Effects on Sleep-Wake States on Reaction Times and Priming Effects in a Semantic Priming Paradigm

Margreet Kolff, Winni Hofman, Ph.D.,
Gerard Kerkhof, Ph.D., and Anton Coenen, Ph.D.

Recently, Stickgold et al. (1999) demonstrated that subjects awakened from REM sleep showed a greater priming effect by weak primes than by strong primes, which is in contrast to the normal pattern of priming. Their interpretation was that REM sleep is involved in enhancing the strength of memory association. To replicate these findings a semantic priming experiment was designed. Subjects were exposed to prime-target pairs just before sleeping, just after awakening from slow wave sleep as well as from REM sleep, and after waking up in the morning. Reaction times on the target word were dependent on the level of association of the prime-target words, and on the sleep-wake state just before testing. In agreement with the literature was the finding that the stronger the association, the shorter the reaction time on the target was. Moreover, and in agreement with Stickgold et al.` findings, was the fact that reaction times after awakening from sleep and REM sleep were longer compared to those when wakefulness was preceding the test. This is in line with the phenomenon of 'sleep inertia'. However, not in agreement with Stickgold et al.` results was that the priming effect after REM sleep was smaller than that after slow wave sleep. This effect was even comparable to the priming effect after waking. This finding jeopardises the interpretation and conclusions with respect to the positive function of REM sleep in memory consolidation. **(Sleep and Hypnosis 2003;5(2):72-77)**

Key words: *sleep-wake states, REM sleep, memory hypothesis, semantic priming paradigm, priming effect, reaction times, sleep inertia*

INTRODUCTION

The cognitive capacities of a sleeping brain are still largely unknown. Investigators suggest a function of sleep in information processing and more specifically in the strengthening of memory (1,2), but a discussion about the differential cognitive functions of slow wave sleep (SWS) and rapid eye movement (REM) sleep is still going on. The brain acquires continuously new information, and new memories are consolidated from short-term into long-term memory. The consolidation process refers to the process operating during the time after acquisition. A multitude on studies has explored the role of REM sleep in memory formation and plastic cerebral changes seem to

From NICI, Department of Biological Psychology, University of Nijmegen, Nijmegen (Drs. Kolff and Coenen) and Unit of Psychophysiology, Department of Psychology, University of Amsterdam, Amsterdam (Drs. Hofman and Kerkhof) The Netherlands

Address reprint requests to: Dr. Anton Coenen, NICI, Department of Biological Psychology, University of Nijmegen, PO Box 9104, 6500 HE Nijmegen, The Netherlands
Phone: +31 24 3612545, Fax: +31 24 3616066,
e-mail: coenen@nici.kun.nl

Accepted April 11, 2003

underlie learning and memory processes in animals as well as in humans (3,4). In several animal studies it is found that consolidation needs periods with REM sleep (5), while deprivation of REM sleep is followed by memory impairments (6). Moreover, there are studies showing that new association can be formed during REM sleep (3). However, negative studies are also often reported (7).

Stickgold et al. (4) performed studies towards a specific role of sleep in memory processes. They showed that associative memory is altered during REM sleep. Contrary to the normal pattern of priming, persons awakened from REM showed a greater priming effect by weak primes than by strong primes. Stickgold et al. (4) suggest that REM sleep might alter the strength of associative links in memory. The results of this research suggest that cognition during REM sleep is qualitatively different from that of waking and non-REM sleep. According to Stickgold et al. (4) 'associative priming' can be used to obtain evidence for the view that sleep is involved in memory processing.

Associative priming might provide information about the way in which words are represented in memory (8). Responses to a target word (e.g. dog), which is preceded by a strongly related, prime, word (e.g. cat), are faster and more accurate than responses to weakly related primes (e.g. child - youth). This implies that memory systems can be automatically activated by a prime. Stickgold et al. (4) found that priming was qualitatively different between SWS and REM sleep. Weak primes were most effective during wakefulness and during REM sleep and less effective during SWS. It is therefore assumed that changes in cognitive processes occur during REM sleep. The study of these changes is crucial to uncover the link between memory processes and sleep-wake states in the strengthening of newly formed associations. The aim of the present study is to compare the differences between sleep-wake states on semantic priming, both with respect to reaction times and to the priming effects.

METHODS

Sixteen undergraduate psychology students of the University of Amsterdam (5 men and 11 women, age 18-26 years) received course credits for their participation in this study. All subjects declared to be in good health, with no sleep problems and did not use hypnotics or other medicines. Subjects were not allowed to take caffeine and alcohol after 5 PM of the day preceding the test night and napping was forbidden during this day. A Neurotop Nihon-Kohden polygraph was used for registration of the EEG and EOG. Silver chloride electrodes were placed on C3, C4, O1, and O2 and were linked to references on A1 and A2, according to the 10-20 electrode system. A ground electrode was placed on the forehead and two EOG electrodes near the eyes. The EEG signal was recorded with a sample frequency of 256 Hz and electrode impedance was less than 5 kOhms. The low pass filter was set at 70 Hz and the time constant was 0.16 Hz. Standard polysomnographic techniques were used to classify sleep-wake stages (9).

The priming task stimuli were presented with an IBM Personal Computer. Four lists of 200 Dutch prime-target pairs were selected from published association norms (10-12). The associative strength of the strong primes was more than 30% (implying that 30% of all subjects give the same response on the prime), and for the weak primes between 2% and 8%. Each list contained 25 strongly related word pairs, 25 weakly related word pairs, 50 unrelated word pairs as well as 100 word - non-word pairs. A non-word is a non-existing word, which in length is matched with an existing word. Total test time was 10 minutes. The list order was counterbalanced across subjects. Stimuli were presented in the center of a computer screen. A fixation point, which appeared for 700 ms in the center, was followed by a prime for 200 ms. Immediately after this prime the target word appeared until a response was made.

The experimental night started at 10 PM with preparing subjects for polysomnographic recordings. Than subjects were trained once in the semantic priming paradigm. They were instructed to read the first word (prime) and than to respond to the second word (target) as fast as possible. A response was made by pressing a button with the forefinger: with the right hand on the right button when the target is a ‘word’, or with the left hand on the left button when the target is a ‘non-word’. Subjects went to bed between 11.15 and 11.45 PM and woke up between 7.00 and 7.30 AM. Lights were turned off at 12 PM. The first list was presented just before the subjects went to bed for sleeping (pre-sleep condition). In the slow wave sleep condition (SWS condition) subjects were awakened after 10 consecutive minutes in SWS by turning on the lights and calling the subject’s name. Within one minute after awakening the subject started with the experiment. Thereafter, the subjects returned to bed and were awakened again after 3.00 PM after the first minute of rapid eye movement sleep (REM sleep condition). Again within one minute the test was started. Five minutes after awakening in the morning (post-sleep condition) subjects were tested for the fourth time. Determination of the sleep-wake states was done on-line based on the records of the polygraph and controlled afterwards off-line. Based on this control, six subjects of the REM sleep group were excluded from analysis for reasons of uncertainty.

RESULTS

Reaction times

Subjects had to respond as fast as possible after appearance of the target. Only correct responses were included in the analysis of the reaction times and only those reactions given by the right button (responses by the left button, implying a non-word, were requested for the reason that the subjects had to decide whether it was an existing word or not. Thus they could not react only on the appearance of the word or non-word). Data are presented in Table 1 and paired samples statistics were performed on the data. In all four conditions (pre-sleep, SWS, REM, post-sleep) a significant difference ($p<0.05$) was found between the ‘strongly related word pairs versus the unrelated word pairs’, and the ‘weakly related word pairs versus the unrelated word pairs’.

The reaction times for the pre-sleep (strongly related, weakly related and the unrelated words) are significantly faster than for the SWS condition (strongly related, weakly related and unrelated; paired samples test, $p=0.06$) and the REM condition (strongly related, weakly related and unrelated, $p=0.03$). Also the post-sleep (strongly related, weakly related and unrelated) showed a significant difference with the SWS condition ($p=0.01$) and the REM condition ($p=0.001$).

The reaction times in the ‘wake-state’ (pre-sleep and post-sleep pooled) are faster than in the ‘sleep-state’ (SWS and REM sleep pooled). A repeated measure analysis of variance (ANOVA) for the two pooled conditions wake- and sleep states showed a significant difference ($df=1$, $F=7.2$, $p=0.025$).

Table 1. Reaction times

Condition	n	RT strongly	SEM related	RT weakly	SEM related	RT unrelated	SEM
pre-sleep	16	524	20	538	17	554	18
SWS	16	571	21	581	24	623	22
REM	10	578	14	605	12	625	26
post-sleep	16	539	17	549	18	575	21

The mean RT (reaction times) in ms with SEMs to target words, primed with strongly related words (25), with weakly related words (25) and with unrelated words (50).

Priming effects

The difference in reaction time in primes between a related prime-target word pair and an unrelated prime-target word pair is defined as the priming effect (Table 2). The analysis of priming effects between different sleep-wake conditions with a paired sample test, did not reveal significant differences. There was one exception: a significant difference was found between the pre-sleep and the SWS condition (p=0.025).

Table 2. Priming effects

Condition	Priming effect	SEM
Pre-sleep	46	11
SWS	94	19
REM	67	26
Post-sleep	62	12

The priming effect is the difference in ms between the reaction times of the primes of the unrelated words and the related words (effects of strong and weak priming added). The priming effect is given for the several conditions. The higher the number, the greater is the priming effect.

DISCUSSION

As is known from the literature (see 13 for review) the reaction times for strongly related words are faster than for weakly related words and much faster for unrelated words. In this study it is indeed shown that reaction times are dependent of the strength of the prime-target relationship. Moreover, the reaction times are also dependent from the sleep-wake states. The wake (pre-sleep) condition has the shortest reaction time, followed by the post-sleep condition, while the two sleep conditions (SWS and REM sleep) have the slowest reaction times. This is completely in line with the findings of Stickgold et al. (4). Although the reaction times are determined when the subjects are aroused, it can be concluded that there is a slow transition from sleep, and even from REM sleep, to full wakefulness. This 'sleep inertia' after forced awakenings shows that the brain is not immediately able to react as fast as during full wakefulness (14-16). Even after a spontaneous awakening in the morning the brain is still not optimally working. Table 1 shows this two factors model of the execution of reaction times elegantly: the first factor is the strength of relatedness of the two words of a word pair and the second is the level of vigilance from which the subject is aroused.

The semantic priming effect is unexpectedly larger following awakenings from SWS than from other states. How could it be that semantic priming is larger directly after awakening from SWS compared to full wakefulness (pre-sleep condition)? Semantic priming is defined as the difference between reaction times for target words preceded by primes with no semantic relationship, and reaction times to target words preceded by semantically related primes. Semantic priming is thought to be associated with the automatic spreading of activation from a neural ensemble representing a prime word to another neural ensemble representing the target word. It is found that this spread of activation is faster during the brain in a sleep-like state (SWS condition), compared to wakefulness. The neurophysiological situation in the brain during sleep is totally different to the waking situation (17). During wakefulness numerous nerve cells in the brain are in a tonic mode of neuronal firing implying a state of sustained and high spontaneous activity, with a low synchronisation between cells. On the other hand, during sleep many neurons fire in a burst mode, implying bursts of action potentials with relatively long-lasting pauses and a high synchronisation between neurons. It is speculated that this burst-pause firing mode with a high synchronisation between cells forms the neurological substrate for the spread of activation during sleep. During wakefulness the synchronisation between cells is low, while the high tonic activation of large parts of the brain, with much more interference, prevents a fast adequate spreading of activation. It is further speculated that the complete change in firing mode from sleep to wakefulness costs some time.

A completely alternative explanation is that the priming effect found shortly after arousing from sleep is a kind of an artefact of the formula to establish the priming effect. In general the reaction times just after sleep are quite long, due to a low level of vigilance. Presumably, this might be due to the hyperpolarisations of neurons in the peripheral motor system; it needs a longer time to pass this system. This is true for the response to unrelated word pairs as well as for the related word pairs, for which the reaction times given the relatedness are smaller. Priming effects assume a linear relationship between the factors 'degree of vigilance' and 'strength of association'. However, this is not a verified assumption; it might be that the contribution of the 'degree of vigilance' is very different from the 'strength of association'. Finally, it has to be admitted that this study did not control for time-of-day effects (awakenings after SWS are always sooner as awakenings after REM sleep).

Nevertheless, which explanation of the data might be true, they do not fit with the Stickgold et al. (4) data, in particular with those of REM sleep. They found a striking difference in comparing weak and strong priming. Contrary to the normal pattern of priming, subjects awakened from REM sleep showed greater priming by weak primes than by strong primes. Although the data from weak and strong priming were pooled in the present study, the separate data for weak and strong priming do not suggest such an effect at all (see Table 2). There was no significant priming effect in the REM weak condition. REM sleep data are best comparable to the post-sleep data and given the brain states during REM sleep (high activity but different from waking) and post sleep (five minutes after awakening thus already back on a quite high activity level) this is not surprising.

In all, it is concluded that the data do not support the strengthening of memory hypothesis for REM sleep, while this hypothesis for SWS, despite the greater priming effect after SWS, is debatable. Nevertheless, the two factors determining the speed of reaction times after priming (degree of vigilance and strength of relatedness between the words of the word pair) are convincingly shown in this experiment.

REFERENCES

1. *Cipolli C. Sleep, dreams and memory: an overview. Journal of Sleep Research 1995;4:2–9.*
2. *Plihal W, Born J. Effects of early and late nocturnal sleep on priming and spatial memory. Psychophysiological Research 1999;36:571–582.*
3. *Hennevin E, Hars B, Maho C, Bloch V. Processing of learned information in paradoxical sleep: relevance of memory. Behaviour Brain research 1995;69:125-135.*
4. *Stickgold R, Scott L, Rittenhouse C, Hobson J. Sleep-induced changes in associative memory. Journal of Cognitive Neuroscience 1999;11:182-193.*
5. *Smith CT, Rose GM. Evidence for a paradoxical sleep window for place learning in the Morris water maze. Physiology and Behavior 1996;59:93-97.*
6. *Smith CT, Conway JM, Rose GM. Brief paradoxical sleep deprivation deprivation impairs reference, but not working memory in the radial arm maze task. Neurobiology of Learning and Memory 1998;69:211-217.*
7. *Vertes RP, Eastman KE. The case against memory consolidation in REM sleep. Behavioral and Brain Sciences 2000;23:867-876.*
8. *Zeelenberg R. Testing theories of priming. Ridderkerk, The Netherlands: Ridderprint BV, 1998.*
9. *Rechtschaffen A, Kales A. A manual of standardized terminology, techniques and scoring system for sleep stages of human subjects. Brain Information Service, Brain Research Institute, University of California, Los Angeles, California, USA, 1968.*
10. *de Groot, AMB. Mondelinge Woordassociatienormen: 100 Woordassociaties op 460 Nederlandse Zelfstandige Naamwoorden. [Oral Word Association Norms: 100 Word Associations to 460 Dutch Nouns]. Lisse, The Netherlands: Swets & Zeitlinger, 1980.*
11. *van Loon-Vervoorn WA, van Bekkum IJ. Woordassociatie Lexicon (gebaseerd op 1299 woorden en 100 proefpersonen). [Word Association Lexicon (based on 1299 words and 100 subjects. Amsterdam, The Netherlands: Swets & Zeitlinger, 1991.*

12. *Lauteslager M, Schaap T, Schievels D. Schriftelijke Woordassociatie Normen voor 549 Nederlandse Zelfstandige Naamwoorden. [Written Word Association Norms for 549 Dutch Nouns]. Lisse: The Netherlands: Swets & Zeitlinger, 1986.*

13. *Neely JH. Semantic priming effects in visual word recognition: a selective review of current findings and theories. In: Besner D, Humphreys GW, eds. Basic processes in reading: visual word recognition. Hillsdale, N.J, USA: Erlbaum, 1991:264–336.*

14. *Balkin T, Badia P. Relationship between sleep inertia and sleepiness, cumulative effects of four nights of sleep distribution/restriction on performance upon abrupt nocturnal awakenings. Biological Psychology 1988;27:245-258.*

15. *Dinges DF, Kribbs NB. Performing while sleepy: Effects of experimentally-induced sleepiness. In: Monk TH, ed. Sleep, Sleepiness and Performance. New York: John Wiley & Sons, 1991:97-128.*

16. *Naitoh P, Kelly T, Babkoff H. Sleep inertia: best time not to wake up. Chronobiology International 1993;10:109-118.*

17. *Coenen AML. Neuronal activities underlying the electroencephalogram and evoked potentials of sleeping and waking: implications for information processing. Neuroscience and Biobehavioral Reviews 1995;19:447–463.*