trical event suited to the enhancement of motor procedural learning.

On one hand, as discussed in the target article (sect. 2.4.2), the sleep spindle is typically modeled as a thalamocortical network event. On the other hand, in both human and animal studies, motor procedural learning has come to be regarded as an encapsulated process that requires the participation of the neostriatum (e.g., McDonald & White 1993; Packard & Teather 1998; Reber & Squire 1998). The purpose of this commentary is to unite the two perspectives. Three arguments, bearing equally on the sleep spindle's role in motor procedural learning and on its place in neostriatal network activation, will be advanced.

(1) In anatomic terms, neostriatal projection neurons would be exempt from spindle-frequency oscillation in sleep only if their receipt of thalamic and cortical input – in each case massive, ordered, and glutamatergic – were prevented. If these excitatory afferent pathways are functional in sleep – and no evidence exists to suggest their silence[1] – then synchronous voltage oscillation at spindle frequencies in thalamus and cortex will rhythmically excite large assemblies of GABAergic striatal projection cells at their spiny dendrites. In turn, thalamocortical projection targets of pallidal and nigral GABAergic efferent neurons will be disinhibited, completing any number of (cortico)striatothalamocortical (CSTC) "loops" in sleep. If a motor procedural task has been recently learned and practiced, activation of its CSTC circuit in sleep should tend to replicate that motor procedure at acquisition-primed ("tagged") synapses.

(2) Whether spindle-based procedural replication serves consolidation-based enhancement exclusively, as Walker suggests, or both enhancement and consolidation per se, is unknown. It is reasonable, I think, to argue in favor of some role for neostriatal spindling in the process of motor procedural task consolidation. Striatal projection cells – "medium spiny neurons" – are heavily endowed with dendritic spines and thus highly susceptible to dendritic modification. In my view this susceptibility, and the complexity and prolonged time course of dendritic modification, do implicate spindle-generated replay in the consolidation (per se) of motor procedures. It is known that in the hippocampus and amygdala, various learning tasks induce relatively enduring but impermanent cytoskeletal changes at dendritic spines. These changes, effected by actin polymerization prior to nuclear (or dendritic) protein synthesis, increase synaptic efficacy – for instance, by augmenting dendritic response to glutamate – and yet remain modifiable for many hours (Lamprecht & LeDoux 2004). If practicing a motor procedure produces early and modifiable changes in, say, the number and shape of dendritic spines on striatal projection cells, and if these early changes persist for many hours, spindling in Stage 2 sleep could exert a powerful, synchronous excitatory drive at cytoskeletally altered dendrites during the period of their modifiability. Thus spindling could work to stabilize – for instance, by stimulating AMPA receptor insertion – the early cytoskeletal changes. Such a role in stabilization would not, of course, exclude a role for spindling in the processes of consolidation-based enhancement.

(3) An excellent fit between corticostriatal anatomy and physiology, on one hand, and the physical properties of the sleep spindle, on the other, furthers the case for both consolidation and consolidation-based enhancement of motor procedures in sleep.

On the corticostriatal side, it is well known that a large number of cortical neurons projects to a much smaller number of striatal projection neurons. A recent estimate based on the arborization of cortical pyramidal neurons axons in striatum has 17 million corticostriatal neurons projecting to 1.7 million striatal projection neurons (Zheng & Wilson 2002). This anatomic convergence has important physiologic correlates. As demonstrated by Wilson (1992), neostriatal projection neurons are strongly hyperpolarized at rest, where potassium currents resist depolarization by weak or desynchronous synaptic excitation. Where excitation is strong, distributed, and synchronous, however – as presumably it is during a sleep spindle – the inwardly rectifying membrane currents are deactivated, and striatal spiny projection neurons are successfully depolarized.

On the spindling side, the elementary physics of the sleep spindle are instructive. Spectral analysis (by FFT) of any epoch of Stage 2 sleep containing spindles produces a Gaussian distribution of peak frequencies in the circa 12–14 Hz bandwidth; this frequency range is narrow, and within it any two spectral peaks will differ relatively little. If the original sleep epoch is then filtered without phase distortion at any two peaks, each of the resultant waveforms will approximate a simple harmonic oscillator. Where two harmonic oscillations are of nearly the same frequency, as in this example, a special case of the physical principle of superposition states that the oscillators will add to produce periodic "beats" that regularly wax and wane in amplitude. At maximal beat amplitude, the oscillators are maximally in phase; at minimal beat amplitude, they are maximally out of phase. In my view, the characteristically waxing and waning EEG sleep spindle similarly records a physically inevitable, repeating phase synchrony among many voltage oscillations.

Spindling differs from "beats," of course: Because a spindle superposes many oscillators at variable frequencies within the circa 12–14Hz band – legible to the scalp electrode via corticostriatal axonal arborization in cortical layer I – phase synchrony is irregularly intermittent, not regularly periodic. Nonetheless, if each "pure" frequency component of a sleep spindle reflects synchronous membrane voltage oscillation in a discrete population of corticostriatal neurons, then spindling may provide a mechanism for coherent activity within the set of motor and sensory corticostriatal cell populations that uniquely represents a given motor procedure. In this view, a sleep spindle is precisely what is needed to depolarize striatal projection cells, at once convergently and selectively, and thus to disinhibit a particular CSTC motor circuit.

The physical properties of the sleep spindle are hospitable not only to motor procedural learning but also to alteration by it. If intensively practicing a motor procedure produces more or larger sleep spindles, that change is consonant with (1) increased amplitude of voltage oscillation in corticostriatal cell populations, (2) a shift in spectral peak distribution, or (3) increased numbers of spectral peaks. Any or all of these physical changes could ensue from the consolidation-based enhancement (or consolidation) of a recently learned motor procedure – as if evolution had adapted the spindle to practice the task again, outside of consciousness and without behavioral consequence.

NOTE

1. Intermittent synchronous activity in neostriatal networks, interrupting relatively long periods of silence, may go unread during neuroimaging studies of the sleeping brain.

REM sleep, dreaming, and procedural memory

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Abstract: In this commentary the "incredibly robust" evidence for the relationship between sleep and procedural memory is questioned; inconsistencies in the existing data are pointed out. In addition, some suggestions about extending research are made, for example, studying REM sleep augmentation or memory consolidation in patients with sleep disorders. Last, the possibility of a relationship between dreaming and memory processes is discussed.

The model proposed by Walker does have a great impact on the current research in the field of sleep and memory. First, it is important to differentiate between procedural memory and declarative memory because research (e.g., Markowitsch 1996) has shown that the different memory systems are located in different brain areas. Evidence that this is also valid for sleep-related learning was provided by Peigneux et al. (2003). Second, the model includes learning processes during wakefulness and during sleep,

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which settles the debate about the exclusiveness of memory consolidation during sleep.

In describing the findings regarding procedural memory and sleep in humans, Walker states that the evidence is "incredibly robust." Reviewing the literature, however, one must say that the number of studies is quite small, and direct replication studies carried out in different laboratories are scarce. Often different tasks (e.g., a visual discrimination task [Stickgold et al. 2000b], motor skills like finger tapping [Walker et al. 2003b], acquisition of probabilistic rules [Peigneux et al. 2003], and priming [Plihal & Born 1999a]) as well as different manipulation techniques (e.g., early versus late sleep [Plihal & Born 1997], REM sleep deprivation [Karni et al. 1994], and correlations between sleep parameters and improvement [Stickgold et al. 2000b]) have been used. In our laboratory, we are currently conducting a correlation study applying the mirror trace task used by Plihal and Born (1997). The preliminary findings ($N = 12$) are promising: a significant correlation ($r = .430$, $p < .05$, one-tailed) between percentage of REM sleep and improvement in speed from the evening session to the morning session was found. This is not completely consistent with the finding of Stickgold et al. (2000b) for the visual discrimination task; they reported a much higher correlation ($r = .74$; $N = 14$).

Next, my coworkers (Orla Hornung, Francesca Regen, Heidi Danker-Hopfe, and Isabella Heuser) and I utilized a modified version of the mirror-tracing task in a study of memory in elderly, healthy persons and were also able to demonstrate a correlation between the percentage of REM sleep and performance (this is a preliminary result; the study is still in progress). On the other hand, the insignificant finding regarding non-REM Stage 2 sleep and performance is not in line with the findings of Walker et al. (2003b). In addition to these conflicting results, other inconsistencies between the different studies in the field can be pointed out. Karni et al. (1994), for example, found an effect of REM sleep deprivation on the improvement in the visual discrimination task but not for slow wave sleep deprivation, whereas Stickgold et al. (2000b) reported correlations for slow wave sleep and REM sleep. To summarize, although the amount of evidence supporting a close relationship of procedural memory and sleep is growing, many inconsistencies have to be clarified by futures studies.

If sleep plays a crucial role in memory consolidation, one of the next steps will be to study patients with primary sleep disorders. Although Fulda and Schulz (2001) published a extensive meta-analysis on the cognitive impairment in patients with sleep disorders, detailed studies using paradigms including evening training sessions and morning retest sessions have not yet been carried out in these patient groups. Keeping in mind the reduced daytime vigilance in these patients, it will be interesting to search for correlations between sleep architecture (total sleep time, percentage of REM sleep) and performance improvements in procedural as well as declarative tasks.

Assuming that REM sleep plays a crucial role in consolidation of procedural memory (e.g., Plihal & Born 1997), studying the effects of REM sleep augmentation on learning will be of interest. Schredl et al. (2001) have published the first human study in which donepezil, an acetylcholinesterase inhibitor, was administered to enhance REM sleep. A significant correlation ($r = .669$, $p < .05$, one-tailed) between percentage of REM sleep and the improvement of a task (relearning a word list) that comprises declarative and implicit features was found for the donepezil nights. Although this pilot study leaves many questions unanswered, this research area is of interest because it was found that patients with Alzheimer's disease have reduced REM sleep (Bliwise 1993), and cholinergic agents, which often enhance REM sleep – one of the measurable effects of these agents on the cholinergic system – (see Schredl et al. 2000), are widely used in the treatment of Alzheimer's disease.

The last topic to be addressed here is the possible relationship between dream content and learning. Some preliminary evidence has been reported by De Koninck et al. (1988) for intense language learning, and De Koninck et al. (1996) for adaptation to vertical inversion of the visual field. In the second study, the persons who experienced incorporations of the inverted visual field in their dreams performed better on tasks (reading and writing) measuring adaptation. This relation makes sense since research (Schredl 2000) has shown that dream content is related to specific brain activation patterns and other physiological parameters measured during sleep. Moreover, this is in line with the continuity hypothesis of dreaming (cf. Schredl 2003), which states that waking-life experiences, for example, the evening learning sessions, are probably incorporated into subsequent dreams. An experimental approach to this topic could be the technique of lucid dreaming, since it is possible to carry out assigned tasks during the dream (e.g., LaBerge & Rheingold 1990). For a simple motor activity (hand clenching), Erlacher et al. (2003) were able to demonstrate that the related area of the motor cortex was active during the lucid dream (EEG measure). This approach makes sense in the light of the extensive literature on the effect of mental training on performance (e.g., Driskell et al. 1994). Single cases of successful training of sport skills in lucid dreams have been reported (LaBerge & Rheingold 1990; Tholey 1981). On the other hand, one should consider that dreaming as reportable subjective experiences during sleep is only a small part of the total activity of the sleeping brain (comparable to consciousness during the waking state), so it remains unclear how close the relationship between dream content and learning processes during sleep might be.

To summarize, the model proposed by Walker is a promising starting point for future research investigating, in addition to the time course, influential factors such as task type, experimental difficulty, and performance level in the relationship between sleep and procedural memory.

Memory consolidation during sleep: A form of brain restitution

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Abstract: Does sleep restore brain function or does it consolidate memory? I argue that memory consolidation during sleep is an offshoot of restitution. Continual learning causes local synapse-specific neural fatigue, which then masks expression of that learning, especially on time-limited tests of procedural skills. Sleep serves to restore the fatigued synapses, revealing the consolidation-based enhancement observed as a "latent" overnight improvement in learning.

Evidence for the involvement of sleep in memory consolidation comes in many forms, such as the effects of learning on postlearning sleep and the re-expression of behavior-specific patterns during postlearning sleep. However, a cause-and-effect relationship or even a robust correlation between the effects of learning on sleep or the replay of patterns during sleep, on the one hand, and the magnitude of consolidation, on the other, has yet to be effectively demonstrated. Improved learning following a period with sleep, compared to one without, remains the most consistent evidence to date; I propose an explanation for this.

I begin by noting that there exists emerging evidence for sleep as a localized brain process. While Rechtschaffen (1998) suggests that it is "difficult to arrive at a widely acceptable theory of sleep function because that function is not reflected at the organ or system level," he and others (e.g., Moruzzi 1966) propose that sleep is a localized process that provides basic cellular resources. Indeed, no brain lesion has ever successfully eliminated sleep totally for long periods (Rechtschaffen 1998). In certain marine animals, sleep is sometimes localized to one brain hemisphere at a time (Oleksenko et al. 1992). Continual tactile stimulation of the right hand prior to sleep results in increased spectral power in the delta band during early non-REM sleep in the contralateral somatosensory cortex (Kattler et al. 1994).

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