CAN SCIENCE HELP YOU SMOKE LESS?

Scientists find that olfactory aversive conditioning during sleep reduces cigarette smoking behavior.

By Aanya Gupta

Recent research by Arzi et al from the Lowenstein Hospital Helsinki Committee shows that a single night of olfactory aversive conditioning during sleep significantly reduced cigarette-smoking behaviour in a sleep stage-dependent manner, and this effect persisted for several days. There were significant reductions in the number of cigarettes smoked following olfactory aversive conditioning during stage 2 and rapid eye movement (REM) sleep but not following aversive conditioning during wakefulness. Moreover, the reduction in smoking following aversive conditioning during stage 2 was greater and longer lasting compared with the reduction following aversive conditioning during REM. Finally, the reduction in smoking following aversive conditioning during sleep was significantly greater than in two separate control sleep experiments that tested aversive odours alone and the effects of cigarette odours and aversive odours without pairing.

Sleep is highly beneficial for learning and memory. Consolidation and reactivation of memories during sleep have been observed across a wide range of modalities and learning forms. Moreover, recent studies have implied that entirely new associations can be learned during sleep. These new associations can drive altered physiological and neuronal responses during the same night of sleep and immediately upon ensuing wakefulness. With this, the researchers wanted to test whether implicit associative learning during sleep can alter long-term ensuing behaviour. In order to do so, they tested whether olfactory aversive conditioning between cigarette odours and profoundly unpleasant odours during sleep would reduce later cigarette-smoking behaviour compared to similar conditioning during wakefulness. The researchers hypothesized that olfactory aversive conditioning during sleep would alter cigarette-smoking behaviour during ensuing wakefulness. A total of 66 human subjects wishing to quit smoking participated in the study (23 females and 43 males). Subjects were split into different groups depending on if they were being tested during wakefulness or sleep and which odours they were being exposed to.

Each day for 7 days before the experimental procedure, subjects completed a smoking diary and a smoking habits questionnaire. On the experimental day or night, subjects in the sleep implicit group rated the intensity and pleasantness of the odourants using a visual analogue scale (VAS) while those in the wake implicit group did the same in addition to rating the similarity of the cigarette odour. The experiment was conducted in a designated olfaction sleep laboratory which presented cigarette odours with profoundly unpleasant odours, including ammonium sulfide (AmSu) and a scent emulating rotten fish (RF; Sensale), and clean airflow through a nasal mask. Sleep and nasal respirations were measured using electroencephalograms (EEGs), a spirometer, a high-standard pneumotachometer, and a standard polysomnography. Sniffs and nasal airflow aided in understanding varying sleep stages since they were measured, analyzed and compared to that in the trial onset. In all sleep experiments, if arousal or awakened state was detected in the ongoing polysomnographic recording, the experiment was immediately stopped until stable sleep was resumed and then continued until the end of the block. In both the sleep implicit and wake explicit groups, approximately 30 min after awakening in the morning, subjects again rated the intensity and pleasantness of the odourants in addition to the similarity of the cigarette odour. Finally, subjects completed a smoking diary on each of the 7 days after coming to the sleep laboratory, detailing the number of cigarettes smoked each day.

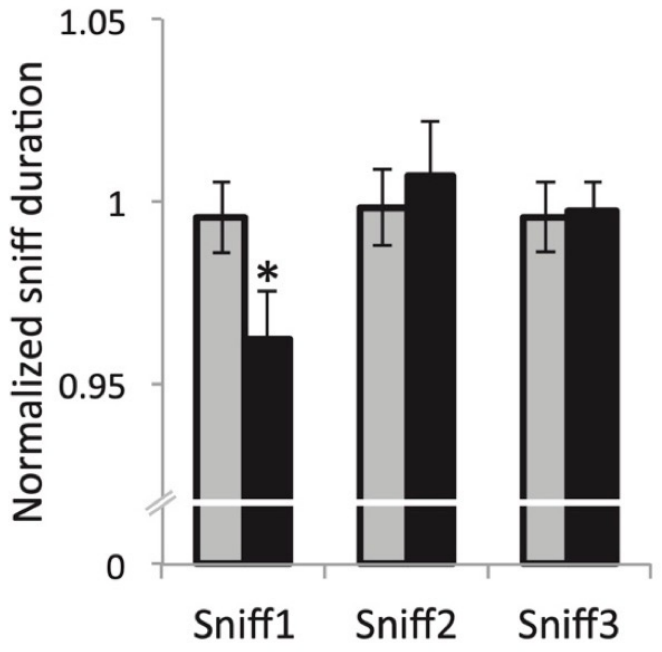

Figure 4. Unpleasant odors reduced first sniff duration during sleep. Normalized sniff duration for three consecutive sniffs following unpleasant odors (black) and cigarette odor (gray) during sleep. The first sniff following unpleasant odor onset was significantly shorter compared with baseline, implying that the sleeping brain indeed registered odor presence and quality. $^{*}p < 0.05$.

The main results found were as follows:

The odourants used were unpleasant as intended: From an ANOVA on VAS pleasantness and intensity ranking that subjects completed before conditioning, while all three odours (cigarette odours, AmSu, and RF) were less pleasant than neutral, both AmSu and RF were significantly less pleasant and more intense than cigarette odour, as intended.

The odourants used did not awaken subjects: According to polysomnography standards applied for arousal and wakefulness over multiple trials and EEG spectral properties, nontrigeminal odourants presented during sleep do not awaken subjects. These results are consistent with previous studies.

Odourant properties were reflected in the sniff response during sleep: An ANOVA on sniff duration for the condition of sniff and planned comparisons showed a significant reduction from baseline in the first sniff after odour onset. Although nontrigeminal odours do not awaken the subject, they nevertheless modify the sniff response in a predicted manner, driving weaker sniffs for unpleasant odours. These odour-induced sniffing patterns of reduced sniffs for the unpleasant odours during sleep are consistent with previous studies and imply that the sleeping brain indeed registered odour presence and quality.

Conditioning during sleep reduced cigarette-smoking behaviour but conditioning in wakefulness did not: According to an ANOVA, there was a significant reduction in smoking following conditioning during stage 2 sleep and REM, but not wake. Following conditioning during stage 2 sleep there was a significant reduction in smoking in the first half and second half of the experiment. However, following conditioning during REM, there was a significant reduction only in the first half but not in the second half of the experiment. In addition, conditioning during wakefulness did not reduce smoking in either the first or second half of the experiment.

These findings suggest that implicit olfactory aversive conditioning during sleep significantly reduced smoking behaviour, yet explicit olfactory aversive conditioning during wakefulness did not. Furthermore, a reduction in smoking was observed following olfactory aversive conditioning during stage 2 and REM sleep. However, the smoking reduction magnitude and duration were sleep stage-dependent with an enhanced and longer-lasting reduction following stage 2 conditioning.

The effectiveness of conditioning was not associated with altered sensory perception: After comparing the ANOVAs on VAS pleasantness and intensity ranking before and after conditioning, olfactory aversive conditioning did not change the perception of cigarette odour, and imply that the ensuing influence on cigarette-smoking behaviour was not the result of altered sensory perception alone.

Conditioning reduced cigarette-smoking behaviour more than sensory exposure alone: To test whether the observed reduction in smoking following olfactory aversive conditioning during sleep resulted from the pairing between cigarette odour and unpleasant odours, or from the administration of unpleasant odours alone, the researchers conducted a control experiment in which they replicated the conditioning paradigm but used clean air instead of cigarette odour (unpleasant odour group). In this experiment, participants were exposed to unpleasant odours alone during stage 2 or REM sleep. After comparing these results to the original stage 2 and REM conditioning groups, they found that both olfactory aversive conditioning and unpleasant odour administration alone during sleep reduced smoking behaviour, yet the reduction in smoking following olfactory aversive conditioning was approximately double the magnitude of those following unpleasant odours alone. An additional control experiment was conducted in which they delivered the same number of aversive and cigarette odours as in the conditioning, but in randomized order rather than paired (nonconditioned group). Because a greater and longer-lasting reduction was evident following conditioning during stage 2 sleep compared with REM 2 sleep, they conducted this control during stage 2 sleep only and compared the results to that of the olfactory. The results imply that the greater reduction in smoking following olfactory aversive conditioning during sleep compared with odour exposure alone resulted from the pairing between cigarette odour and unpleasant odours and not from the administration of the cigarette odour or due to fewer exposures to odour.

Taken together, these results indicate that a single night of conditioning between cigarette odour and profoundly unpleasant odours (AmSu and RF) during stage 2 and REM sleep drove a significant reduction in smoking behaviour over the ensuing week, which supports the researchers' initial hypothesis. Moreover, they found that the reduction in smoking behaviour was greater and longer lasting following conditioning in stage 2 versus REM sleep. The increased effect in stage 2 is consistent with the expanding literature regarding the role of slow-wave oscillations in memory consolidation of general and olfactory-specific information. In turn, the reduced effect in REM may be viewed as consistent with the rapid forgetting of REM-related memories. In contrast to the results obtained during sleep, explicit olfactory aversive conditioning during wakefulness did not alter smoking behaviour. Building upon the results obtained from this experiment, olfaction may have a privileged role not only for implicit learning in general but also more specifically in the context of addictive behaviour, such as smoking. The shared anatomy and the enhanced connectivity during sleep between the brain circuits of reward and olfaction may enable olfaction to play a role as a unique pathway to modulate reward-related behaviour in general and during sleep in particular. Thus, future studies may assess the direct applicability of aversive conditioning during sleep to the treatment of addiction.