source of information for understanding the design rules of light harvesting and the origin of the red forms.

The structure also reveals particulars of the connections between light-harvesting complexes and the core and between each other. These data are crucial for detailed modeling and understanding of excitation energy transfer and trapping in PSI. It is the extremely fast excitation energy transfer that makes PSI the record holder for quantum efficiency, because it allows the protein complex to outcompete the intrinsic de-excitation mechanisms of the chlorophylls, which occur on a nanosecond time scale. On average, it takes less than 50 ps after absorption of a photon by one of the 155 chlorophylls of PSI to create charge separation in the reaction center (*2*), leading to 99% quantum efficiency.

Fast excitation energy transfer is often associated with an energetic funnel, meaning that the excitation is transferred from high-energy to low-energy pigments, with a close distance between all pigments (*8*). Qin *et al.*'s structure indicates that this does not apply to the entire PSI. A surprising result is the absence of most of the "gap chlorophylls" that in the previous structure were observed between the Lhca belt and the core (*12*). Their absence leaves a large spatial gap between the light-harvesting subunits Lhca2 and Lhca4 and the core. To reach the reaction center, excitations from the Lhca belt should then mainly flow via Lhca1 and Lhca3. Yet at first sight these pathways seem to be slow, because they contain a series of uphill energy transfer steps that involve both the red forms and chlorophyll b pigments, which are higher in energy than chlorophyll a pigments. Qin *et al.*'s data need to be integrated with theoretical and experimental results to understand the high efficiency of PSI even in the presence of these putative slow transfer steps. ■

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10.1126/science.aab3387

NEUROSCIENCE

Exploiting sleep to modify bad attitudes

Targeted memory reactivation of training-induced social counterbias during sleep

By **Gordon B. Feld** *and* **Jan Born**

Since the age of enlightenment in the 18th century, liberty and equality have spread across the Western world, leading to a decline in explicit racism and sexism. Nevertheless, the tendency to hold implicit prejudices of race or gender continues to drive discrimination (*1*, *2*). Indeed, recent news has been filled with reports on the rise of nationalistic groups, excessive police violence against minority group members, persisting unequal pay for women, and sexual harassment all across the developed world. On page 1013 in this issue, Hu *et al.* (*3*) show how such unwanted attitudes may be persistently changed by a social counterbias training when the fresh memories of this training are systematically reactivated during sleep after training.

Sleep, and specifically deep or slow-wave sleep [non–rapid eye movement (REM) sleep], benefits memory formation by reactivating neuronal traces that were formed during the preceding period of wakefulness. This reactivation of specific memories leads to their strengthening and transformation (*4*). Such reactivation can be experimentally induced during slow-wave sleep by presenting cues that were present during the prior period of memory acquisition. Initial studies showed that an odor present during learning of object locations enhances these memories when the participant is reexposed to the odor during slow-wave sleep after learning (*5*). These findings have been confirmed in numerous studies investigating different memory systems and also when auditory instead of olfactory cues are used (*6*–*8*). This basic research has firmly established the possibility of influencing sleep to enhance specific newly learned memories by targeted memory reactivation.

The findings by Hu *et al.* now suggest that this method can also be used to influence implicit attitudes that are known to typically manifest themselves early during childhood and remain very stable into adulthood (*9*). Before a 90-min nap, participants underwent training aimed at countering typical implicit gender and racial biases by learning to associate genders and races with opposing attributes; that is, to associate female faces with science-related words and black faces with "good" words (see the figure). Critically, presentation of the to-be-learned counterassociations was combined with a sound, which served as a cue to promote the reactivation of the newly learned associations during a subsequent nap while the participant was deep in slow-wave sleep. Only when this sound was re-presented during slow-wave sleep did the posttraining reduction in implicit social bias survive and was even evident 1 week later. These findings are all the more convincing as the authors conducted the reactivation step during a 90-min daytime nap. During normal sleep at night, the effects are expected to be even stronger, owing to the generally deeper and longer periods of slow-wave sleep and REM sleep. Additionally, the accompanying neuroendocrine milieu makes nocturnal sleep even more efficient for memory reinforcement.

> ***"...this method can be used to break long-lived, highly pervasive response habits deeply rooted in memory..."***

Previous studies have shown that such targeted reactivation of memory during sleep can effectively extinguish unwanted behavior such as experimentally induced fear in humans (*10*, *11*). The present study is the first to demonstrate that this method can be used to break long-lived, highly pervasive response habits deeply rooted in memory and thereby influence behavior at an entirely unconscious level. A hallmark of such automatically implemented habit memories is that their retrieval escapes cognitive control exerted over consciously recalled explicit memory by the prefrontal cortical-hippocampal system. In this regard, Hu *et al.*'s data

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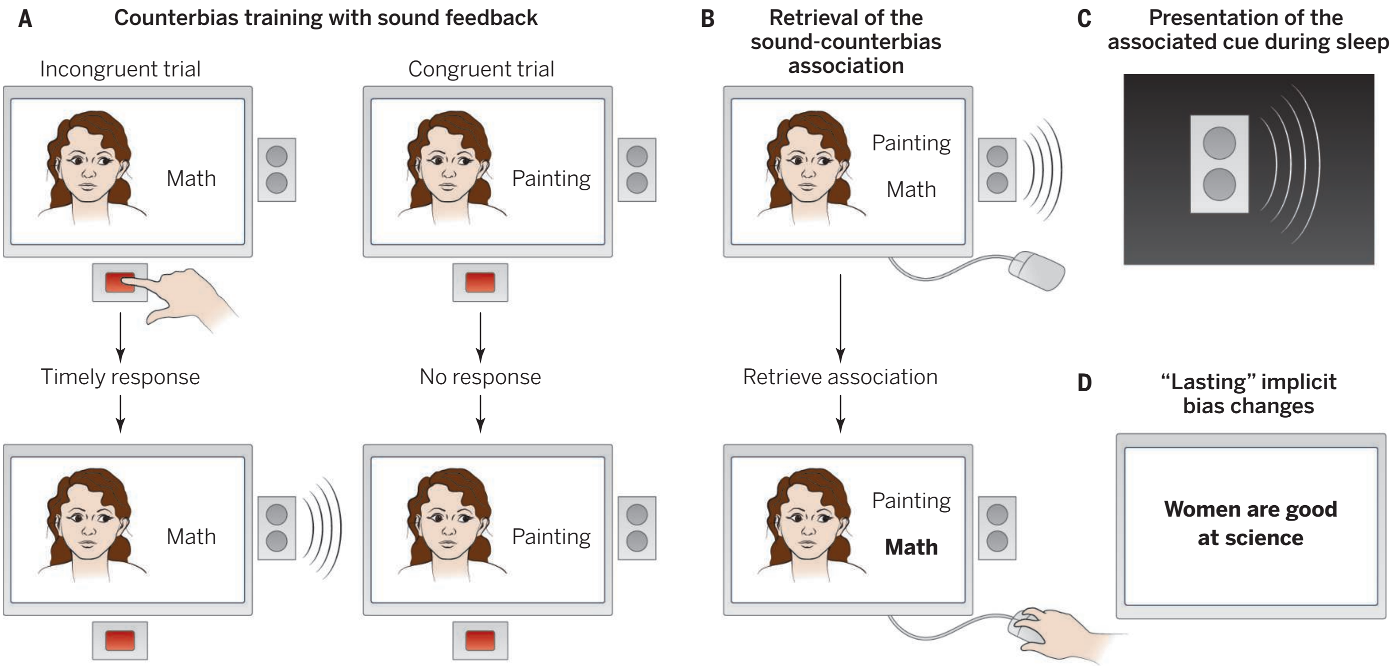

Sleeping your way out of a bad attitude. Implicit social bias scores could be improved by applying a counterbias intervention comprising two tasks: counterbias training with sound feedback and retrieval of the sound-counterbias association. This training-induced improvement was then stabilized by re-presenting the sound cue during sleep. (**A**) On the counterbias training, participants were shown separate pictures of men and women of different racial groups together with words from the opposing categories "science/art" and "good/bad". When seeing an "incongruous" pair (e.g., face of a woman and the word "math"), participants had to respond by pressing a button. "Correct" and timely responses received a feedback sound. Congruent trials afforded no response. (**B**) On the sound-counterbias retrieval task, participants were instructed to drag and drop a face (e.g., a female face) onto the incongruous word (e.g., "math") whenever they heard the sound that was associated with this specific counterbias during the preceding counterbias training. (**C**) The sound was then used to cue, and thereby reactivate, the memory of the newly learned counterbias association when the participant entered slow-wave sleep during a subsequent 90-min nap. (**D**) A stable reduction of implicit social bias, persisting 1 week later, was only achieved if the counterbias intervention was cued during the nap.

suggest that sleep is a brain state labilizing even strong habit-like implicit memories. This putatively makes them susceptible to modification through treatments targeting, in the first place, the explicit hippocampus-dependent memory system.

Hu *et al.* certainly demonstrate the striking potential of targeted memory reactivation during sleep to modify deeply rooted attitudes. Together with the ongoing debate on the longevity and effectivity of social bias interventions (*12*), these findings raise a number of questions regarding the underlying neurophysiological and psychological mechanisms. One is why such enduring modifications cannot be achieved by targeted reactivations during wakefulness. Perhaps countering the preexisting racial or gender bias by memory reactivation during sleep leads to an immediate weakening of the original bias memory trace, indicating that during sleep even very old traces can reenter a labile state. Alternatively, the procedure might induce an extinction-like suppression of the original bias by a newly learned counterbias. Such new learning of response suppression implicates the activation of the machinery of synaptic plasticity during sleep. Here, another detail of Hu *et al.*'s findings is of interest, suggesting that the long-term improvement in social bias was additionally linked to posttraining REM sleep, which represents a state of increased synaptic plasticity. This indeed fits a "sequential" view on sleep's role in memory formation (*4*): Each bout of slow-wave sleep and accompanying reactivation transforms the new counterbias traces and primes the participating synapses for lasting synaptic changes that are induced during the subsequent phase of REM sleep (e.g., by activation of immediate early genes and protein synthesis).

However, new learning of an extinction-like suppression also suggests that effects might depend strongly on the learning context. If so, the risk of spontaneous recovery of the original social bias is increased when the person leaves the behavior modification setting, as well as with increasing time after the treatment. Unless the underlying mechanisms are understood, there is a risk that seemingly marginal changes in the procedures of targeted memory reactivation during sleep might produce precisely opposite results of the desired effects. Indeed, just such reversals have been seen in studies applying this method to counter fear responses (*13*). The possibility of such an outcome is further suggested by interventions that paradoxically increase social bias instead of reducing it (*14*).

There is little doubt that the study of Hu *et al.*—with its clear implications for society—will motivate research to resolve these remaining issues. However, Aldous Huxley's description of a dystopian "brave new world" where young children are conditioned to certain values during sleep reminds us that this research also needs to be guided by ethical considerations. Sleep is a state in which the individual is without willful consciousness and therefore vulnerable to suggestion. Beyond that, Hu *et al.*'s findings highlight the breadth of possible applications to permanently modify any unwanted behavior by targeted memory reactivation during sleep. ■

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10.1126/science.aab4048

ILLUSTRATION: P. HUEY/SCIENCE

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Science **348**, 971 (2015);
DOI: 10.1126/science.aab4048