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).

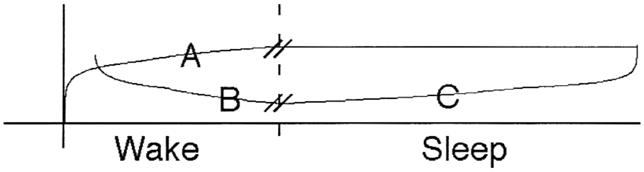

Figure 1 (Sheth). A hypothetical evolution of local brain processes as a function of behavioral state, and the effects on memory performance. Various processes (A, B, and C) combine to affect memory test performance (ordinate). With continual practice while the observer is awake, learning occurs (A), which improves performance. However, neuronal fatigue (B), which occurs hand in hand with the learning, impairs performance. During sleep, neural circuits slowly recover (C), which gives rise to "latent learning." A, B or C are transparent to the experimenter. Observed performance is some (nonlinear) combination of them.

With these ideas as a basis, I propose that two separate local brain processes are involved in the learning of a procedure or skill (see Fig. 1). Over repeated trials, the awake observer practices specifics of the procedure (A). Learning is a multifaceted process, one facet being the progressive restriction in the brain circuits that influence performance (Edelman & Tononi 2000; James 1890). I propose that while this process does not depend on sleep, a second independent process exists that does. With increasing neural specialization during learning, the circuits or synapses repeatedly engaged in the procedure adapt or fatigue (B). Synapse-specific fatigue during procedural learning is unavoidable. Repeated stimulus processing produces decreased responses in brain circuits associated with that processing – a "repetition suppression" effect (Brown & Xiang 1998; Desimone 1996; Wiggs & Martin 1998). The inefficiency in local signal transmission that arises from the synaptic fatigue or adaptation masks expression of the learning. With prolonged training on a task that involves both speed and skill, the net product of these two contravening processes, measured behaviorally, is asymptotic learning (Karni & Sagi 1991). Over still longer training periods, a decline in performance is observed (Mednick et al. 2002). Several studies (e.g., McCollough 1965) have shown that the effects of adaptation can be long lasting, particularly if a select few synapses, specific to certain stimuli or conditions and not others, are adapted.

The recovery of functions related to sensory transmission, such as the restoration of neurotransmitters or the re-formation of receptors, likely involves protein synthesis, which has its own characteristic time course, one that is longer than the time course of resource depletion in the synapse. Thus, sleep-dependent synapse-specific recovery (Fig. 1) is independent of the training in the wake state. It is, however, dependent on sleep; sleep cannot be replaced with awake resting, which fails to control internally generated activity in key brain areas, or by reversible inactivations of brain areas engaged in the consolidation, which only delays the recovery and may even shrink the critical time window during which the learnt information can be actively enhanced (target article, sect. 2.3.2.2).

Sleep is clearly not monolithic. SWS, and non-REM sleep in general, are believed to have a restorative role in brain function (Horne 1988). It is notable that there is correlational evidence for the role of non-REM sleep in memory consolidation in humans (Stage 2 sleep for motor skill learning, Walker et al. 2002; early SWS for visual discrimination skill consolidation, Gais et al. 2000; Stickgold et al. 2000b). This dovetails nicely with the idea of synapse-specific recovery. Replay of behavior-specific patterns during late REM sleep, if short-lived, may reactivate and reinforce the task-related synapses (target article, sect. 2.4.2) with minimal synaptic adaptation or fatigue.

In contrast to procedural memory, evidence that sleep improves declarative memory is inconsistent (sect. 2.2). Perhaps conclusive evidence exists but has eluded researchers, or perhaps procedural and declarative memories differ in the same respects that make the former more susceptible to sleep. Procedural learning is usually dependent on the context and modality in which the material was presented initially (Squire 1986), are "realized as cumulative changes stored within the particular neural systems engaged during learning" (Squire 1986), and typically require training for several minutes to several hours on the procedure. In contrast, declarative learning is flexible, accessible to all modalities and can be "one-shot." The weaker synaptic specificity and quicker learning of declarative as opposed to procedural learning implies less localized declarative storage, which means, by our hypothesis, less synapse specific fatigue, and smaller benefits of sleep.

In sum, two issues are critical in the present account: (1) Synaptic specificity: With greater synaptic specificity, there is greater impact of sleep on local synaptic recovery; and (2) the need for speed: On perceptual as well as motor learning tasks, perception and/or motor action must be conducted within a finite period of time for optimal performance (e.g., Stickgold et al. 2000b; Walker et al. 2002). With time constraints, inefficiency of synaptic transmission takes on even greater significance, and, because speed-accuracy tradeoffs are commonplace, the effects of sleep deprivation are observable on measures of speed as well as accuracy.

By varying each factor, this hypothesis can be experimentally verified. One possibility is to vary the degree of synapse-specific adaptation in two sets of synapses that exhibit learning during training. Visual discrimination skills that transfer to different conditions (Ahissar & Hochstein 1996; 1997) are suitable for this. Synapse-specific sleep dependent recovery will accordingly differ between the two sets. Learning following sleep loss will be impaired following sleep loss in both brain circuits, but less so in the brain circuit that learnt the procedure indirectly via transfer.

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The incredible, shrinking sleep-learning connection

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Abstract: Initial claims that REM sleep is important in the consolidation of all memories have been revised and reduced to the claim that sleep has a role only in the consolidation of procedural learning. Now, Walker hypothesizes that sleep has no role in the "stabilization phase of consolidation" but only in the "enhanced learning" phase of procedural learning. Evidence for this vague, truncated hypothesis remains as inconsistent as that for prior claims.

The idea that REM sleep is important for memory consolidation is attractive, since it would explain the vivid imagery of dreams as a repetition of the events of the prior day to enable the laying down of permanent memory traces. Unfortunately, dream reports do not support this idea. Most dreams concern emotions and activities that did not occur during prior days. Furthermore, most dreams are not subsequently recalled unless they are immediately rehearsed in waking following the dream (Rechtschaffen & Siegel 2000).

Those working on the role of sleep in human learning have modified their hypotheses to include non-REM sleep as well as REM sleep. Many studies of the relationship between human sleep and learning have focused on sleep's role in learning of word recognition and associations between words and events – tasks mimicking most of what goes on in school; this is what learning