysis

All statistical analyses were performed using SAS version 8 (SAS Institute, Cary, NC). NREM sleep stage data were collected for each rat, averaged in 3 h blocks, and expressed as a percent of recording time. Because REM sleep comprised less than 6% of total recording time and was absent during much of the active phase, REM sleep data (expressed as number of epochs) was averaged into

Fig. 1. Sample electroencephalographic/electromyographic recordings from rats anesthetized with propofol (A) and control rats given intralipid (B). Paper speed was 10 mm/s. In intralipid rat recording, sleep-to-wake transition is marked. EEG = electroencephalogram; EMG = electromyogram.

larger, 6-h blocks to ensure that all blocks contained some REM sleep. To correct for differences in mean delta power density due to variability in electrode placement or skull shape, delta power during epochs scored as NREM sleep was normalized by dividing the NREM values for each rat for each block by the mean delta power density during REM sleep for the same block. To prevent division by zero in blocks with no REM sleep, delta power was thus averaged into 6-h blocks. This approach has previously been reported to minimize within-group variance in rodents.¹⁹

Baseline sleep for propofol and intralipid groups were compared using a repeated-measures analysis of variance (ANOVA). For each group, comparisons between postdeprivation recovery and baseline sleep were also performed using a repeated-measures ANOVA.

To determine the magnitude and extent of postdeprivation rebound sleep, each 3-h block of postdeprivation recovery sleep was first normalized by subtracting baseline sleep at the same time point. This step served to remove the normal circadian variation in sleep with time. Each 3-h block of normalized postdeprivation sleep was then compared to 0 using a one-sided *t* test with Bonferroni adjustments for multiple comparisons.

Between-groups comparisons of postdeprivation sleep characteristics was performed by subtracting baseline

values from postdeprivation sleep in both groups and comparing the resulting differences using a block-by-block repeated-measures ANOVA.

Results

For both intralipid and propofol groups, average weights (266.1 ± 19 vs. 279.8 ± 22 g), ages (71.3 ± 6.3 vs. 70 ± 6.1 days), and degrees of sleep deprivation (92.9 ± 6.3 vs. $90.5 \pm 9.2\%$ wake/24 h) were similar. During deprivation, there was no significant difference in disk rotation between rats in the intralipid ($18.3 \pm 9.4\%/24\text{-h}$ period) and propofol ($15.4 \pm 13\%$) groups. The average infusion rate for rats sedated with propofol over the 6-h period was $297 \pm 38 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$, corresponding to a total infusion volume of 5.95 ± 0.6 ml over 6 h. Control rats received a total infusion volume of 6 ml over 6 h (1 ml/h). Visual inspection of the electroencephalogram during propofol anesthesia revealed a continuous, high-amplitude pattern without noticeable NREM or REM stages for the entire 6-h period (fig. 1). During the 6-h intervention period, sleep in control rats (NREM + REM) totaled 4.27 ± 0.33 h. Rats anesthetized with propofol took less than 10 min to reach their behavioral endpoint, defined as a loss of

Fig. 2. Non-rapid eye movement (NREM) sleep frequency during baseline recording. NREM sleep was scored in 30-s epochs, collected and averaged in 3-h blocks, and expressed as percent of total block time $\pm$ SD. Shaded areas depict dark phase (6:00 PM–6:00 AM) recording. AM and PM are denoted as *a* and *p*, respectively.

righting reflex and tolerance of clip-style pulse oximetry. The average time from discontinuing the infusion to first movement was 30 ± 18 min.

NREM Sleep

Baseline values for NREM sleep in control rats given intralipid and anesthetized rats given propofol were similar (fig. 2). Both groups demonstrated normal circadian variability (less sleep during the lights-off period between 6:00 PM and 6:00 AM) and appropriate synchronization to the experimental lighting cycle. In controls, NREM sleep after deprivation was significantly increased above baseline values (obtained at the same time point) for 12 h before returning to baseline (fig. 3). Specifically, NREM sleep was increased above baseline by (mean $\pm$ SD) $19.3 \pm 3.0\%$ in the first 3-h block (12:00 PM–3:00 PM, $t(15) = 6.38$, $P < 0.001$), $18.1 \pm 8.3\%$ in the second block (3:00 PM–6:00 PM, $t(15) = 8.76$, $P < 0.001$), $14.0 \pm 10.6\%$ in the third block (6:00 PM–9:00 AM, $t(15) = 5.30$, $P < 0.001$), and $9.3 \pm 11.7\%$ in the fourth block (9:00 AM–12:00 AM, $t(15) = 3.17$, $P = 0.025$). NREM sleep

returned to baseline levels during the fifth block and did not differ from baseline for the remainder of the 72-h recording period. In particular, no delayed rebound was observed.

In rats given propofol, conventional scoring of the electroencephalogram/electromyogram during the 6-h anesthetic was not performed. No comparisons to baseline were therefore made for the first two blocks after deprivation. After emergence, NREM sleep was increased by $22.3 \pm 18.0\%$ in the first 3-h block only ($t(15) = 4.45$, $P < 0.002$; fig. 3). NREM sleep returned to baseline during the second 3-h block after emergence from anesthesia and was not different from baseline for the subsequent 72-h recording period. The overall duration of increased sleep after deprivation (including the 6-h anesthetic) was thus 9 h. As with control rats, no delayed increase in postdeprivation NREM sleep was observed.

When NREM sleep had returned to baseline levels in both groups, no delayed increases were observed, and circadian variation appeared normal for the duration of the

Fig. 3. Rebound non-rapid eye movement (NREM) sleep after deprivation for propofol and control animals. Values were calculated by collecting and averaging NREM sleep in 3-h blocks before and after deprivation, subtracting postdeprivation NREM sleep from baseline values obtained at the same circadian time point and expressed as mean change in absolute percentage from baseline values $\pm$ SD. Note that NREM behavior was not plotted for propofol rats during anesthesia. Shaded areas depict dark phase (6:00 PM–6:00 AM) recording. *, $\dagger P < 0.05$ when compared with baseline values for propofol and intralipid groups, respectively. AM and PM are denoted as *a* and *p*, respectively.

Fig. 4. Rapid eye movement (REM) sleep at baseline and after deprivation. REM sleep was scored in 30-s epochs, collected in 6-h blocks, and expressed as mean number of epochs/time block $\pm$ SD. Note that REM behavior was not plotted for propofol rats during anesthesia. Shaded areas depict dark phase (6:00 PM–6:00 AM) recording. *, † $P < 0.05$ when compared with baseline values for propofol and intralipid groups, respectively. AM and PM are denoted as *a* and *p*, respectively.

72-h recording period. When postdeprivation NREM sleep was directly compared between propofol and intralipid groups, a repeated-measures ANOVA showed more NREM sleep in controls than in anesthetized rats during only one 3-h block after deprivation, with no other differences between the two groups for the entire recording period. In no postdeprivation block did NREM sleep for propofol rats significantly exceed that of controls.

REM Sleep

As with baseline values for NREM sleep, baseline values for REM sleep in propofol and intralipid groups were similar by repeated-measures ANOVA. In both groups, a characteristic circadian pattern with REM sleep greatest in the second block (6:00 PM–12:00 AM) was observed (fig. 4). In control rats, sleep deprivation significantly increased REM sleep for the first two 6-h blocks before returning to baseline (37.4 ± 27.6 epochs, $t(15) = 5.41$, $P < 0.001$ for the first block, 12:00 PM–6:00 PM; 40.2 ± 40.1 epochs, $t(15) = 3.95$, $P < 0.001$ for the second block, 6:00 PM–12:00 AM) (fig. 4). The duration of REM sleep rebound was thus 12 h. After deprivation, REM sleep for each recovery day was greatest during the first block (12:00 PM–6:00 PM), suggesting residual sleep deprivation.

In rats given propofol, REM sleep was not evaluated during the 6-h propofol anesthetic. After emergence, REM sleep was increased for 6 h (6:00 PM–12:00 AM, 20.8 ± 40.1 , $t(15) = 2.45$, $P = 0.05$) before returning to baseline. The REM rebound response in propofol rats was thus complete 12 h after the end of deprivation. As with control rats, rats given propofol demonstrated the same altered daily pattern of REM sleep after deprivation, suggesting a similar degree of residual sleep deprivation (fig. 4).

When postdeprivation REM sleep was normalized in both groups by subtracting baseline values, repeated-measures ANOVA showed slightly higher REM sleep in control rats during the fourth block after deprivation but no other differences between intralipid and propofol rats. At no time after deprivation was REM sleep in propofol rats increased above that in controls.

NREM Delta Power

During baseline monitoring, delta power did not differ significantly between anesthetized and control animals. In both groups, baseline delta power was highest during the third block (12:00 AM–6:00 AM). In control rats, sleep deprivation significantly increased NREM delta power in the first 6-h block on the first recovery day (1.61 ± 1.4 ,

Fig. 5. Delta power during non-rapid eye movement (NREM) sleep at baseline and after deprivation. Delta power was calculated during epochs scored as NREM sleep, collected in 6-h blocks, and normalized by dividing by average REM delta power for the same period. Values were expressed as mean $\pm$ SD. Note that delta behavior was not plotted for propofol rats during anesthesia. Hatched bars indicate the intralipid group; open bars indicate the propofol group. Shaded areas depict dark phase (6:00 PM–6:00 AM) recording. *, † $P < 0.05$ when compared with baseline values for propofol and intralipid groups, respectively. AM and PM are denoted as *a* and *p*, respectively.

$t(15) = 3.61$, $P < 0.005$). NREM delta subsequently returned to baseline during the second block and was indistinguishable from baseline for the duration of the 72-h monitoring period (fig. 5).

In rats anesthetized with propofol, delta power was not calculated during the anesthetic. Absolute delta power, however, was negligible for the entire anesthetic, a finding consistent with propofol anesthesia in rats.²⁰ After emergence, delta power was not increased above baseline in any block for the duration of the 72-h recording period.

When postdeprivation delta power was normalized to baseline and compared between groups, no differences were found. Absolute theta power, characteristically increased during REM sleep and some waking periods,¹⁸ was negligible in rats receiving propofol.

Discussion

We found that after 24 h of sleep deprivation, recovery sleep behavior in rats for which 6 h of *ad libitum* sleep was allowed was no different from that of rats subjected to a 6-h propofol anesthetic. After emergence from propofol anesthesia, increases in NREM sleep, REM sleep, and delta power suggesting recovery from sleep deprivation persisted for 9, 12, and 6 h, respectively. These increases were equal to or slightly less than those for control rats for which *ad libitum* recovery was allowed. In addition, when sleep had returned to baseline in rats given propofol, no delayed increase in any form of sleep was seen for the duration of the 72-h monitoring period.

In principle, a period of anesthesia might modify the homeostatic regulation of sleep debt in three ways. For example, general anesthesia might be a permissive state that allows normal sleep homeostatic processes to occur. An anesthetized organism would thus repay sleep debt built up during previous wakefulness and emerge less sleep-deprived after an anesthetic than before. Alternatively, anesthesia might progressively increase sleep debt in a fashion similar to wakefulness. Prolonged anesthetics would then induce a sleep-deprived state. Finally, anesthesia might represent a state unlike either sleep or waking, in which sleep debt neither accumulates nor dissipates. Organisms emerging from anesthesia would then have the same degree of sleep deprivation as when they were initially anesthetized.

Under normal conditions, robust sleep homeostatic mechanisms act to preserve adequate sleep after sleep deprivation. Even mild sleep loss increases the propensity to sleep,⁵ and sustained deprivation can cause the organism to sleep when doing so would be life-threatening.

Recovery from sleep deprivation is characterized by rebound increases in NREM and REM sleep and changes in the power spectrum of NREM sleep that persist until homeostatic mechanisms have been satisfied.¹⁶

Our findings are consistent with the presence of an active sleep homeostatic process during anesthesia with propofol. If the anesthetized state had resembled wakefulness in its effect on sleep homeostasis, additional sleep "debt" would have accrued throughout the 6-h anesthetic. This increased debt, combined with a delay in the initiation of recovery until after emergence, would have resulted in a greater amount and intensity of NREM and REM sleep when compared with controls, a higher delta power during NREM sleep, and a corresponding delay in the return of NREM and REM sleep to baseline. If sleep debt had remained static during anesthesia, recovery from deprivation would also have been delayed until after the anesthetic and would have manifested as higher levels of sleep and NREM delta power compared with controls and a longer duration of recovery. Our observation that rats anesthetized with propofol had recovery characteristics nearly identical to rats for which unrestricted sleep was allowed strongly suggests that a recovery process occurred during the 6-h anesthetic and implies that anesthesia with propofol affects sleep homeostasis in a fashion similar to naturally occurring sleep.

Although the mechanisms by which sleep reverses behavioral manifestations of sleep deprivation are poorly understood, plausible links between anesthesia and sleep regulatory mechanisms support an ability of the brain to recover from sleep deprivation during anesthesia. Sleep deprivation increases extracellular adenosine concentrations in the basal forebrain of rats and cats, a site known to modulate central nervous system arousal.¹³ Evidence that administration of adenosine reuptake inhibitors into the basal forebrain increases sleep²¹ and that adenosine delays recovery from halothane anesthesia¹⁵ suggests that extracellular adenosine concentrations plays a role in control mechanisms for both sleep and anesthesia. Increases in basal forebrain adenosine may potentiate anesthetic action, for example, and reduced metabolic demands during anesthesia may allow adenosine concentrations built up during wakefulness to dissipate. Alternatively, anesthetic-induced changes in brain activity may directly decrease adenosine release.

Neurophysiologic similarities between anesthesia and sleep may also allow the anesthetized state to reverse behavioral effects of sleep deprivation. Positron electron tomography/metabolic scanning⁹ and microelectrode recordings of thalamic relay neuronal activity²² both demonstrate reductions in thalamic activity during anesthesia, an important characteristic of naturally occurring sleep.²³ Histologic studies suggest that dexmedetomidine anesthesia increases activity in the ventrolateral preoptic nucleus and reduces activity in the locus ceruleus¹⁰ in a fashion similar to sleep. Although the mo-

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lecular mechanisms governing sleep homeostasis are unknown, some feature of brain activity during anesthesia may duplicate the aspect of naturally occurring sleep that modulates homeostatic control of sleep.

We did not test other anesthetic agents for two reasons. Because our central finding was that no difference existed between anesthetized and control groups, we believed that to include another group would have weakened the statistical finding of no difference. In addition, other anesthetics, such as isoflurane, may have had delayed effects on sleep patterns, preventing us from interpreting postdeprivation behavior. We also targeted a single, behaviorally defined endpoint. Because sleep deprivation can affect anesthetic potency,¹¹ fixed doses of anesthetic would have resulted in changes in the depth of anesthesia as the degree of deprivation changed over time. We therefore titrated our anesthetic to loss of righting reflex and tolerance of clip-style pulse oximetry to maximize behavioral similarities to sleep. Although a dose-response curve involving a different behavioral endpoint (such as electroencephalographic silence) was possible, cardiorespiratory depression would have necessitated intubation and mechanical ventilation for the duration of the anesthetic.

Delayed, propofol-induced effects on sleep may also have altered the interpretation of our results. In humans, the combination of inhaled anesthetics and surgery results in initial suppression of REM sleep, followed by a rebound increase on the second or third postoperative day.²⁴ We thought it unlikely in our study that a delayed effect of propofol anesthesia suppressed subsequent sleep and obscured detection of a recovery response. No delayed rebound suggestive of an initial suppressive effect was seen in anesthetized rats, and block-by-block comparisons between baseline and postanesthesia sleep after the end of recovery revealed no suppressive effect in any sleep measure. It is possible that the shorter recovery duration in anesthetized animals actually indicated a more efficient recovery process during anesthesia than during *ad libitum* conditions. This possibility might plausibly be explained by differences in the time spent in the unresponsive state (6 h for anesthetized rats *vs.* 4.27 h for controls).

Finally, lighting conditions during our study deserve mention. Rats are nocturnal animals, normally asleep during daylight hours.²⁵ At baseline, rats in both groups demonstrated appropriately less sleep during the dark period. In our study design, the 6-h intervention occurred during the light phase (12:00 PM–6:00 PM), with the next 12 h spent in darkness (6:00 PM–6:00 AM). We chose this strategy because recovery during the light phase is subject to a “ceiling effect” on total sleep,²⁶ which may have limited the size of the rebound we observed. Locating the infusion period in the last 6 h of the light phase thus allowed us to contrast high light-phase recovery sleep levels in controls to near-zero overt sleep in anesthetized animals and examine recovery dur-

ing darkness when between-groups comparisons would be optimally sensitive to differences in recovery sleep. Although previous studies in our laboratory have examined recovery from sleep deprivation under constant lighting conditions,^{25,26} removing such a circadian cue introduces the possibility of circadian drift over time. We therefore chose to monitor recovery under baseline, 12:12-h lighting conditions to minimize this possibility. Because propofol and control rat recovery data were compared at the same point in their diurnal cycle and time after deprivation, phase shifts and diurnal variation were unlikely to affect our results.

In summary, we report that after a 24-h period of sleep deprivation, rats anesthetized for 6 h with propofol recovered to the same degree as rats allowed 6 h of *ad libitum* sleep. This observation suggests that sleep and anesthesia may share common control mechanisms and raises the possibility that understanding anesthetic effects on known correlates of sleep homeostasis may facilitate knowledge regarding effects and consequences of sleep deprivation. Clinically, such interactions between sleep and anesthesia may allow anesthesiologists to better understand how sleep deprivation and anesthesia interact and may potentially allow anesthetics to facilitate sleep in environments where sleep deprivation is common.

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