ELSEVIER

Cognitive Brain Research 14 (2002) 317–324

COGNITIVE BRAIN RESEARCH

www.elsevier.com/locate/bres

Research report

Cognitive flexibility across the sleep–wake cycle: REM-sleep enhancement of anagram problem solving

Matthew P. Walker*, Conor Liston, J. Allan Hobson, Robert Stickgold

Laboratory of Neurophysiology, Department of Psychiatry, Harvard Medical School, 74 Fenwood Road, Boston, MA 02115, USA

Accepted 6 March 2002

Abstract

Flexible or 'fluid' cognitive processes are regarded as fundamental to problem solving and creative ability, requiring a specific neurophysiological milieu. REM-sleep dreaming is associated with creative processes and abstract reasoning with increased strength of weak associations in cognitive networks. REM sleep is also mediated by a distinctive neurophysiological profile, different to that of wake and NREM sleep. This study compared the performance of 16 subjects on a test of cognitive flexibility using anagram word puzzles following REM and NREM awakenings across the night, and waking performances during the day. REM awakenings provided a significant 32% advantage in the number of anagrams solved compared with NREM awakenings and was equal to that of wake time trials. Correlations of individual performance profiles suggest that REM sleep may offer a different mode of problem solving compared with wake and NREM. When early and late REM and NREM awakening data were separated, a dissociation was evident, with NREM task performance becoming more REM-like later in the night, while REM performance remained constant. These data suggest that the neurophysiology of REM sleep represents a brain state more amenable to flexible cognitive processing than NREM and different from that in wake, and may offer insights into the neurocognitive properties of REM-sleep dreaming.

Theme: Neural basis of behaviour

Topic: Cognition

Keywords: Cognitive flexibility; Sleep–wake cycle; REM sleep; Norepinephrine; Prefrontal cortex

1. Introduction

The concept of differing cognitive styles has now been established for nearly a century [34]. One proposed classification of cognitive styles distinguishes a rigid or 'crystalline' form of intelligence from a flexible or 'fluid' style [18]. In this framework, one might conceive of crystalline processes as involving the rigid, rule bound application of factual information, while fluid processes utilize more associative based mechanisms to form novel relationships such as those employed in problem solving and creative thinking.

At a neurophysiological level, fluid cognitive processes appear to be dependent on levels of central aminergic neurotransmitter dominance. Situations of high stress and anxiety, where aminergic transmitter levels are high, impair cognitive flexibility [37], with a particular sensitivity to the degree of dominance by norepinephrine. For example, Beversdorf et al. [6] have established that tests of cognitive flexibility such as anagram word puzzles are completed more quickly following β-adrenergic blockade with propranolol, while task performance worsens following administration of the adrenergic agonist ephedrine. Furthermore, these aminergically controlled changes in cognitive flexibility appear to be centrally as opposed to peripherally mediated [7]. In support of these cognitive data, cellular recordings have demonstrated that a suppression of noradrenergic tone decreases the signal-to-noise ratio within cortical neurons [16], while animal models indicate that reduced firing modes of noradrenergic locus coeruleus neurons result in a more divergent state, leading to high degrees of behavioral flexibility [2].

*Corresponding author. Tel.: +1-617-626-9540; fax: +1-617-734-7851.

E-mail address: mwalker@hms.harvard.edu (M.P. Walker).

0926-6410/02/$ – see front matter
PII: S0926-6410(02)00134-9

Anatomically, prefrontal lesions and frontal lobe pathology cause severe disruptions to problem solving abilities [4,10,12,27,38], suggesting that fluid problem-solving abilities entail a reliance upon frontal lobe function during wake. In addition, neuroimaging studies using tasks of cognitive flexibility and fluid reasoning trigger signal increases in prefrontal regions in healthy subjects, particularly in the dorsolateral prefrontal cortex (DLPFC) [28,32].

Dreaming, a process most strongly correlated with rapid eye movement (REM) sleep [25], has been associated with enhanced creativity [5]. From the dreams of both August Kekulé which led to the conception of a simple structure for benzene [19], and Dmitry Mendeleyev that initiated the creation of the periodic table of elements [36], to the late night dreaming of Otto Loewi which inspired the creative experiments unveiling neurochemical transmission [24], demonstrations of even scientific creativity arising during sleep do not appear to be uncommon.

Quantitative data have demonstrated that problem solving ability, as measured using fluid cognitive tests, is more effective following a 3.5 h interval containing high proportions of REM sleep in comparison to 3.5 h of waking or non-rapid eye movement (NREM) sleep [9]. Moreover, a recent study of semantic priming has demonstrated that, in contrast to the situation in waking, performance following REM sleep awakenings shows a greater priming effect by weak primes than by strong primes, while strong priming exceeds weak priming in NREM sleep [35]. While some authors have argued against the concept of such fluid thinking during REM [31], these data support the hypothesis that REM-sleep dreaming may prime the efficiency of more flexible cognitive skills [8], and offer further insights into the hyperassociative and creative processes that have been assigned to the REM-sleep state [14,24].

During sleep, the brain undergoes dramatic ultradian shifts in neurochemistry and functional neuroanatomy. In NREM sleep, cholinergic systems becomes markedly less active [17,21], while serotonergic raphé neurons and noradrenergic locus coeruleus neurons, although not firing at waking levels, remain active [1,33], leaving the brain in a more aminergically dominated state. In REM sleep, however, both these aminergic populations are inhibited while the cholinergic system becomes as active as in wake [23], resulting in a brain state that is largely devoid of aminergic modulation. PET studies during REM have revealed that regions of the prefrontal lobe, particularly the DLPFC, become markedly suppressed while limbic systems and posterior regions become more active compared with quiet wake and NREM (for review, see Ref. [22]). Furthermore, following REM awakenings, prefrontal regions do not normalize to baseline levels until 15 min later [3]. In contrast, during deep NREM sleep (stages 3 and 4), most brain regions undergo a decrease in activity compared with wake.

The predictable shifts in neurochemistry, functional neuroanatomy and cognitive-psychological properties occurring in wake, REM and NREM sleep thereby provide a fortuitous model with which to (a) further investigate the dependence of flexible cognitive processes on specific psychophysiological parameters, and (b) gain further clarification of the neurocognitive processes associated with sleep-related mental activity. A summary of the key properties that are proposed to mediate cognitive flexibility are provided in Table 1, together with the changes that occur in these properties during REM and NREM sleep.

Table 1
Proposed psychophysiological mediators of optimum cognitive flexibility performance together with the respective functioning levels of those properties in WAKE, NREM sleep and REM sleep

Psychophysiological property	Optimum for cognitive flexibility	WAKE	NREM	REM
Aminergic dominance	↓↓	↔	↑	↓↓
Weak associative memory networks	↑↑	↓	↓	↑↑
Prefrontal lobe function	↑↑	↑↑	↓	↓↓

This study investigated the difference in cognitive flexibility, using anagram word puzzles, during waking trials and following awakenings from nocturnal REM and NREM sleep. It was hypothesized that waking performance would remain constant across the WAKE trials, while the overall performance following REM awakenings would be greater than that from NREM and WAKE test sessions due to the lack of aminergic dominance and the increases in weak associational networks. Furthermore, it was predicted that, due to the markedly different functional anatomy of REM sleep, specific performance profiles following REM sleep awakenings would be different from both the WAKE and NREM profiles respectively.

2. Materials and methods

2.1. Subjects

Sixteen native English speaking college undergraduates (six males and 10 females, mean age 20.8 ± 2.7 years (S.D.)) with normal or corrected to normal vision and without any prior history of neurological, psychiatric, sleep, drug or alcohol problems were recruited from a local university.

2.2. Protocol

The study protocol was approved by the Massachusetts Mental Health Center review board and all subjects provided written informed consent prior to the study. Subjects completed a brief computerized anagram test (see below) at four times across a 10-h period, once at

approximately 10 p.m. before sleep (PRE), once following an awakening 10 min into NREM sleep, once following an awakening 10 min into REM sleep, and once in the morning at approximately 8 a.m. (POST), 30 min after awakening (Fig. 1). REM and NREM awakenings were administered using a balanced order protocol so that eight subjects received one testing session in the second REM period (REM_a) and the next testing session in the forth NREM period ($NREM_a$), and eight subjects received one test session in the third NREM period ($NREM_b$) and the next testing session in the third REM period (REM_b). All REM and NREM tests were administer within 15 s of awakening.

On the evening of the test, subjects were brought into the sleep laboratory and, following the first testing session at 10 p.m. (PRE), prepared for polysomnographic (PSG) monitoring using standardized techniques [29], the criteria of which were used to identify REM and NREM test periods. All NREM awakenings were confirmed to be from stage 2 NREM sleep.

After approximately 8 h of PSG confirmed sleep, and following successful completion of REM and NREM awakening tests, subjects were woken and retested in the morning (POST) after a 30-min interval of waking activity (approximately 8 a.m.). Stanford Sleepiness Scales were obtained prior to the PRE and POST sleep trials, to evaluate subjective sleepiness.

2.3. Sleep stage recordings

Sleep stage recordings were scored according to standardized criteria [29]. All subjects displayed normal sleep profiles. Sleep stage parameters for the group are shown in Table 2.

Table 2
Group sleep stage parameters

Sleep stage measure	Sleep-stage %
Stage-Wake	3.1 (±0.89)
Stage-1 NREM	4.9 (±0.64)
Stage-2 NREM	51.4 (±1.21)
Stage-3 NREM	5.1 (±0.45)
Stage-4 NREM	11.5 (±1.02)
SWS (3+4)	16.6 (±0.74)
REM	24.0 (±2.05)

Values in parentheses represent standard errors. SWS, slow wave sleep; the sum of Stage-3 and Stage-4 NREM sleep.

2.4. Anagram test of cognitive flexibility

The specific test of cognitive flexibility involved solving anagram word puzzles [6], each composed of five letters. The anagram puzzles only had one correct solution (e.g. 'OSEOG'='GOOSE'). Thirty-two different anagrams were used, divided into four sets of eight. The four sets were balanced for level of difficulty based on data from a prior experiment using these anagram words (Beversdorf, personal communication), data that was replicated in an additional 16 subjects tested at four times across the day (10 a.m., 2 p.m., 4 p.m. and 8 p.m.). These data also demonstrated that there was no circadian influence on anagram performance across the day (percent correct: 10 a.m. 54.6±32; 2 p.m. 51.5±6.0; 4 p.m. 49.2±4.67; 6 p.m. 56.2±3.9; $F(3,15) = 0.64$, $P = 0.58$).

Anagram trials were presented on a computer screen at a set distance from the subject, placed adjacent to the bed so as to minimize disruption on awakening. Subjects had a time limit of 10 s to solve each displayed anagram word, thus each test session lasted a maximum of 80 s. When subjects solved an anagram within the 10-s time limit, they pressed the computer space bar, and then verbally reported the solution to the experimenter who recorded the answer. When subjects failed to solve an anagram within the 10-s time limit, the next anagram word appeared, as it did when the subject pressed the space bar indicating a solution. For each subject, at each of the four testing sessions, the number of anagrams solved and the mean reaction times

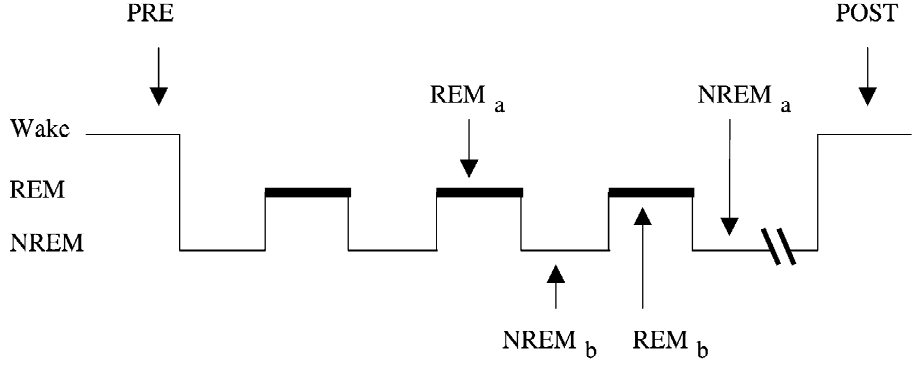

Fig. 1. WAKE, REM and NREM awakening protocol: all 16 subject were tested once before lights out (PRE). REM and NREM awakening tests were performed across the night, counterbalanced between the 16 subjects: eight subjects received one testing session 10 min into the second REM period (REM_a) and the next testing session 10 min into the forth NREM period ($NREM_a$); eight subjects received one test session 10 min into the third NREM period ($NREM_b$) and the next testing session 10 min into the third REM period (REM_b). Following 30 min of waking activity in the morning, all 16 subjects were then tested again (POST).

for those correctly identified were obtained. The four sets of anagrams were administered in a balanced order design across the four test conditions for all subjects.

Analyses of the number of correct anagrams solved and the associated solution reaction times were carried out by repeated measures ANOVAs. For brain state specific comparisons paired, two-tailed Students *t*-tests were used. Correlations of anagram performance (percent correct and reaction times) across the differing states of WAKE, REM and NREM and with Stanford Sleepiness Scale scores were performed using Pearson's correlation analyses.

3. Results

3.1. State-specific comparisons

As predicted, the WAKE PRE and POST test performances on the anagram task did not differ in either the number of anagrams solved or the mean reaction time values (percent solved, 56% PRE vs. 53% POST, df = 15, $t = 0.45$, $P = 0.65$; reaction times, 3.8 s PRE vs. 4.5 s POST, df = 15, $t = 1.6$, $P = 0.12$). Therefore, both the number of anagrams solved and the reaction time values from PRE and POST test sessions were averaged together respectively as a 'WAKE' group for further comparisons with sleep awakenings.

3.1.1. Percentage solved

There was a significant difference in the number of anagrams solved across the three conditions of WAKE, NREM and REM ($F(2,15) = 3.8$, $P = 0.03$; Fig. 2a). In agreement with our initial hypothesis, the number of anagrams solved following REM awakenings was 32% higher than the number solved following NREM awakenings (df = 15, $t = 2.3$, $P = 0.03$; Fig. 2a). There was no significant difference in the number of anagrams solved in the WAKE tests compared with the performance from REM awakenings (55% REM vs. 54% WAKE, df = 15, $t = 0.15$, $P = 0.88$). In contrast, the number of puzzles solved following NREM awakenings was significantly less compared with the WAKE condition (42% NREM vs. 54% WAKE, df = 15, $t = 2.4$, $P = 0.02$).

3.1.2. Reaction times

There was no significant difference in the mean reaction times across the three conditions (WAKE = 4.2 s, REM = 4.3 s, NREM = 4.5 s, $F(2,15) = 0.37$, $P = 0.68$; Fig. 2b), or the median reaction time (WAKE = 3.9 s, REM = 4.4 s, NREM = 4.1 s, $F(2,15) = 0.26$, $P = 0.76$). Furthermore, there was no significant difference in the mean reaction times between any of the conditions (df = 15; REM vs. NREM, REM vs. WAKE, NREM vs. WAKE; all $P > 0.40$). Each condition also displayed a similar distribution of anagram solution times across the 10-s window of re-

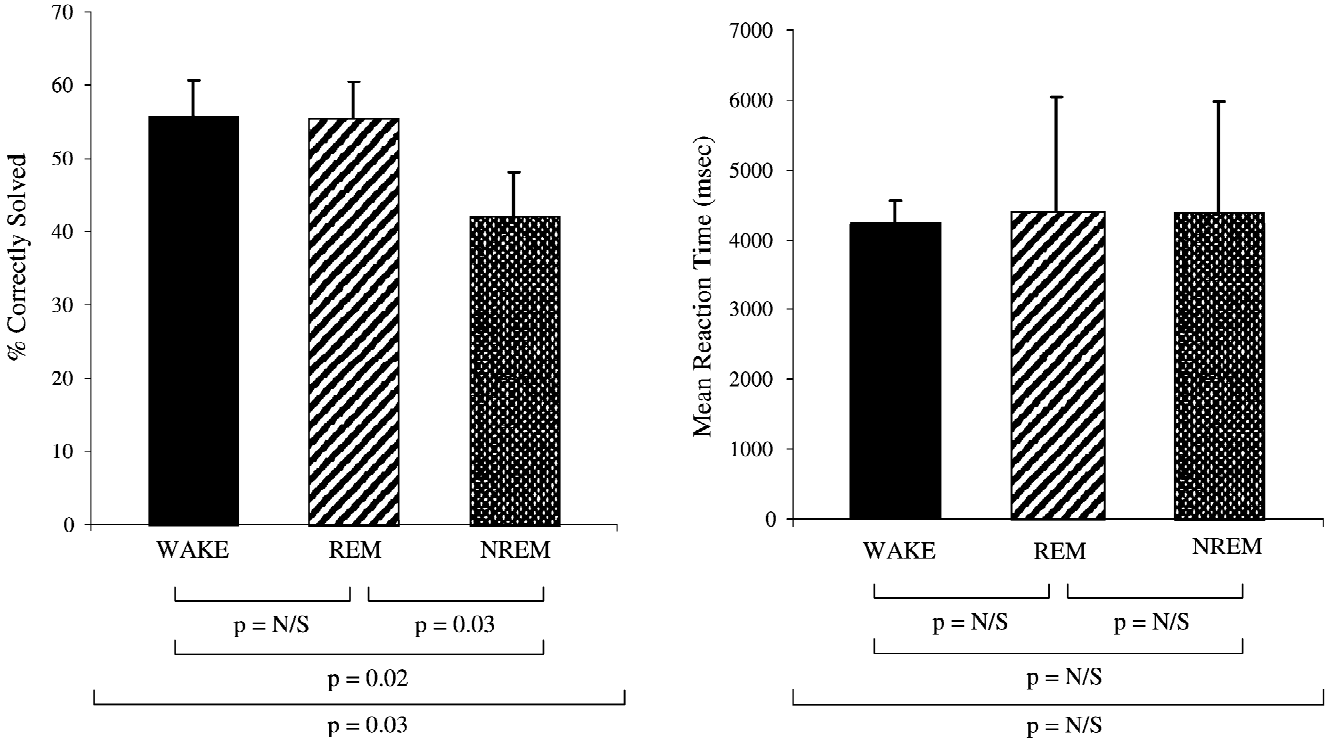

Fig. 2. (a) Mean percentage of anagram puzzles correctly solved in the three experimental conditions of the WAKE, nonREM sleep awakenings (NREM) and REM sleep awakenings (REM), together with standard errors. *P* values for state-specific comparisons are shown underneath the graph. (b) Mean solution reaction times, in milliseconds, for anagrams solved in the three experimental conditions of the WAKE, nonREM sleep awakenings (NREM) and REM sleep awakenings (REM), together with standard errors. *P* values for state-specific comparisons are shown underneath the graph.

sponse. For the WAKE, 58% of anagrams were solved between 0 and 4 s, 26% solved between 4 and 7 s, and 16% solved between 7 and 10 s. For REM awakenings, 61% were solved between 0 and 4 s, 26% solved between 4 and 7 s, and 13% solved between 7 and 10 s, while for NREM awakenings, 62% were solved between 0 and 4 s, 21% solved between 4 and 7 s, and 17% solved between 7 and 10 s. Thus, based on these reaction time distributions, there did not appear to be an effect of general cognitive slowing in either of the sleep conditions. Data for all the above comparisons are shown in Table 3.

Table 3
Anagram task performance across the sleep–wake cycle (see Fig. 1); average percentage of anagram solutions solved (Mean % correct) and the mean solution reaction times for correctly solved anagrams (Mean R.T. (ms)) are presented

Test condition	(*n*)	Mean % correct	Mean R.T. (ms)	Mean S.S.S.
WAKE (averaged)	16	54.6 (±5.0)	4237 (±328)	–
PRE	16	56.2 (±6.6)	3879 (±1552)	3.3
POST	16	53.1 (±5.5)	4594 (±1619)	2.6
NREM	16	42.1 (±6.0)	4612 (±1436)	–
REM	16	55.4 (±4.7)	4374 (±1609)	–
'Early' REM_a	8	56.2 (±7.8)	4134 (±597)	–
'Late' REM_b	8	54.6 (±5.7)	4615 (±1001)	–
'Early' $NREM_b$	8	37.5 (±6.2)	4893 (±1222)	–
'Late' $NREM_a$	8	46.8 (±10.5)	4332 (±1657)	–

S.S.S., Stanford Sleepiness Scale scores; R.T., reaction time in milliseconds; ± values in parentheses represent standard errors.

3.2. State-specific differences in individual performance profiles

Although mean REM and WAKE anagram performance levels were found to be similar, the respective neurophysiological profiles are considerably different. To investigate this result further, the individual anagram scores from the WAKE, REM and NREM awakening tests were compared in a within-subjects correlation, in order to determine if the performance profiles for each subject changed across these different states.

Surprisingly, there was no significant correlation between subjects performance from the WAKE trials and those from the REM awakenings ($r^2(16)=0.17$, $P=0.10$), despite the mean group percentage scores being equal. In contrast, a significant correlation was evident between the WAKE performances and NREM awakening values ($r^2(16)=0.34$, $P=0.01$) while REM awakenings showed only a weak correlation with NREM awakening values ($r^2(16)=0.19$, $P=0.08$). Therefore, similar within-subject performance profiles were apparent between the WAKE and NREM conditions, while relatively different performance profiles were evident following REM awakenings.

3.3. Task performance variation across the night

Both the physiology and phenomenology of REM and NREM sleep vary across the night [26], with late night NREM becoming similar to early night REM [13]. Thus our combining of data from both early and late REM and NREM periods may have obscured additional state-dependent results. We therefore looked at early and late REM–NREM differences across the night.

3.3.1. Percentage solved

The percentage of anagrams solved from early REM_a (2nd REM period) and late REM_b (3rd REM period) were similar at 56 and 54%, respectively (Fig. 3, Table 3). However, the percentage scores from early $NREM_b$ (3rd NREM period) awakenings were lower than from late $NREM_a$ (4th NREM period) awakenings at 37 and 47%, respectively (Fig. 3). Thus, when compared between the balanced groups, there was a non-significant 9% difference between subject performance in 'early' REM_a (2nd REM period; 56%) compared with late $NREM_a$ (4th NREM period; 47%) awakenings (df=7, $t=1.0$, $P=0.3$; Fig. 3). In contrast, there was a significant 17% difference between early $NREM_b$ (3rd NREM period; 37%) and late REM_b (3rd REM period; 54%) awakenings (df=7, $t=2.4$, $P=0.04$). Hence REM awakening performance remained stable across these time points, while NREM performance

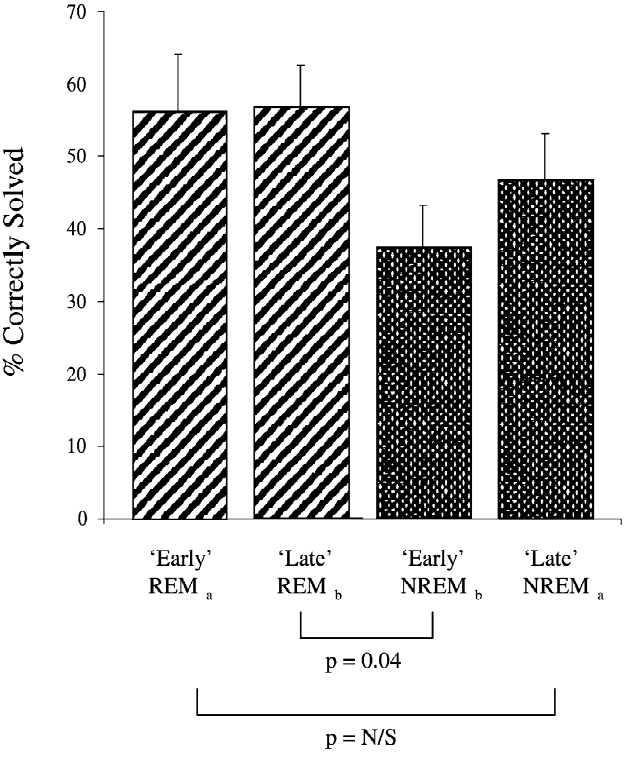

Fig. 3. Mean percentage of anagram puzzles correctly solved from the balanced order awakening protocol early and late into the night, together with standard errors (see Fig. 1 for details). *P* values for state-specific comparisons are shown underneath the graph.

shifted closer to REM values later in the night, and may reflect changes in sleep-stage intensity.

3.3.2. Reaction times

As seen for the overall comparison of REM and NREM, there was no significant differences in mean reaction times in either of the balanced groups (REM_a (4.1 s) vs. $NREM_a$ (4.3 s), df = 7, $t = 0.2$, $P = 0.7$; REM_b (4.6 s) vs. $NREM_b$ (4.7 s), df = 7, $t = 1.2$, $P = 0.2$). Thus the differences in percentages solved across the night do not appear to be due to shifts in general cognitive processing speeds. Data for all the above comparisons are shown in Table 3.

3.4. Sleepiness scales and task performance

Stanford Sleepiness Scale scores (Table 3) obtained before the evening PRE test (10 p.m.) and the morning POST test (8 a.m.) showed no significant correlation with the percentage of anagrams solved or the solution reaction time speeds (percent solved: PRE (10 p.m.) testing $r^2(16) = 0.007$, $P = 0.75$; POST (8 a.m.) testing $r^2(16) = 0.009$, $P = 0.74$; reaction times: PRE (10 p.m.) testing $r^2(16) = 0.02$, $P = 0.57$; POST (8 a.m.) testing $r^2(16) = 0.002$, $P = 0.8$). There was also no significant difference between the PRE and POST Stanford Sleepiness Scale scores (df = 15, $t = 1.7$, $P = 0.1$).

4. Discussion

Problem-solving ability significantly differed across the sleep–wake cycle. Awakenings from REM sleep provided a 32% advantage in the number of anagrams solved compared with the number correctly answered following NREM awakenings. Performance following REM sleep awakenings was equal to that seen in the WAKE test sessions, while the number of puzzles solved following NREM awakenings was significantly less compared with wake. However, no significant differences were observed between the respective mean solution reaction times across all of these conditions.

4.1. Interpretive issues

One might argue that the advantage in performance observed following REM awakenings compared to NREM awakenings is simply due to a difference in the general level of brain activation between these two conditions rather than a specific neurophysiological shift influencing cognitive networks. We consider this unlikely for several reasons. Firstly, the average reaction time, known to be a robust indicator of arousal level [30], did not differ between the WAKE, REM sleep, and NREM sleep awakenings, while the number of anagrams solved was significantly different. Secondly, there was no correlation between the Stanford Sleepiness Scale scores and anagram performance, suggesting that perceived arousal level is also not associated with proficiency on the anagram task. Thirdly, these findings are also consistent with the proposal that awakenings from lighter sleep stages, specifically REM and stage 2 NREM sleep as probed in this study, are related to similar levels of global arousal and such differences in cognitive performance reflect more specific neurophysiological changes in brain functioning [20]. A fourth reason is that the functional brain anatomy of REM sleep, NREM sleep and waking are remarkably different and non-homogenous, hence a view of the sleeping brain being more or less active in REM or NREM sleep is overly simplistic. Fifth, a previous study of semantic priming demonstrated no significant differences in simple reaction times following awakenings from REM and stage 2 NREM sleep, while more complex cognitive processes did differ significantly [35]. Hence it seems more reasonable to conclude that the changes in cognitive flexibility between wake, REM and NREM awakenings are primarily an expression of specific underlying neurophysiological differences between these brain states.

4.2. Methodological issues

Explicit cognitive evaluations in sleep do pose a particularly difficult challenge. Although it is normally impossible to perform cognitive tasks such as these in sleep, one solution to this problem is to administer tests immediately following awakenings from specific sleep states when subjects experience a period of ‘sleep inertia’. Throughout this period, the brain is believed to display similar neurophysiological properties to the prior sleep state from which subjects awoke [11], offering a brief window of time amenable to cognitive testing where some aspects of sleep-related brain physiology remains. While such a paradigm has also been used successfully in a previous study of semantic priming [35], it is not ideal. It should be appreciated that a certain amount of the sleep state properties will have been lost as a consequence of awaking and therefore it is accepted that the true differences between these sleep states could be even more pronounced than evidenced in this paradigm.

4.3. State-specific differences in cognitive flexibility

The contrast in anagram performance between WAKE, REM and NREM suggests that cognitive processing differs in these three brain states, presumably as a consequence of underlying changes in physiology.

The REM performance advantage compared with NREM awakenings is consistent with the hypothesis that the REM sleep state, lacking aminergic dominance, provides a brain medium more conducive to fluid reasoning, and hence better able to perform cognitive tasks requiring flexible thought [2,6–8]. This is congruent with the known shifts in cognitive networks toward activation of weaker

memory associations during REM, a shift that would also favor flexible thought processes [35].

Unexpectedly, REM awakening performance showed no advantage over the WAKE state condition only equivalent levels, even though the changed neuromodulation and associative processing would indicate the potential for improved performance. This may be explained by changes in regional brain activation across the different wake–sleep states. During REM sleep, the dorsolateral prefrontal cortex (DLPFC) is particularly suppressed compared to both waking and NREM sleep [22], and does not return to waking baseline values for up to 15 min after awakening [3]. Furthermore, both imaging and pathological studies indicate the involvement of prefrontal regions in problem-solving tasks during wake [10,15,28,32], although these findings do not specify if prefrontal areas are absolutely required for this function or just preferentially engaged. Nevertheless, such hypo-frontality could explain the lack of advantage that REM awakening performance offered compared with the wake state. It may therefore be surprising that REM awakening test performance even approached waking levels and offered such an advantage over NREM awakenings.

The correlation between the performance profiles in these different brain states offered additional considerations to this theory.

4.4. Dissociating performance profiles

To further investigate the possibility that subjects solved anagrams in a different manner across the three behavioral states, subject's individual anagram performance profiles from REM and NREM were correlated with values obtained from the respective WAKE trials. Despite almost identical group mean percentages of correctly solved anagrams in the WAKE and REM test conditions, a non-significant correlation was evident between the individual subject scores from each of these conditions. In contrast, a significant correlation was found between the performance on WAKE and NREM tests, even though the group mean percentage scores from these two conditions were significantly different. Therefore, REM awakening performance is not as well predicted by WAKE values as is NREM awakening performance.

This finding suggests the possibility of a different mode of problem solving occurring as a consequence of REM sleep physiology, and although potentially different from the WAKE strategy, is still equally as effective. Such a difference is consistent with the contrasting functional anatomy and neurochemistry of REM compared with wake and NREM. Indeed, it may be the prefrontal lobe disconnection during REM that shifts the brain into a more associative state [35], which combined with lowered aminergic modulation, results in a lack of correlation between the WAKE state and REM test performance, despite similar overall scores. Therefore, while one network for problem solving is constrained in REM (prefrontal), another, based on altered neuromodulation, may effectively replace it. While more work is required to test this hypothesis, it is interesting to speculate that access to these alternate methods of fluid reasoning could be sleep specific, and may help explain the creative qualities often assigned to REM-sleep dreaming [8,9,24].

4.5. Shift in NREM performance across the night

Separating anagram data into early and late REM and NREM testing sessions revealed a dissociation in performance across the night. NREM performance underwent a noticeable shift towards improved cognitive flexibility later in the night (Fig. 3). In contrast, the number of puzzles solved following REM awakenings early and late into the night did not appear to change. In this limited sense, it would appear that cognitive flexibility might fluctuate as a function of ultradian sleep state across the night, and while still remaining sleep stage specific, may reflecting changes in the physiological intensity of different REM and NREM periods. This is congruent with recent findings that the frequency of hallucinatory features increases dramatically across the night in NREM but not in REM dreams [13]. Thus the current cognitive findings match previously reported time of night effects seen in both physiological and dream content parameters.

In conclusion, awakenings from REM sleep resulted in a significantly greater number of puzzles solved on a test of cognitive flexibility than seen following awakenings from stage 2 NREM sleep, and were equal to WAKE baseline levels. The advantage offered by REM sleep was independent of reaction times, suggesting a specific effect of underlying neurophysiology, unrelated to basic arousal levels. Unlike NREM performance, individual REM awakening profiles did not correlate significantly with WAKE values. The results support the notion that the neurophysiological state of REM sleep is amenable to improved problem solving compared to NREM sleep, and while equal to that in wake, may be accomplished by a different mechanism. These contrasting profiles can assist in the understanding of certain neurocognitive features associated with REM-sleep dreaming.

Acknowledgements

Prof. David Beversdorf is gratefully acknowledged for providing the anagram lists and corresponding data values from a pervious study. We also wish to thank Roar Fosse and Ed Schott for their constructive comments regarding the manuscript. This research was supported by NIH grants NIMH MH-48832, NIDA DA11744-01A1 and NSF grant BCS-0121953.

References

[1] G. Aston-Jones, F.E. Bloom, Activity of norepinephrine-containing locus coeruleus neurons in behaving rats anticipates fluctuations in the sleep–waking cycle, J. Neurosci. 1 (1981) 876–886.

[2] G. Aston-Jones, J. Rajkowski, J. Cohen, Locus coeruleus and regulation of behavioral flexibility and attention, Prog. Brain Res. 126 (2000) 165–182.

[3] T.J. Balkin, A.R. Braun, N.J. Wesensten, P.B. Varga, R.E. Carson, G. Belenky, P. Herscovitch, Bi-directional changes in regional cerebral blood flow across the first 20 min of wakefulness, Sleep Res. Online 2 (1999) 6.

[4] W.W. Beatty, Memory and 'frontal lobe' dysfunction in multiple sclerosis, J. Neurol. Sci. 115 (Suppl.) (1993) S38–S41.

[5] H. Been, Dreams: the convergence of neurobiologic and psychoanalytic perspectives, J. Am. Acad. Psychoanal. 25 (1997) 639–654.

[6] D.Q. Beversdorf, J.D. Hughes, B.A. Steinberg, L.D. Lewis, K.M. Heilman, Noradrenergic modulation of cognitive flexibility in problem solving, Neuroreport 10 (1999) 2763–2767.

[7] D.M.W. Broome, D.C. Cheever, J.D. Hughs, D.Q. Beversdorf, Effect of central and peripheral beta-adrenergic blockers on noradrenergic modulation of cognitive flexibility, J. Cogn. Neurosci. (2000) 105.

[8] R. Broughton, Human consciousness and sleep/waking rhythms: a review and some neuropsychological considerations, J. Clin. Neuropsychol. 4 (1982) 193–218.

[9] R. Cartwight, Problem solving in REM, NREM and waking (abstract), Am. Psychol. Sleep Soc. 9 (1971) 108.

[10] M.S. Cohen, S.M. Kosslyn, H.C. Breiter, G.J. DiGirolamo, W.L. Thompson, A.K. Anderson, S.Y. Brookheimer, B.R. Rosen, J.W. Belliveau, Changes in cortical activity during mental rotation. A mapping study using functional MRI, Brain 119 (1996) 89–100.

[11] D. Dinges, Are you awake? Cognitive performance and reverie during the hypnopompic state, in: J.S. Kihlstrom (Ed.), Sleep and Cognition, American Psychological Association, Washington, DC, 1990, pp. 159–178.

[12] J. Duncan, A.M. Owen, Common regions of the human frontal lobe recruited by diverse cognitive demands, Trends Neurosci. 23 (2000) 475–483.

[13] R. Fosse, R. Stickgold, J.A. Hobson (Eds.), Reciprocal Variations in Thoughts and Hallucinations Across Wake–Sleep Cycle, Associated Professional Sleep Society, Las Vegas, NV, 2001, p. A178.

[14] R. Gaines, D. Price-Williams, Dream images as a technique for the study of creative processes, Percept. Mot. Skills 70 (1990) 540–542.

[15] K.R. Hanes, D.G. Andrewes, C. Pantelis, Cognitive flexibility and complex integration in Parkinson's disease, Huntington's disease, and schizophrenia, J. Int. Neuropsychol. Soc. 1 (1995) 545–553.

[16] M.E. Hasselmo, C. Linster, M. Patil, D. Ma, M. Cekic, Noradrenergic suppression of synaptic transmission may influence cortical signal-to-noise ratio, J. Neurophysiol. 77 (1997) 3326–3339.

[17] J.A. Hobson, R.W. McCarley, P.W. Wyzinski, Sleep cycle oscillation: reciprocal discharge by two brainstem neuronal groups, Science 189 (1975) 55–58.

[18] J.L. Horn, R.B. Cattell, Refinement and test of the theory of fluid and crystallized intelligence, J. Educ. Psychol. 57 (1966) 253–270.

[19] A. Hubert, Kekulé von Stradonitz, Friedrich August, Macmillan, New York, 1985.

[20] P. Lavie, Y. Matanya, S. Yehuda, Cognitive asymmetries after wakings from REM and NONREM sleep in right-handed females, Int. J. Neurosci. 23 (1984) 111–115.

[21] R. Lydic, H.A. Baghdoyan, Handbook of Behavioral State Control: Cellular and Molecular Mechanisms, CRC Press, Boca Raton, FL, 1988, pp. 688.

[22] P. Maquet, Functional neuroimaging of normal human sleep by positron emission tomography, J. Sleep Res. 9 (2000) 207–231.

[23] F. Marrosu, C. Portas, M.S. Mascia, M.A. Casu, M. Fa, M. Giagheddu, A. Imperato, G.L. Gessa, Microdialysis measurement of cortical and hippocampal acetylcholine release during sleep–wake cycle in freely moving cats, Brain Res. 671 (1995) 329–332.

[24] P. Mazzarello, What dreams may come?, Nature 408 (2000) 523.

[25] T.A. Nielsen, Mentation during sleep: the NREM/REM distinction, in: R. Lydic, H.A. Baghdoyan (Eds.), Handbook of Behavioral State Control: Cellular and Molecular Mechanisms, CRC Press, Boca Raton, FL, 1999, pp. 101–128.

[26] T.A. Nielsen, A review of mentation in REM and NREM sleep: 'covert' REM sleep as a possible reconciliation of two opposing models, Behav. Brain Sci. 23 (2000) 851–866, discussion 904–1121.

[27] O.A. Parsons, S.J. Nixon, Neurobehavioral sequelae of alcoholism, Neurol. Clin. 11 (1993) 205–218.

[28] V. Prabhakaran, J.A. Smith, J.E. Desmond, G.H. Glover, J.D. Gabrieli, Neural substrates of fluid reasoning: an fMRI study of neocortical activation during performance of the Raven's Progressive Matrices Test, Cogn. Psychol. 33 (1997) 43–63.

[29] A. Rechtschaffen, A. Kales, A manual standardized terminology, techniques and scoring system for sleep stages of human subjects, U.S. Department of Health, Bethesda, MD, 1968.

[30] I. Reinvang, Validation of reaction time in continuous performance tasks as an index of attention by electrophysicological measures, J. Clin. Exp. Neuropsychol. 20 (1998) 885–897.

[31] A. Revonsuo, The reinterpretation of dreams: an evolutionary hypothesis of the function of dreaming, Behav. Brain Sci. 23 (2000) 877–901, discussion 904–1121.

[32] F. Schneider, R.E. Gur, A. Alavi, M.E. Seligman, L.H. Mozley, R.J. Smith, P.D. Mozley, R.C. Gur, Cerebral blood flow changes in limbic regions induced by unsolvable anagram tasks, Am. J. Psychiatry 153 (1996) 206–212.

[33] K. Shima, H. Nakahama, M. Yamamoto, Firing properties of two types of nucleus raphe dorsalis neurons during the sleep–waking cycle and their responses to sensory stimuli, Brain Res. 399 (1986) 317–326.

[34] C. Spearman, General Intelligence, Objectively Determined and Measured, 1904.

[35] R. Stickgold, L. Scott, C. Rittenhouse, J.A. Hobson, Sleep-induced changes in associative memory, J. Cogn. Neurosci. 11 (1999) 182–193.

[36] P. Strathern, Mendeleyev's Dream: The Quest for the Elements, Hamish Hamilton, London, 2000.

[37] P. Toren, M. Sadeh, L. Wolmer, S. Eldar, S. Koren, R. Weizman, N. Laor, Neurocognitive correlates of anxiety disorders in children: a preliminary report, J. Anxiety Disord. 14 (2000) 239–247.

[38] D.R. Weinberger, M.S. Aloia, T.E. Goldberg, K.F. Berman, The frontal lobes and schizophrenia, J. Neuropsychiatry Clin. Neurosci. 6 (1994) 419–427.