For the article “Diversity of regulatory CD4⁺ T cells controlling distinct organ-specific autoimmune diseases,” by Marie-Alexandra Alyanakian, Sylvaine You, Diane Damotte, Christine Gouarin, Anne Esling, Corinne Garcia, Séverine Havouis, Lucienne Chatenoud, and Jean-François Bach, which appeared in issue 26, December 23, 2003, of Proc. Natl. Acad. Sci. USA (100, 15806–15811; first published December 12, 2003; 10.1073/pnas.2636971100), due to a printer’s error, the first bar for the cell population CD25⁺CD62L⁻ in Fig. 2 should be open instead of filled. The corrected figure and its legend appear below.

**Corrections**

**IMMUNOLOGY.** For the article “Diversity of regulatory CD4⁺ T cells controlling distinct organ-specific autoimmune diseases,” by Marie-Alexandra Alyanakian, Sylvaine You, Diane Damotte, Christine Gouarin, Anne Esling, Corinne Garcia, Séverine Havouis, Lucienne Chatenoud, and Jean-François Bach, which appeared in issue 26, December 23, 2003, of Proc. Natl. Acad. Sci. USA (100, 15806–15811; first published December 12, 2003; 10.1073/pnas.2636971100), due to a printer’s error, the first bar for the cell population CD25⁺CD62L⁻ in Fig. 2 should be open instead of filled. The corrected figure and its legend appear below.

**COMMENTARY.** For the article “Slow-wave sleep, acetylcholine, and memory consolidation,” by Ann E. Power, which appeared in issue 7, February 17, 2004, of Proc. Natl. Acad. Sci. USA (101, 1795–1796; first published February 9, 2004; 10.1073/pnas.0400237101), the author notes that the phrase “and associated with theta and gamma oscillations” should be omitted from the first sentence of the center column on page 1795. The theta and gamma oscillations are related to information transfer during REM and not to slow-wave sleep. The sentence should have read “Buzsaki (12, 13) has suggested that sharp wave bursts initiated in the hippocampus during SWS may provide the mechanism by which ‘quanta’ of information may be relayed back to the neocortex during memory consolidation.”
For the article “Wnk1 kinase deficiency lowers blood pressure in mice: A gene-trap screen to identify potential targets for therapeutic intervention,” by Brian P. Zambrowicz, Alejandro Abuin, Ramiro Ramirez-Solis, Lizabeth J. Richter, James Piggott, Hector Beltran-del-Rio, Eric C. Buxton, Joel Edwards, Rick A. Finch, Carl J. Fridlend, Anupma Gupta, Gwenn Hansen, Yi Hu, Wenhu Huang, Crystal Jaing, Billie Wayne Key, Jr., Peter Kipp, Buckley Kohlhauff, Zhi-Qing Ma, Diane Markesich, Robert Payne, David G. Potter, Ny Qian, Joseph Shaw, Jeff Schrick, Zheng-Zheng Shi, Mary Jean Sparks, Isaac Van Sligtenhorst, Peter Vogel, Wade Walke, Nianhua Xu, Qichao Zhu, Christophe Person, and Arthur T. Sands, which appeared in issue 24, November 25, 2003, of Proc. Natl. Acad. Sci. USA (100, 14109–14114; first published November 10, 2003; 10.1073/pnas.2336103100), the authors note that the software used to generate the original graph depicting historical progression of estimated genome coverage by Omnibank failed to consistently select the earliest Omnibank sequence tag (OST) match to the sentinel gene list. Therefore, the rate of genome coverage is significantly greater in the initial phases of gene trap clone collection than that originally presented in the graph for Fig. 2B. The corrected graph accurately illustrates an initial high rate of growth in genome coverage that then slows more significantly in the later stages of clone collection. The conclusions regarding total genomic coverage achieved by this methodology as well as other aspects of the work are unchanged. The corrected figure and its legend appear below.

![Corrected Figure](https://www.pnas.org/content/100/14/14109/F2.large.jpg)
Here has been a long history of experimentation and conjecture about a potentially critical role in memory consolidation for brain processes unique to sleep (1–3). A role for sleep in memory consolidation is consistent with the fact that new memory traces are not instantly fixed but rather remain susceptible to neuro-modulatory influences for several hours after acquisition and require protein synthesis to become stable long-term memories (4). And while it has been clearly demonstrated that sleep deprivation can impair later memory for recently acquired declarative and procedural memory, the precise mechanisms by which sleep may aid or mediate memory storage processes are not known (3, 5). Activation of the cholinergic system has been demonstrated to enhance attention, learning, and memory consolidation and to facilitate plasticity after physiological manipulations and during development (6–8). Acetylcholine levels are high during waking and rapid eye movement (REM; also known as paradoxical) sleep (9). These observations seem consistent with the possibility that REM sleep may play an important role in facilitating synaptic plasticity of recently acquired memory traces. However, the great similarities between the waking and REM sleep states beg the question: What about REM sleep relative to waking is privileged for memory consolidation? Explicitly, REM sleep episodes follow deep slow-wave sleep (SWS) episodes. New findings by Gais and Born (10) presented in this issue of *PNAS* provide compelling evidence in human subjects that SWS and the accompanying low levels of acetylcholine during SWS may mediate a critical memory consolidation process. These findings support two-stage models of memory consolidation, as will be discussed below.

**Hippocampal–Neocortical Cooperation**

Two-stage models of memory consolidation rest on observations that the integrity of hippocampal circuitry is necessary for the maintenance of recent memories but is no longer necessary for older, presumably better consolidated memories (11). In this scheme the hippocampus is specialized in the rapid acquisition of new information relayed from cortical circuits through the entorhinal cortex during periods of elevated cholinergic levels, namely waking and especially during arousal (9, 12–14). Buzsaki (12, 13) has suggested that sharp wave bursts initiated in the hippocampus during SWS and associated with theta and gamma oscillations may provide the mechanism by which “quanta” of information may be relayed back to the neocortex during memory consolidation. In strong support of this view, a recent study (15) demonstrated a correlation between neocortical and hippocampal activity during SWS, which suggests that these hippocampal sharp wave bursts are coupled selectively to the neocortical cell groups that participated in the triggering of the bursts. Hasselmo (14) has further postulated that the flow of information between the hippocampus and neocortex is regulated by cortical acetylcholine release. According to this model, neocortical signaling to the hippocampus predominates during waking and REM sleep periods, when hippocampal feedback to the neocortex is suppressed by acetylcholine. Memory traces encoded in and temporarily stored in hippocampal circuitry may then be relayed back to the neocortex and associated with relevant traces during SWS, when cholinergic suppression of hippocampal feedback to the neocortex is released (14).

Gais and Born (10) designed an experiment to test directly whether low levels of acetylcholine during SWS periods normally predominated by SWS were in fact necessary for normal memory consolidation of a declarative (word list) memory task. Consistent with previous findings, subjects showed improved memory for both the declarative and a procedural (mirror-tracing) task after sleep. Treatment with the acetylcholine esterase inhibitor physostigmine, however, selectively blocked the performance improvement in the declarative memory task normally observed after sleep. These results suggest that the release from elevated acetylcholine levels that occurs during normal SWS is critical in enabling sleep-associated improvement in declarative memory. This finding is consistent with the hypothesis that acetylcholine regulates the flow of information between the hippocampus and neocortex and that such shifts in infor-
SWS or REM sleep may be more critical for the consolidation of newly acquired memory rather than the type of memory (17). Studies attempting to examine selectively REM or non-REM sleep are further complicated by the caveat that it may not be possible to disrupt exclusively one phase of sleep without disrupting the other or at least disrupting SWS–REM transitions that may themselves be important.

**Sleep and Declarative Versus Procedural Memory**

These findings also highlight some as-yet-unresolved issues regarding possible differences in memory consolidation processes for different forms of memory. The physostigmine treatment did not interfere with retention of the mirror-tracing task in Gais and Born’s study (10), although SWS deprivation has been reported to interfere with memory consolidation for a procedural (presumably not hippocampus-mediated) visual discrimination task (16). The lack of a dissociation premature. Alternatively, it has been suggested that the degree to which memory consolidation depends on REM sleep may be related to the complexity of the newly acquired memory rather than the type of memory (17).

**SWS and REM Sleep Contributions to Consolidation**

Findings such as Gais and Born’s (10), which suggest a critical role for SWS in memory consolidation, raise further questions about the relationship between SWS and REM sleep. If SWS does enable feedback of information to the neocortex from the hippocampus, what could be the role of REM sleep in memory consolidation? The facilitating influence of cholinergic activation on synaptic plasticity (8) and memory consolidation in waking animals (7) suggests that SWS sleep episodes may provide periods of plasticity-facilitating elevated acetylcholine levels, such that SWS modifications of neocortical memory traces by feedback from the hippocampus and perhaps other memory buffers may be saved (Fig. 1). Extensive evidence indicates that the hippocampus encodes spatial and temporal information (19, 20) and that the hippocampus, together with its associated cortices, has an especially critical role in episodic memory (21, 22). These findings, together with the above sleep data, suggest that SWS may enable the gradual relaying of critical contextual and binding information to associated neocortical traces so that those memories may become independent of the hippocampus, thereby enabling the hippocampus to continue to specialize in encoding new information.

Memory researchers have recognized acetylcholine as a local enhancer of plasticity (8, 23–25) and cognitive functions, including attention, acquisition, working memory, and consolidation of long-term memory (6, 7, 26). Also, different forms of memory have been shown to depend on different memory systems: e.g., a hippocampal dependence for declarative, episodic, or spatial memory and a striatal dependence for memory classified as procedural, skill, habit, or response (27, 28). The findings reported by Gais and Born (10) encourage us to consider more fully the importance of acetylcholine and perhaps other neuromodulators in regulating the flow of information in the brain and the cooperation of brain structures during memory consolidation (14, 29, 30).