

Research report

Theta synchronization during episodic retrieval: neural correlates of conscious awareness

W. Klimesch^{a,*}, M. Doppelmayr^a, A. Yonelinas^b, N.E.A. Kroll^b, M. Lazzara^b, D. Röhme^a,
W. Gruber^a

^aDepartment of Physiological Psychology, Institute of Psychology, University of Salzburg, Hellbrunnerstr. 34, A-5020 Salzburg, Austria

^bDepartment of Psychology, University of California, Davis, USA

Accepted 30 January 2001

Abstract

The neural correlates of conscious awareness during successful memory retrieval were examined. In a recognition test, subjects indicated whether they consciously recollected the event in which a word was earlier presented (Remembering), or whether they recognized it on the basis that it was familiar in the absence of recollection (Knowing). An early EEG synchronization in the theta band predicted knowing, and a later remembering. Moreover, early and late event-related potentials were also found to predict knowing and remembering, respectively. The results indicate that the temporal dynamics of theta synchronization are related to the particular conscious experiences associated with memory retrieval. © 2001 Elsevier Science B.V. All rights reserved.

Keywords: Theta; Memory; Consciousness; ERP; ERD

1. Introduction

The search for neural correlates of conscious experience represents one of the most challenging questions in cognitive neuroscience. One common approach is to use neuroimaging methods like positron emission tomography to identify the brain regions that are activated when subjects report specific conscious experiences such as detecting an object or recalling a previous event [6]. These methods have been useful in identifying the brain regions that are associated with consciousness. However, because of limitations in temporal sensitivity, these techniques have provided very little information about the temporal dynamics of the relevant cortical activation. In the current study, we take an alternative approach and measure scalp EEGs in order to examine the temporal dynamics of widespread neural synchronization in the theta bandwidth that is associated with the conscious experience of memory retrieval.

Animal research has provided good evidence that the amplitudes (power) of theta oscillations in the hippocampal

region increase during exploratory behavior and orienting responses [16], but are virtually absent during automatic behaviors, such as eating or drinking. Furthermore, theta oscillations can be observed during REM-sleep where dreaming episodes occur [21]. These findings provide preliminary evidence for the hypothesis that an increase in theta activity is related to states of increased awareness or to an altered state of awareness as indicated by increased theta during dreaming episodes. Moreover, there is convincing evidence that an increase in hippocampal theta is related to the encoding and retrieval of new episodic information [8]. In human subjects, lesions of the medial temporal lobe, including the hippocampus, are known to cause a loss of the capacity for conscious recollection of new events [4,15,23]. These findings suggest that hippocampal theta is a promising neural correlate of conscious awareness in memory. Although it has been questioned for a long time, there is meanwhile converging evidence that theta oscillations can also be observed in humans. This evidence comes from studies with patients using depth [2] and subdural [10] electrodes as well as from studies with normal subjects using scalp electrodes [7] and the MEG [19].

Results from our laboratory have shown that in human scalp EEG, theta responds selectively (with an increase in

*Corresponding author. Tel.: +43-662-8044-5120 or 5100; fax: +43-662-8044-5126.

E-mail address: wolfgang.klimesch@sbg.ac.at (W. Klimesch).

band power) to the encoding and retrieval of episodic information [11,12]. These findings are in accord with the hypothesis that episodic processes are reflected by theta oscillations in hippocampo-cortical reentrant loops. However, no studies have yet been carried out to demonstrate a functional relationship between theta activity and conscious awareness in memory.

In the present study, we utilized the remember/know paradigm to separate different forms of conscious awareness during retrieval [20]. In the first phase of this procedure, subjects are exposed to a series of ‘miniature events’: discrete visual or auditory items appearing one at a time for a few seconds each. In the second phase, subjects are presented with both target (old, previously encountered) and distractor (new, not previously encountered) items, and asked to assign each such test item to one of three mutually exclusive experiential categories: (i) they recollect the event of the item’s presentation in the study list (remembering), (ii) they know the item was in the study list on the basis that it is familiar, but not recollected (knowing), (iii) they have no awareness that the item was presented in the earlier list (unawareness of the past) and, thus, give a ‘new’ response. The aim was to determine whether the conscious experiences of remembering and knowing were associated with theta, and to examine the time course of those neural responses. Because event-related potentials (ERPs) have already been used to study the neural correlates of conscious awareness during retrieval [5], an additional aim is to compare the theta with the ERP response.

ERP studies indicate that voltages recorded over central and parietal sites are more positive for targets than for distractors [17]. In those ERP-studies where subjects had to differentiate between ‘remembered’ words from those they ‘know’ to be old, this old/new effect was larger for remembered than for known items [5,17]. There is evidence that the medial temporal lobe (with the hippocampal formation as a crucial component of the distributed limbic-cortical network), contributes to the generation of the ERP old/new effect [9]. In a recent study using a standard recognition paradigm, we have found that the ERP old/new effect and a significant increase in theta power occur within the same time window [14]. Thus, we have to expect that a significant increase in theta power occurs within the time window of the ERP old/new effect.

2. Materials and methods

2.1. Subjects

After informed consent, a sample of 13 right-handed students (3 males, 10 females) participated voluntarily in the present experiment. Their mean age was 23.5 years with a range of 20–38 years.

2.2. Materials

A set of 260 familiar words (120 targets, 120 distractors and 20 ‘training’ words) was used as stimuli. They were controlled for word length (number of syllables), familiarity and word frequency.

2.3. Design

The recognition task was preceded by an incidental study task where subjects had to count syllables for 120 words. An incidental study task was used to increase the probability of know judgments. Without prior warning, subjects were then asked to recognize the previously presented target words. They were instructed to respond ‘remember’ if the word is accompanied by the conscious recollection of its prior occurrence or ‘know’ when a word was presented, but failed to evoke any specific conscious recollection from the study list. A ‘new’ judgment should be made if subjects believe the word was not presented at all, earlier in the list.

2.4. Procedure

As schematically depicted in the upper part of Fig. 1, a single trial consisted of the following sequence: a blank interval of 1.5 s, the presentation of a warning tone (0.25 s), a blank interval of 1.25 s, the presentation of a word (0.5 s), a blank interval of 1 s, the presentation of a question mark (2 s), which served as response signal, and a blank interval of 1.75 s. The 120 target and 120 new (distractor) words were presented on a computer monitor in randomized order.

2.4.1. Apparatus

EEG-signals were amplified by a 32-channel biosignal amplifier system (frequency response: 0.16–30 Hz), subjected to an anti-aliasing filterbank (cut-off frequency: 30 Hz, 110 dB/octave) and were then converted to a digital format. Sampling rate was 128 Hz.

2.4.2. EEG Recording

A set of 25 silver electrodes were placed according to the International Electrode (10–20) Placement-system, at F3, F4, Fz, FC1, FC2, FC5, FC6, C3, C4, Cz, T3, T4, CP1, CP2, CP5, CP6, P3, P4, Pz, PO1, PO2, PO3, PO4, O1 and O2. In addition, two earlobe electrodes were attached to the left and right ear. Data were recorded against a common reference placed on the nose and off-line algebraically re-referenced to linked earlobes. The Electrooculogram (EOG) was recorded from 2 pairs of leads in order to register horizontal and vertical eye movements. All epochs were carefully checked individually for artifacts. After rejecting artifacts and erroneous trials, an average of 66 epochs remained for correctly identified targets (35 for ‘remembering’; 31 for ‘knowing’) and 48

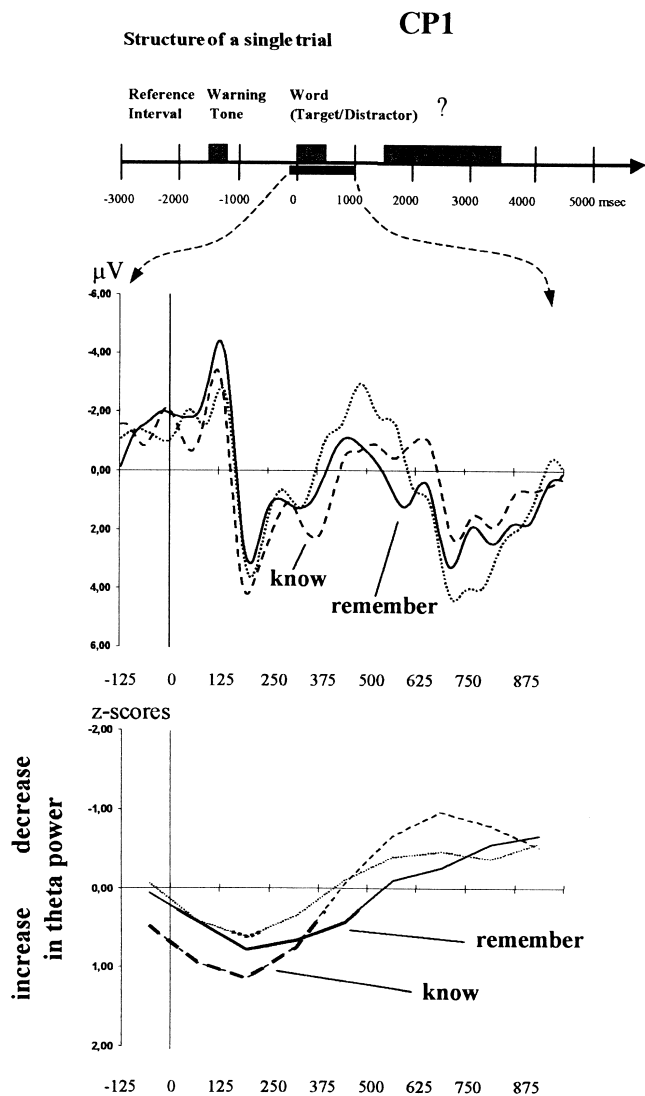


Fig. 1. Time course of a single trial, ERP and theta ERBP at CP1 for the three response types (remember and know responses to target items, and new responses to distractor items). The time course of event related theta band power (transformed to z-values) is shown below the respective ERP. Extra bold lines indicate the limits of 99.99% confidence intervals with respect to a reference interval ('baseline') at the beginning of each trial. Remembered items are represented by bold lines, known items by dashed, and new items by dotted lines.

epochs for correct rejections. For false alarms and incorrectly identified distractors, 11 and 26 epochs remained. Statistical analyses were carried out only for hits and correct rejections.

2.4.3. The calculation of event-related band power (ERBP) and event-related potentials (ERPs)

Because we have shown repeatedly that the use of fixed frequency bands leads to distorted results we define frequency bands individually by using individual alpha frequency IAF(*i*) as cut off point, for 5 bands of 2 Hz each. We distinguish between an upper alpha band (falling above IAF(*i*)), two lower alpha bands (termed lower-1 and

lower-2 alpha), a theta and delta band (falling below IAF(*i*) in consecutive steps of 2 Hz). Averaged over the sample of subjects, alpha frequency was 10.63 Hz. The standard deviation was 0.8 Hz.

It should be noted that all frequency bands are adjusted to IAF. Because the present study focuses on theta, it might be objected that adjusting the theta band to individual alpha frequency is an unnecessary or even questionable method. However, when measuring that frequency in the power spectra which marks the transition from theta synchronization to alpha desynchronization we have found (cf. the review in [11]) that this 'transition frequency' (TF) — which is considered the boundary between theta and lower alpha — is significantly correlated with alpha peak frequency. This finding indicates that theta frequency (as measured by TF) varies as a function of alpha frequency and suggests the use of alpha frequency as a common reference point for adjusting different frequency bands not only for the alpha, but theta range as well.

The steps for calculating ERBP are the following [13]. First, over the entire length of the experimental session, the EEG data are band pass filtered and then the filtered data are squared. Second, the obtained data are averaged over the number of artifact free epochs. Third, within consecutive time windows of 125 ms the squared data are averaged. Starting with presentation onset for a word, these time windows are termed $t_1, t_2 \dots t_8$. Fourth, z-values were computed for each subject, recording site and experimental condition. In addition to the standard ERPs we calculated theta ERPs from the band pass filtered data in calculation step 1. For each sample point i of the band pass filtered data, the mean $\mu(i)$ — representing the filtered ERP — is calculated over the respective epochs for each electrode site, experimental condition and subject. Standard ERPs were averaged stimulus synchronized and for a time interval of 125 ms preceding the onset of a word and 1000 ms following the onset of a word.

2.4.4. Statistical analyses

For the ERPs, the time interval in which recognition positivity occurred was determined. Within this time interval two different components with maximal positive components, an early (for the know response) and a late component (for the remember response) were determined. The amplitudes of these components were used as the dependent measures for a series of one-way ANOVA's with factor MEMORY (remember, know, new). These ANOVA's were calculated for each of the 25 recording sites.

For ERBP, confidence intervals were calculated to determine that time period, where a significant increase in band power occurs with respect to a reference period (defined as the interval of 0–1000 ms at the beginning of each epoch). Over the sample of subjects the means and standard deviations (for each lead and experimental condition) of the respective values of these reference periods

were used for the calculation of 99.99% confidence intervals.

In order to test whether the order of the strength of amplitudes (for ERPs and ERBP) for a know-remember-and new-response is similar between recording sites, a series of χ^2 -tests was performed. The order of the strength of ERP or ERBP amplitudes is coded by a sequence of letters, such as 'krn' (i.e., 'know' greater than 'remember' greater than 'new').

3. Results

Analysis of the behavioral data showed that our sample of 13 subjects performed quite well. From the 120 targets, 43% were judged 'remembered' and 41% 'known'. Of the 120 distractors, 63.5% were correctly judged new (3.5% were judged 'remembered' and 31.0% 'known').

The ERP's indicate that within the time window of recognition positivity (of about 300–625 ms), two pronounced positive ERP components can be observed for old items. As an example, the ERP (averaged over the sample of 13 subjects) is shown for recording site CP1 in Fig. 1. Averaged over all respective sites, the early component which is maximal for 'know' items peaks at 356.5 ms, whereas the late component, which is maximal for 'remember' items peaks at 591.3 ms. The ERPs for known, remembered, and new judgments are significantly different from each other (at the respective peaks) for 13 out of the 25 recorded sites for the early component, and for 17 sites for the late component (one-way ANOVA's (2,24); $P < 0.05$). At these sites the order of the strength of amplitudes is krn (i.e., 'know' greater than remember' greater than 'new') for the early and rnk for the late component (with the exception of 3 locations, O1, O2 and Pz, where the ordering is rkn). With respect to topography it is important to note that only at centroparietal and parietal sites (CP1,

CP2, P3, P4) did both the early and late component show significant effects over both hemispheres.

Analysis of the EEG theta band reveals that at all but one site (correct new judgments at CP5), a significant increase in theta power for correct remember, know, and new judgments was found. The findings for the centroparietal site CP1 (grand average over all subjects) are plotted in Fig. 1 (positive z-values reflecting an increase in power are scaled downwards; cf. the Method section). The onset and duration of theta synchronization, however, is different for the three response types. At all of the 25 sites, the duration of synchronization was shortest for new items ($\chi^2(1)=25$; $P < 0.001$), and at 21 sites, remembered items show the longest duration ($\chi^2(1)=11.56$; $P < 0.001$). Moreover, at 15 sites, significant increases in theta synchronization were observed for the know items before the remember items ($\chi^2(1)=1$; n.s.).

During the early post-stimulus interval, 'known' words show the largest increase in theta band power, whereas during a later period (particularly in interval t5, 500–625 ms) 'remembered' words show the largest amount of theta power. Time interval t3 (250–375) corresponds to the early ERP component, whereas t5 (500–625) corresponds to the late component. As with the ERP's, during the early interval (t3), the most frequent ordering is krn (13 from 25 locations; $\chi^2(5)=22.59$; $P < 0.001$) and for the late interval (t5) the most frequent ordering is rnk (19 from 25 locations, $\chi^2(5)=64.6$; $P < 0.001$).

Thus, the time course of theta ERBP and ERP reveals an interesting convergence. For a better comparison, the sequence of the ordering of the relative magnitude of response type was determined for ERBP in the same way as for the ERP's. The respective results are summarized in Table 1 and show that during the time interval of the early ERP-component, t3, the 'know' response is more positive in ERPs and exhibits larger theta power at 16 of the 25 locations. From these 16 locations 13 show the sequence krn. If for the ERP's and ERBP's the 6 possible sequences

Table 1

A comparison of ERP's at mean peak latency of the early (356.5 ms) and late component (591.3 ms) with theta ERBP at t3 (250–375 ms) and t5 (500–625 ms). The order of the strength of amplitudes or power of a remember-, know-, or new-response is coded by the sequence of the letters r', k', n'

Lead	Left hemi				Right hemi				Midline			
	t3		t5		t3		t5		t3		t5	
	ERP	ERBP	ERP	ERBP	ERP	ERBP	ERP	ERBP	ERP	ERBP	ERP	ERBP
F3/4/z	krn	rkn	rnk	rkn	krn	rkn	rnk	rnk	krn	krn	rnk	rnk
FC1/2	krn	krn	rnk	rkn	krn	rkn	rnk	rnk				
FC5/6	krn	nkr	–	krn	knr	rkn	–	rnk				
C3/4/z	krn	rkn	rnk	rnk	knr	krn	rnk	rnk	krn	rkn	rnk	rnk
CP1/2	krn	krn	rnk	rnk	krn	krn	rnk	rnk				
CP5/6	krn	rnk	rnk	rnk	krn	knr	rnk	nrk				
T3/4	–	krn	–	rkn		nrk		rnk				
P3/4/z	krn	krn	rnk	rnk	krn	krn	rnk	rnk	krn	krn	rkn	rnk
PO1/2	knr	krn	rnk	rnk	krn	krn	rnk	rnk				
PO3/4	knr	knr	rnk	rnk	nkr	krn	rnk	rnk				
O1/2	rkn	knr	rkn	rnk	rnk	krn	rkn	rnk				

(knr, krn, nkr, nrk, rkn, rnk) would combine by chance, we would obtain 36 different cases ($P=0.028$; expected frequency=0.7). For the eight combined cases of krn during t3 (cf. Table 1), the respective χ^2 -test yields a highly significant effect ($\chi^2(35)=78.32$; $P<0.001$). During interval t5 (the late component), for 16 of the 25 locations the ERBP shows the sequence rnk. For the 14 combined cases of krn, the respective χ^2 -test yields a highly significant result ($\chi^2(35)=259.97$; $P<0.001$). With respect to topography, a perfect match for both, the ordering of the early and late component in the left and right hemisphere was found at centro-parietal regions (CP1, CP2, P3 and P4).

For CP1, a comparison of the standard ERP and the theta ERP reflecting evoked theta activity is depicted in Fig. 2. It is interesting to note that ERP peaks show a close relation to the positive and negative peaks of evoked theta activity which is particularly strong for the know response

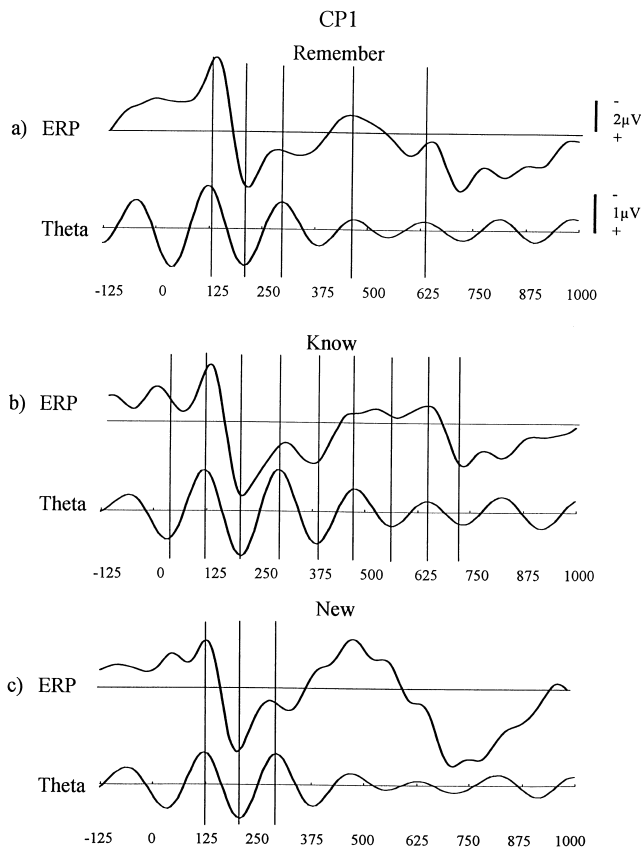


Fig. 2. A comparison of the standard ERP and the theta ERP at CP1 for the remember (a), know (b) and new response (c). Note that ERP peaks show a close relation to the positive and negative peaks of evoked theta activity (of about 4.6–6.6 Hz) which is particularly strong for the know response. Vertical lines connecting the standard and theta ERP indicate cases where ERP peaks show an obvious correspondence with evoked theta. CP1 was selected because it is one of those sites that exhibit a close association between an increase in theta ERBP and the occurrence of the early and late ERP component for the know and remember response respectively (cf. Table 1).

(cf. the vertical lines in Fig. 2 connecting the standard and theta ERP).

The analyses of delta and alpha bands show a completely different pattern of results. With a single exception (lower-1 alpha band during t5), only the theta band produces a highly significant deviation from a random distribution (with respect to the 6 possible sequences: knr, krn, nkr, nrk, rkn, rnk). For the lower-1 alpha band, significant effects were obtained for the frequent cases krn ($\chi^2(5)=23.41$; $P<0.001$) and rkn ($\chi^2(5)=24.38$; $P<0.001$) which were found during t5.

4. Discussion

The results of the present study demonstrate that two different physiological correlates can be distinguished for remembering and knowing. During an early retrieval period (of about 300–450 ms), knowing (as compared to remembering) is associated with larger theta power and ERP positivity; whereas during a later period (450–625 ms), remembering is associated with larger theta power and ERP positivity. Furthermore, the significant theta synchronization was observed earlier for knowing than for remembering, yet the duration of theta was longer for remembered than for knowing.

The increase in theta associated with both the remembering and knowing responses indicates that these two types of conscious experience were preceded by massive but cortically widespread synchronized neural firing. Fig. 2 shows that the increase in theta activity can already be observed in the form of evoked theta activity that is evident even in the standard ERP components. This finding is consistent with an interesting coherence study which indicates that working memory processes are reflected by phase locked theta activity [18]. Moreover, that the onset and duration of the respective periods of theta differed indicates that the temporal dynamics of the neural synchronization plays an important role in the experiential characteristics associated with memory retrieval. The results are consistent with behavioral data indicating that recognition memory judgments based on familiarity can be made more rapidly than those requiring recollection of qualitative event information [22]. They are also consistent with ERP results indicating early and late components associated with familiarity and recollection respectively [5].

In conclusion, the results indicate that conscious retrieval associated with both remembering and knowing were preceded by an increase in theta synchronization. This interpretation is in line with findings that indicate that familiarity judgments do not depend on the hippocampal system but instead on a distinct system involving the perirhinal cortex and the medial dorsal nucleus of the thalamus [1]. Nonetheless, this latter brain circuit may very well constitute an important ‘input’ component of the

‘theta system’ because it is well known that theta oscillations can be observed in the entorhinal cortex [3] and in the anterior thalamus as well.

Finally, it should be noted that our findings do not show a simple relationship between states of increased awareness (during remembering) and an increase in the strength of theta activity. Nonetheless, the reported findings support the hypothesis that a late or prolonged increase in the duration of theta activity is related to states of increased conscious awareness. We speculate that the late increase in theta during the remember response (cf. Table 1) is related to theta oscillations in complex hippocampo-cortical reentrant loops. The early increase in theta during the know response may reflect theta oscillations in a distinct system involving the perirhinal cortex and the medial dorsal nucleus of the thalamus [1]. Whatever the correct interpretation, the present data demonstrate that even in the human scalp EEG, memory processes are reflected by theta oscillations in a similar way as was found in animal research.

Acknowledgements

This research was supported by the Austrian ‘Fonds zur Förderung der wissenschaftlichen Forschung’, Project P-13047.

References

- [1] J.P. Aggleton, M.W. Brown, Episodic memory, amnesia and the hippocampal anterior thalamic axis, *Behav. Brain Sci.* 22 (1999) 425–489.
- [2] D.E.A.T. Arnolds, F.H. Lopes Da Silva, J.W. Aitnik, W. Boeijinga, The spectral properties of hippocampal EEG related to behaviour in man, *Electroencephalogr. Clin. Neurophysiol.* 50 (1980) 324–328.
- [3] G. Buzsaki, The hippocampo-neocortical dialogue, *Cereb. Cortex* 6 (1996) 81–92.
- [4] N.J. Cohen, L.R. Squire, Preserved learning and attention of a pattern-analyzing skill in amnesia: dissociation of knowing how and knowing that, *Science* 210 (1980) 207–210.
- [5] E. Düzel, A.P. Yonelinas, G.R. Mangun, H.J. Heinze, E. Tulving, Event-related potential correlates of two states of conscious awareness in memory, *Proc. Natl. Acad. Sci.* 94 (1997) 5973–5978.
- [6] D.H. Ffytche, R. J Howard, M.J. Brammer, A. David, P. Woodruff, S. Williams, The anatomy of conscious vision: an fMRI study of visual hallucinations, *Nat. Neurosci.* 1 (1998) 738–742.
- [7] A. Gevins, M.E. Smith, L. McEvoy, D. Yu, High-resolution EEG mapping of cortical activation related to working memory: effects of task difficulty, type of processing, and practice, *Cereb. Cortex* 7 (1997) 374–385.
- [8] B. Givens, Stimulus-evoked resetting of the dentate theta rhythm: relation to working memory, *NeuroReport* 8 (1996) 159–163.
- [9] T. Grunwald, K. Lehnertz, C. Helmstädter, M. Kutas, N. Pezer, M. Kurthen, D. Van Roost, C.E. Elger, Limbic ERPs predict verbal memory after left-sided hippocampectomy, *NeuroReport* 9 (1998) 3375–3378.
- [10] M.J. Kahana, R. Sekuler, J.B. Caplan, M. Kirschen, J.R. Madsen, Human theta oscillations exhibit task dependence during virtual maze navigation, *Nature* 399 (1999) 781–784.
- [11] W. Klimesch, EEG alpha and theta oscillations reflect cognitive and memory performance: a review and analysis, *Brain Res. Rev.* 29 (1999) 169–195.
- [12] W. Klimesch, H. Schimke, J. Schwaiger, Episodic and semantic memory: an analysis in the EEG-theta and alpha band, *Electroencephalogr. Clin. Neurophysiol.* 91 (1994) 428–441.
- [13] W. Klimesch, H. Russegger, M. Doppelmayr, T. Pachinger, A method for the calculation of induced band power: Implications for the significance of brain oscillations, *Electroencephalogr. Clin. Neurophysiol.* 108 (1998) 123–130.
- [14] W. Klimesch, M. Doppelmayr, J. Schwaiger, T. Winkler, W. Gruber, Theta oscillations and the ERP old/new effect: independent phenomena?, *Clin. Neurophysiol.* 111 (2000) 781–793.
- [15] N.E.A. Kroll, R.T. Knight, J. Metcalfe, E.S. Wolf, E. Tulving, Cohesion failure as a source of memory illusions, *J. Mem. Lang.* 35 (1996) 176–196.
- [16] J. O’Keefe, N. Burgess, Theta activity, virtual navigation and the human hippocampus, *Trends Cogn. Sci.* 3 (1999) 403–406.
- [17] M.D. Rugg, A.M. Schloerscheidt, R.E.J. Mark, An electrophysiological comparison of two indices of recollection, *Mem. Lang.* 39 (1998) 47–69.
- [18] J. Sarnthein, H. Petsche, P. Rappelsberger, G.L. Shaw, A. von Stein, Synchronization between prefrontal and posterior association cortex during human working memory, *Proc. Natl. Acad. Sci. U.S.A.* 95 (1998) 7092–7096.
- [19] C.D. Tesche, J. Karhu, Theta oscillations index human hippocampal activation during a working memory task, *Proc. Natl. Acad. Sci. U.S.A.* 97 (2000) 919–924.
- [20] E. Tulving, Memory and Consciousness, *Can. Psychol.* 25 (1985) 1–12.
- [21] J. Winson, The meaning of dreams, *Sci. Am.* 263 (1990) 42–48.
- [22] A.P. Yonelinas, L.L. Jacoby, The relation between remembering and knowing as basis for recognition: effects of size congruency, *J. Exp. Mem. Lang.* 34 (1995) 622–643.
- [23] A.P. Yonelinas, N.E.A. Kroll, I.G. Dobbins, M. Lazzara, Recollection and familiarity deficits in amnesia: convergence of remember/know, process dissociation, and ROC data, *Neuropsychology* 12 (1998) 1–17.