Studies of Learning during Sleep: Problems, Progress, and Perspectives

A. N. Puchkova

Sleep has been shown to play an important role in memory consolidation. The direction of studies of learning during sleep is based on the hypothesis that assimilation of new information can occur during the state of sleep. We present here a review of articles addressing the question of the formation of new memory traces during sleep with retention to waking, as well as reports of work seeking to identify the mechanisms of this learning. Associative conditioned reflex, perceptual, and other forms of learning are demonstrated, the main type being implicit learning.

Sleep is a quickly reversible state characterized by the absence of consciousness and reductions in activity and the ability to respond to external stimuli. Sleep plays an important role in memory consolidation and, therefore, learning processes. Current studies address the specific mechanisms accompanying memory consolidation at levels from molecules to whole-brain activity. These works and the theories based on them suggest processing of previously obtained information stored in short-term memory. The question "can de novo learning not based on previously acquired information occur during sleep?" has been controversial for many years.

There are now two main theories for the important role of sleep in learning. The active consolidation theory holds that during sleep, the neuronal complexes in the cerebral cortex which encode new information are reactivated and reorganized for integration into long-term memory. The neuronal representations of these memories are potentiated and fixed. Hippocampus-dependent memory is tightly linked with the processes of slow-wave sleep (NREM sleep) and sleep spindles [1–3]. The synaptic homeostasis theory focuses on the opposite process: an overall reduction

in synaptic activity during sleep. Representations of important memory traces undergo minimal weakening, while other connections return to their initial levels. This leads to improvements in the signal:noise ratio in neuronal ensembles, readying the brain to work with the new information [4, 5].

These theories complement each other, but presuppose that the brain operates as an isolated system during sleep. They both indicate that memory consolidation will prevent the formation of new memories. However, the brain can also process incoming sensory signals during sleep, as complete isolation from the external environment would be an enormous evolutionary risk. Various studies, especially those reported in the last decade, have pointed to the possibility that several types of learning may occur. The mechanisms and limits of learning potential during sleep remain unclear, though the authors of these studies have tried to integrate their results into a modern understanding of the mechanisms of sleep and memory consolidation.

The review presented here focuses on the most straightforward studies in the understanding of "learning in sleep": studies in which subjects must assimilate some kind of new information during sleep, this being reflected in their reactions or behavior.

Another approach to manipulating memory during sleep has become popular in recent years. This is directed not to the memorization of new information during sleep

Institute of Higher Nervous Activity and Neurophysiology,
Russian Academy of Sciences, Moscow, Russia;
e-mail: puchkovaan@gmail.com.

but to increasing the effectiveness of preceding learning. This os the targeted memory reactivation paradigm, which suggests reinforcement of memory traces formed during waking by presentation of a learning-associated nonwaking "cue stimulus" during sleep after training sessions. This approach has demonstrated efficacy in controlling declarative, emotional, and procedural memory in terms of both strengthening and weakening representations [6].

Learning during Sleep in Newborn Children. The ability to learn during sleep may be closely linked with age and the stage of development of the brain. Babies have specific EEG patterns, sleep–waking structure, and intense assimilation of information about the surrounding world. In the first days of life, babies can remember conditioned signals of different modalities and carry out cross-sensory associative learning [7]. Sleeping newborns can discriminate prosodically rich sounds (intonation in speech and singing) and speech distorted to minimize prosodic features. Magnetoencephalogram studies recording reactions induced by speech or singing demonstrated significant weakening when speech prosody was reduced [8]. Newborns sleep for a significant proportion of the day and inclusion of this period into the time during which learning can occur significantly extends the potential for early learning and assimilation of associations.

The baby's brain is already able to carry out quite complex phonological processing, which does not cease during sleep. EEG recording studies have demonstrated that sleeping newborns can include information presented during sleep in learning to differentiate vowel sounds. Mismatch negativity in event-linked EEG potentials to rare stimuli can be seen in both waking and sleeping babies even at age less than seven days. Newborns were presented with one frequent and two rare vowel sounds in the evening and then in the morning [9]. The experimental group was also presented with these sounds for 2.5–5 h during sleep. The experimental group, in contrast to children not trained during sleep and the group trained using a different set of sounds, learned to discriminate the "phonetically complex" rare signal from the similar frequent stimulus, while the "simpler" rare stimulus induced strong mismatch negativity in the morning. This effect persisted to at least the following evening. Learning to discriminate sounds is required for assimilation of speech, and the path to auditory learning during sleep may be significantly more effective in babies than adults [9]. In this study, the stimuli heard by sleeping babies were not novel for them, though the differences between the groups hearing the sounds only in the evening or in the evening and during sleep provide evidence of additional learning during sleep.

Sleeping newborns are also able to carry out associative learning. The experimental group of sleeping children aged 1–2 days was trained to the "sound tone/puff of air on the eyelid" association. The control group was also presented with the same stimuli in the same conditions but at random points in time. The puff of air induced a characteristic

movement of the closed eyelid in more than 90% of cases. During training, the experimental group showed a four-fold increase in the probability of an eyelid reaction to the tone, from 20 to 80%, while there were no positive changes in the control group. Thus, learning of the new association of stimuli occurred during sleep [7].

The ability of babies to learn may be an important adaptive mechanism. Sleep in neonates is not as structured as in adults; the first years of life involve critically important periods of maturation of the sensory systems and learning. The ability to learn effectively during sleep may be a characteristic of the early sensory period, with gradual loss of importance and fading with the formation of adult sleep patterns and their accompanying processes [10], though it does not disappear entirely.

Learning during Sleep in Adult Humans and Animals. The ability of sleeping humans to learn new skills or knowledge has long attracted researchers' attention. This type of learning is usually considered in response to questions about "learning something during sleep." The most obvious and convenient question, the first to fall into the focus of attention, is the question of the unconscious assimilation of new information in declarative memory to form new explicit knowledge, which is usually verbal information new to the subject. It is entirely natural that systematic scientific research into this question started quite early.

Positive and encouraging results on the acquisition of new heard information by sleeping patients started to appear at the beginning of the last century, though by the 1950s these were subject to criticism in relation to the experimental protocols, statistics, and, most importantly, the fact or otherwise of sleep at the moment of learning. Use of EEG analysis methods showed that the ability to reproduce information presented during sleep was linked with the presence of the EEG α rhythm at the moment of presentation, i.e., it occurred outside the state of normal sleep [11, 12]. Similar results, with memorization of pairs of words exclusively in the presence of α activity (activation) also appeared after this [13]. If presentation took place in uninterrupted second stage of sleep or during REM sleep, no memorization occurred [14]. Studies in this direction gave quite unambiguous results which could be reproduced from study to study: memorization of new explicit verbal information by sleeping adult humans without interruption of sleep structure was not possible.

Despite stable negative results on the activation and consolidation of declarative memory without coming out of the state of sleep, investigators also employed other approaches for which the fundamental possibility of learning without sleep interruption could be demonstrated.

The first to be detected was the possibility of simple associative learning. Early studies reproduced the classical paradigms of conditioned reflex learning. Sleepers were trained to link a sound with an electric shock. Reactions to stimuli consisted of changes in heart rate and the effect was more marked for NREM sleep than stage 2 sleep [15]. New

studies enlarged the understanding of the possibility of the assimilation of nonverbal information, memorization effectiveness depending on sleep stage.

A new series of studies in this area reinvigorated interest in this theme from 2010. A report appeared in 2012 [17] confirming the fundamental possibility of memorizing new associations during sleep. A new combination of stimuli was used: a sound tone and odors, learning results being evaluated by sniffing reactions, i.e., an increase in inhalation in response to presentation of the odor. This same group of researchers had previously demonstrated [16] that various odors whose perception involves only the olfactory nerve (nontrigeminal odors) lack arousing effects when presented during sleep but induce involuntary sniffing reactions. Inhalation reactions in response to pleasant odors were of grater volume than those to unpleasant odors and served as nonverbal sensory reactions which were apparent in waking and while asleep. The investigators combined different sound tones with pleasant and unpleasant nontrigeminal odors, presenting pairs of stimuli during nocturnal sleep. If EEG activation was seen on presentation of stimulation, the data were not included in the analysis. Learning curves could be seen in responses to presentation of sounds during nocturnal sleep: increases in the volume of inhalation in response to sounds associated with pleasant odors and decreases in the volume of inhalation in response to sounds associated with unpleasant odors.

Differences in reactions to odors and sounds have been seen during both REM sleep and non-REM sleep. Reactions to tones were stronger in REM sleep. Differences in inhalation volume in response to sound persisted after waking, though the subjects did not recall the learning process and the untrained control group showed no differences in inhalation after presentation of tones. The learning effect was more marked after waking when training was run in NREM sleep; when stimuli were presented in the REM phase, reactions did not persist into waking. These results point to successful implicit learning of the new sound/odor association during sleep and partial transfer of the memory from sleep to waking [17].

A report was published in 2014 [18] by the same group of authors on the long-term behavioral effects of implicit associative learning during sleep. Smokers performed associative learning: the odor of cigarettes/an unpleasant odor (ammonium sulfide or rotting fish at a non-arousing concentration). The odor of cigarettes was reinforced by the unpleasant odor in 2/3 of presentations, while only the unpleasant odor was presented in the control group. Presentations were made during waking, in the second stage of sleep, or during the REM phase. An additional "untrained" control group received stimuli in random order during sleep phase 2. Stimulation was terminated on waking or activation. Sleeping and waking subjects responded to odors with decreases in the first inhalation after presentation of the odor, which confirmed the occurrence of sensory processing.

Implicit learning had a long-lasting behavioral effect: patients of the groups trained during sleep did not recall the fact of stimulus presentation but decreased their cigarette consumption over the seven days following training as compared with the seven days prior to training, especially when trained in sleep stage 2. The effect was more marked during the first three days after training. Patients of the group trained during waking (explicit training) and the "untrained" control group showed no such effect. Thus, a single night of implicit associative training during sleep had a marked and long-lasting behavioral effect [18].

These study results demonstrate the possibility of associative learning during sleep, though the mechanisms mediating it remain unclear. A new study [19] continued this direction – the authors investigated brain activity during the process of associative learning. Patients were trained to a "tone (400 or 1200 Hz)/odor (pleasant or unpleasant)" association during NREM sleep or REM sleep, and learning was evaluated in terms of the volume of inhalation in response to presentation of the sound without the odor. Increases in the power of the δ and θ rhythms were seen in response to the "unpleasant" tone as compared with the "pleasant" tone in the NREM phase, though in the REM phase of sleep there were no differences in the θ rhythm, as expected by the authors from the results of other experiments. Thus, associations assimilated during sleep affected conditioned stimulus-induced slow-wave activity and spindles in NREM sleep, these being regarded as tightly linked with memory processes. These reactions were not due to the frequency of the tone as such. Changes in the δ rhythm during sleep induced by the conditioned stimulus were found to be associated with the extent of the sniffing reaction in response to the conditioned sound. The stronger the δ activity, the more marked the reaction after waking. During NREM sleep, the extent of the induced α rhythm correlated negatively with the sniffing reaction in response to the "unpleasant" sound but showed no correlation with sniffing in response to the "pleasant" sound, pointing to stronger learning in response to the unpleasant stimulus. The sharp difference in the link between the δ rhythm and behavior during sleep and waking (sniffing reactions during sleep and in the morning did not correlate with each other) points to consolidation processes occurring after the period of learning but before waking.

Another investigation [21] was carried out in parallel with this series of studies, demonstrating the possibility of forming and suppressing new memory traces during sleep using perceptual learning. This used the paradigm of recognition of previously heard sound segments where patients had to recognize repeated sound segments arising on the background of white noise. Recognition effectiveness increased with the duration of presentation of the target stimulus and voluntary attention was not obligatory [20], so this paradigm was suitable for passive learning during sleep. In the evening, patients had to discriminate the simple sound and the repeated sound segment. They fell asleep carrying

TABLE 1. Studies Demonstrating Successful Learning during Sleep Showing Type of Learning, Stimuli, Reactions Recorded for Study States, and Effectiveness of Learning in States

Learning	Stimulus	Reaction	Effectiveness of learning in waking	Notes	Reference
Perceptual, discrimination of sounds	Speech sounds	EEG ERP	W+ Sleep+ W–	Neonates. Additional learning occurred during sleep	Cheour et al., 2002 [9]
Associative	Sound/puff of air on eyelid	Eyelid movement		Neonates. Reactions only during sleep, learning curve during sleep	Fifer et al., 2010 [7]
	Sound/electric shock	Change in HR	2nd and 3rd stages+ 3rd stage > 2nd stage		Ikeda et al., 1996 [15]
	Sound/odor	Volume of inhalation	REM– NREM+	During sleep, reaction in REM > NREM	Arzi et al., 2010 [16]
	Odor of cigarette/odor	Cigarette consumption	W– REM+ 2nd stage+ 2nd stage > REM		Arzi et al., 2014 [18]
	Sound/odor	Volume of inhalation, EEG rhythms	NREM+	Growth of δ and σ rhythms in NREM to "unpleasant" odor	Canales-Johnson et al., 2018 [19]
Perceptual	Looped sound segments	Evoked EEG activity, detection of stimuli in noise	W, REM+ NREM+ 2nd stage > 3rd stage	In the morning – weakened memorization of stimuli previously presented in NREM	Andrillon et al., 2015 [20]
Perceptual, recognition of old/new stimuli	Words, pseudowords	Recognition of old stimulus, confidence in recognition, EEG ERP	W+ Sleep±	Implicit memorization during sleep affects EEG ERP and confidence in recognition of some words	Andrillon et al., 2016 [22]

EEG ERP – EEG event-related potentials; HR – heart rate; W – waking; "–" indicates absence of learning effect; "±" indicates learning effect limited or weak; "+" indicates presence of learning effect; ">" indicates learning effect more marked in one state than another.

out the task and during sleep the experiments started with presentation of a further two sets of five patterns of different repeated segments: in NREM and REM sleep, respectively.

Evoked EEG activity in response to the repeated segments was seen during both waking and sleep and, although the characteristics and dynamics of responses differed in the different stages, this was evidence of successful processing and recognition of segments in both states. In the morning, patients again carried out the task of discriminating the repeated segments, when they were presented with novel stimuli as well as those which had failed in the evening during the REM and NREM phases. At the beginning of the morning test, patients in the early stage effectively recognized the segments presented in the evening or in REM sleep and poorly recognized the novel segments and those presented during the NREM phase. Perceptual learning took place during testing and recognition of the novel segments improved, while recognition of those presented in the NREM phase remained low. For REM sleep, learning effectiveness correlated positively with the number of stimuli presented during the period of phasic REM sleep. For sleep stage 2, learning effectiveness correlated positively with the number of frontal spindles during the training period. Training effectiveness decreased with increases in the proportion of sleep stage 3, while evoked activity in the patients showed decreased discrimination between target and unrecognized reference segments of the sound with increases in δ activity within the sleep cycle.

Thus, this study demonstrated the possibility that new representations of complex sound stimuli could be formed and that different sleep stages are fundamentally different in terms of their potential for forming or suppressing new memory traces. The mechanism of the most perceptual learning remains incompletely understood, though the involvement of structures of the hippocampus has been demonstrated and the inclusion of basic neuroplastic processes has been suggested.

Implicit training is evidently not blocked during sleep as firmly as explicit. This was also indicated by a study in 2016 [22], addressing implicit memorization of words presented during sleep. Patients had to discriminate words and pseudowords by pressing keys with the right or left hands, respectively. They fell asleep carrying out this task. This approach led to retention of a high level of signal processing during sleep. In the evening, before going to sleep, patients were presented with the first set of words and, after transition to the second and third stages, a second set (the protocol switched to the first set on activation). During sleep, differentiated lateralized evoked EEG reactions were seen to words and pseudowords corresponding to the hand with

which the button had to be pressed. This confirmed retention of high-level processing and preparation of responses during sleep.

After waking, subjects were presented with the old sets and a third, new, set of words, and had to indicate whether they heard a new word or an old word and how confident they were. In the morning, patients in most cases did not recognize words presented during sleep and the overall level of recognition errors and confidence that a word was new were the same as for new words, indicating a lack of explicit memory for words. Words presented in the afternoon were in most cases recognized as old with high confidence. However, if patients identified a word from the second set as old, their confidence in this was higher than for an "old" word from the third set. Differences between words of the second and third sets were also seen in evoked EEG activity in the form of "centroparietal negativity" about 500 msec after presentation even in cases when the patient recognized the word as new. The authors regarded these as signs of implicit memory of the words presented during sleep [22].

We can now say that some forms of learning during sleep are possible for humans, though it is still difficult to say that approaches and results can be systematized. Studies yielding positive results are included in Table 1. However, studies of learning during sleep are not limited to research involving humans. Experiments on animals have also addressed a wide range of approaches to formation of memory traces and quite complex forms of learning.

Conditioned reflex learning has been demonstrated in rats [23]. The animals acquired a second-order conditioned reflex during sleep: associations between a sound tone and electrocutaneous stimulation of the ear, which had previously been the conditioned signal for delivery of an electric shock via the floor as they lapped water. The animals underwent second-order training either during waking or during REM or NREM sleep. The measure of training effectiveness was suppression of water lapping on delivery of the second-order conditioned stimulus. Training in both sleep stages was effective, and although the effect was less marked than in waking it also persisted to day 3 of testing.

Formation of explicit memory in mice during sleep occurred as a result of invasive stimulation [24]. Place cells are a group of cells in the hippocampus which are activated when the animal finds itself in a defined place in space. There is a "cell/region of space" bond, so they serve for construction of a cognitive map of the surroundings and their reactivation during sleep is regarded as part of the process of consolidation of spatial memory. The mice received positive reinforcement consisting of stimulation of the medial bundle of the forebrain on spontaneous activation of defined place cells already known to be bound to a space. This created an artificial imitation of the place preference formation task, which according to current views is based on explicit hippocampal-dependent memory. Stimulation was performed in waking or sleeping animals. During sleep, many

stimuli were delivered during NREM sleep and a significant proportionate number of stimuli were delivered during periods of sharp waves, i.e., oscillation patterns linked with memory consolidation.

After stimulation in any state, animals showed marked behavioral preference for the reinforced place linked with the stimulation. Apart from the possibility of learning, this work confirmed the theory of spatial memory reactivation and retention of spatial encoding by place cells during sleep.

Despite new advances, the small number of studies on learning in sleep, and the absence of any deep understanding of the link between sleep stages and the processes consolidating different types of memory and the extent of processing of signals of different modalities in the sleeping brain, it is still not possible to describe the interactions between these factors. Some patterns can be identified and may provide the basis for new studies. Attention can be drawn to the observation that successful cases of learning during sleep mainly involve implicit types of memory: formation of the ability to discriminate sounds, conditioned reflex associations, and recognition of old and new stimuli in the absence of explicit recognition of the fact of learning in those studies in which this was addressed.

Specific Features of the Mechanisms of Learning during Sleep. Sleep is conventionally regarded as a state promoting memory consolidation but not encoding new memories [4, 25]. However, examples of the successful assimilation of new information during sleep show that these pathways are not completely blocked. In some cases, this is explained by effective bypassing of sensory blocks by presentation of olfactory information [17, 18], which does not pass through the thalamic switch, which may explain the special status of odors perceived during sleep [26]. Detection of stimulus-evoked potentials and EEG rhythms in the studies described above is evidence that the sensory barrier can also be overcome in sleep.

Understanding why sleep stages have different potentials for sensory processing of external signals and detection in different paradigms may throw light on the question of their role in memory formation and consolidation. One of the causes of this sharp difference in learning effectiveness may consist of changes in neurotransmitter levels occurring on transfer from one sleep stage to another, for example, the strong decrease in the acetylcholine level in NREM sleep [27]. It may be that the network of neurons recruited by the novel stimulus in deep sleep remains in the stressed state during waking, which is apparent as suppression of memorization of the new stimulus. Changes in the neurochemical status of the brain are tightly linked with plastic processes continuing actively during sleep. Different stages are dominated by potentiation or decreases in synaptic connections. The absence of perceptual learning seen in deep NREM sleep [21] may reflect the process of weakening of synaptic connections.

Conventionally, REM sleep is regarded as a quite "isolated" state in which the brain has low sensitivity to external

stimuli and endogenous processes compete with external signals. In this situation, the ability to memorize stimuli in this state should be lacking. However, division of this stage into phasic and tonic sleep may solve the resulting contradiction. In the state of tonic REM sleep, sensitivity to sensory information was higher [28, 29] and periods of tonic REM sleep were associated with effective learning [21]. On the other hand, transfer of learning effects to subsequent waking in associative learning paradigms using olfactory stimuli was weaker than in stage 2, which may be associated with the mechanism of rapid forgetting of REM sleep-linked memorization [30].

Learning in NREM sleep, which is seen in studies involving people and experimental animals, is consistent with current concepts on the important role of this stage overall and individual oscillatory phenomena (δ waves, spindles) in memory consolidation [1]. The previous sensory barrier to information from outside evidently also undergoes consolidation.

Overall, the theme of learning in sleep is now undergoing a renaissance. This direction of studies is apparent as a general trend for sleep to be attractive for improving cognitive functions [31]. Experiments characterizing the possible types of learning available at different periods of stimulation using different stimulus modalities are being conducted. The prime task may be systematization of links between sleep stages, types of learning, and the mechanisms mediating them. Current methods allow the subtlety of the responses of the sleeping brain to stimuli to be identified, while animal experiments have the potential to evaluate the neurophysiological processes underlying them. Paradigms of implicit learning may attract the interest of specialists in this type of memory and may in future find practical application. And although the subject of "learning during sleep" has met with scientific skepticism for many years, it may widen our understanding of the operation of the processes of perception, attention, memory, and learning.

The author has no conflicts of interests.

REFERENCES

1. J. Born, B. Rasch, and S. Gais, "Sleep to remember," *Neuroscientist*, **12**, No. 5, 410–424 (2006), https://doi.org/10.1177/1073858406292647.

2. M. Inostroza, S. Binder, and J. Born, "Sleep-dependency of episodic-like memory consolidation in rats," *Behav. Brain Res.*, **237**, 15–22 (2013), https://doi.org/10.1016/J.BBR.2012.09.011.

3. G. R. Sutherland, and B. McNaughton, "Memory trace reactivation in hippocampal and neocortical neuronal ensembles," *Curr. Opin. Neurobiol.*, **10**, No. 2, 180–186 (2000), https://doi.org/10.1016/S0959-4388(00)00079-9.

4. G. Tononi and C. Cirelli, "Sleep and the price of plasticity: from synaptic and cellular homeostasis to memory consolidation and integration," *Neuron*, **81**, No. 1, 12–34 (2014), https://doi.org/10.1016/j.neuron.2013.12.025.

5. G. Tononi and C. Cirelli, "Sleep function and synaptic homeostasis," *Sleep Med. Rev.*, **10**, No. 1, 49–62 (2006), https://doi.org/10.1016/j.smrv.2005.05.002.

6. D. I. Schouten, S. I. R. Pereira, M. Tops, and F. M. Louzada, "State of the art on targeted memory reactivation: Sleep your way to enhanced cognition," *Sleep Med. Rev.*, **32**, 123–131 (2017), https://doi.org/10.1016/j.smrv.2016.04.002.

7. W. P. Fifer, D. L. Byrd, M. Kaku, et al., "Newborn infants learn during sleep," *Proc. Natl. Acad. Sci. USA*, **107**, No. 22, 10320–10323 (2010), https://doi.org/10.1073/pnas.1005061107.

8. A. Sambeth, K. Ruohio, P. Alku, et al., "Sleeping newborns extract prosody from continuous speech," *Clin. Neurophysiol.*, **119**, No. 2, 332–341 (2008), https://doi.org/10.1016/j.clinph.2007.09.144.

9. M. Cheour, O. Martynova, R. Naatanen, et al., "Speech sounds learned by sleeping newborns," *Nature*, **415**, No. 6872, 599–600 (2002), https://doi.org/10.1038/415599b.

10. M. S. Scher, "Ontogeny of EEG-sleep from neonatal through infancy periods," *Sleep Med.*, **9**, No. 6, 615–636 (2008), https://doi.org/10.1016/j.sleep.2007.08.014.

11. C. W. Simon and W. H. Emmons, "Learning during sleep?" *Psychol. Bull.*, **52**, No. 4, 328–342 (1955), https://doi.org/10.1037/h0043733.

12. W. H. Emmons and C. W. Simon, "The non-recall of material presented during sleep," *Am. J. Psychol.*, **69**, No. 1, 76 (1956), https://doi.org/10.2307/1418117.

13. K. Tani and N. Yoshii, "Efficiency of verbal learning during sleep as related to the EEG pattern," *Brain Res.*, **17**, No. 2, 277–285 (1970), https://doi.org/10.1016/0006-8993(70)90082-X.

14. J. M. Wood, R. R. Bootzin, J. F. Kihlstrom, and D. L. Schacter, "Implicit and explicit memory for verbal information presented during sleep," *Psychol. Sci.*, **3**, No. 4, 236–239 (1992), https://doi.org/10.1111/j.1467-9280.1992.tb00035.x.

15. K. Ikeda and T. Morotomi, "Classical conditioning during human NREM sleep and response transfer to wakefulness," *Sleep*, **19**, No. 1, 72–74 (1996), https://doi.org/10.1093/sleep/19.1.72.

16. A. Arzi, L. Sela, A. Green, et al., "The influence of odorants on respiratory patterns in sleep," *Chem. Senses*, **35**, No. 1, 31–40 (2010), https://doi.org/10.1093/chemse/bjp079.

17. A. Arzi, L. Shedlesky, M. Ben-Shaul, et al., "Humans can learn new information during sleep," *Nat. Neurosci.*, **15**, No. 10, 1460–1465 (2012), https://doi.org/10.1038/nn.3193.

18. A. Arzi, Y. Holtzman, P. Samnon, et al., "Olfactory aversive conditioning during sleep reduces cigarette-smoking behavior," *J. Neurosci.*, **34**, No. 46, 15382–15393 (2014), https://doi.org/10.1523/JNEUROSCI.2291-14.2014.

19. A. F. Canales-Johnson, T. A. Bekinschtein, and A. Arzi, "Neural signatures of classical conditioning during human sleep," *BioRxiv*, (2018), https://www.biorxiv.org/content/10.1101/372037v1.

20. T. Andrillon, S. Kouider, T. Agus, and D. Pressnitzer, "Perceptual learning of acoustic noise generates memory-evoked potentials," *Curr. Biol.*, **25**, No. 21, 2823–2829 (2015), https://doi.org/10.1016/j.cub.2015.09.027.

21. T. Andrillon, D. Pressnitzer, D. Leger, and S. Kouider, "Formation and suppression of acoustic memories during human sleep," *Nat. Commun.*, **8**, No. 1, 179 (2017), https://doi.org/10.1038/s41467-017-00071-z.

22. T. Andrillon and S. Kouider, "Implicit memory for words heard during sleep," *Neurosci. Consc.*, **1**, 14 (2016), https://doi.org/10.1093/nc/niw014.

23. E. Hennevin and B. Hars, "Second-order conditioning during sleep," *Psychobiology*, **20**, No. 2, 166–176 (1992).

24. G. de Lavilleon, M. M. Lacroix, L. Rondi-Reig, and K. Benchenane, "Explicit memory creation during sleep demonstrates a causal role of place cells in navigation," *Nat. Neurosci.*, **18**, No. 4, 493 (2015), https://doi.org/10.1038/nn.3970.

25. E. Hennevin, C. Huetz, and J.-M. Edeline, "Neural representations during sleep: From sensory processing to memory traces," *Neurobiol. Learn. Mem.*, **87**, No. 3, 416–440 (2007), https://doi.org/10.1016/J.NLM.2006.10.006.

26. J. Plailly, J. D. Howard, D. R. Gitelman, and J. A. Gottfried, "Attention to odor modulates thalamocortical connectivity in the hu-

man brain," *J. Neurosci.*, **28**, No. 20, 5257–5267 (2008), https://doi.org/10.1523/JNEUROSCI.5607-07.2008.

27. V. M. Koval'zon, *Basic Somnology: Physiology and the Neurochemical Sleep–Waking Cycle*, Binom, Moscow (2011).

28. U. Ermis, K. Krakow, and U. Voss, "Arousal thresholds during human tonic and phasic REM sleep: Phasic and tonic REM sleep," *J. Sleep Res.*, **19**, No. 3, 400–406 (2010), https://doi.org/10.1111/j.1365-2869.2010.00831.x.

29. M. Sallinen, J. Kaartinen, and H. Lyytinen, "Processing of auditory stimuli during tonic and phasic periods of REM sleep as revealed by event-related brain potentials," *J. Sleep Res.*, **5**, No. 4, 220–228 (1996), https://doi.org/10.1111/j.1365-2869.1996.00220.x.

30. Y. Nir and G. Tononi, "Dreaming and the brain: from phenomenology to neurophysiology," *Trends Cogn. Sci.*, **14**, No. 2, 88–100 (2010), https://doi.org/10.1016/j.tics.2009.12.001.

31. S. Diekelmann, "Sleep for cognitive enhancement," *Front. Syst. Neurosci.*, **8**, 46 (2014), https://doi.org/10.3389/fnsys.2014.00046.