

Binding processes affect brain potentials and oscillations at multiple levels

Niko A. Busch, Jeanette Schadow & Christoph S. Herrmann

Otto-von-Guericke-University, Magdeburg, Germany

Department of Psychology

P.O. Box 4120

39016 Magdeburg

Tel.: 0049 391 6711969

Fax.: 0049 391 6711947

Email : niko.busch@nat.uni-magdeburg.de

When the brain perceives the outside world, it decomposes objects into parts, which are represented in different areas of the brain. In order for us to perceive whole objects, so-called binding processes need to bind together those parts, which belong to the same objects. Some of these binding processes operate in a bottom-up fashion, i.e. binding together the information from neurons in early visual cortices which code elementary features of visual objects. However, every perception is guided by memory, which implies that we compare every perception to previously perceived objects in our memory. This represents a top-down mechanism, which guides the binding processes. In a series of three experiments we were able to demonstrate that bottom-up as well as top-down binding processes are reflected in certain brain responses. In a first experiment, subjects had to discriminate between circles and squares, which were presented in three different sizes. In order to bind together all neurons, which are excited by a large object, binding mechanisms need to bind over a larger cortical area due to the retinotopic representation. It has been shown that binding processes operate at frequencies in the gamma frequency range (30-80 Hz) and that long-range interactions are usually reflected in lower frequencies than short-range interactions. In line with these findings, we could show that large objects evoke oscillations with lower frequencies than do small stimuli. Thus the frequency represents the range over which this bottom-up mechanism binds. In a second experiment, we differentiated between feature-load and object-load in a delayed matching-to-sample task and showed that both loads affect specific brain potentials during different stages of processing. Especially during the retention period, stimuli were maintained as bound objects and feature-load had no effect on brain responses. In a final experiment, we were able to show that stimuli for which subjects already had a representation in their long-term memory evoked significantly larger gamma responses than unknown stimuli reflecting the top-down process of binding perceptions to memory.

Overview

Almost every cognitive or perceptual process involves activity in a large and distributed neural network. The question arises of how these subprocesses are combined and integrated. In the visual domain this question has been termed the "binding problem". Nelson formulated it this way: "The problem with visual cortex areas is that there are so many of them" (Nelson, 1995). A visual scene usually contains a multitude of objects, which are coded by a large amount of neurons each. How are neurons coding the same object bound together to form a neuronal assembly and how are assemblies coding different objects discriminated from each other? A related binding problem occurs when objects differ on several dimensions (e.g. color and shape). Different stimulus dimensions are known to be coded in anatomically different areas of the visual system. How are stimulus features belonging to the same object bound together? Of course, the visual system is confronted with the binding problem not only during perception, but also when visual information is to be remembered. In the field of memory research, the concept of binding has been employed also with a slightly different comprehension. If an episode is to be remembered, different aspects of that episode (such as the time, context, place and so forth) have to be bound together to form a memory. Later on, binding can occur between memory representations and perception, e.g. when looking at a person's face to find out whether you know it or not. In a series of three experiments binding processes at several stages of processing were investigated: binding of neuronal assemblies, feature binding in visual short-term memory, and binding of visual perception and memory representation.

Binding phenomena of various kinds have been investigated with electrophysiological recordings in both animals and humans. The majority of these experiments employed some kind of frequency analysis of the recorded signal. Regarding human EEG, there has been a growing interest in recent years to complement the classical analysis of EEG and event related potentials (ERPs) with various approaches of analysis in the frequency domain (Engel, Fries & Singer, 2001; Jung et al., 2001; Pfurtscheller & Lopes da Silva, 1999). The EEG frequency spectrum is usually subdivided into different frequency bands. Although the denotation of frequency bands is by no means standardized throughout the EEG literature, a common terminology includes the delta (<3 Hz), theta (4-8 Hz), alpha (8-12 Hz), beta (13-20 Hz), and gamma (30-80 Hz) bands. Regarding oscillatory activity, it is important to distinguish between evoked and induced oscillations since they are assumed to reflect different processes. Evoked oscillations exhibit a strict phase-locking to the experimental event (e.g. stimulus presentation) across trials. Hence, they can be extracted from the ERP, e.g. by filtering. Induced oscillations, on the other hand, show a certain degree of phase-jittering. Therefore, by averaging across trials these oscillations may cancel out completely and hence are only detectable by appropriate ways of analysis, e.g. by a single-trial based wavelet analysis. The wavelet transform can be thought of as the envelope of the bandpass-filtered ERP. The wavelet transform is advantageous over the FFT, since the time course of frequency information can be observed. While this is also true for the filtered signal, the wavelet transform yields directly the amplitude and the phase of the signal oscillations in the analyzed frequency band when a complex wavelet function is used.

Binding across neurons

Introduction

High frequency oscillations in the gamma-band have been investigated in numerous experiments in humans and animals (Keil, Gruber & Müller, 2001; Sannita, 2000; Tallon-Baudry & Bertrand, 1999).

Although discovered as early as 1942 (Adrian, 1942) the current interest in gamma oscillations was fostered by experiments on the anesthetized cat in the late 1980's (Eckhorn et al., 1988; Gray, König, Engel & Singer, 1989). These studies showed that neurons in the cat visual cortex respond strongly synchronized within the 20–80 Hz frequency range when bars were passed across the receptive fields in the same direction compared to bars moving in different directions. The authors concluded that synchronized gamma activity could “bind together” separate features of an object. This finding was incorporated in the hypothesis of “binding by synchrony”. Briefly, this hypothesis states that neurons are bound into a neuronal assembly by synchronization of their activity. Thus, neurons belonging to the same assembly fire at the same time while neurons belonging to a different assembly are active at different times. This idea, which was also termed the „temporal correlation hypothesis“ (Singer & Gray, 1995), has been extensively studied in recent years and is supported by numerous studies (Engel et al., 2001; Singer, 1993). It is obvious that binding by temporal correlation requires a high degree of temporal precision. If the “membership” in an assembly were coded by temporal similarity, neurons, which do not tune their activity to the rhythm of the assembly, would be interpreted as not belonging to the assembly. In the worst case they might even erroneously become a member of a different assembly. It can be inferred that the required temporal precision is dependent on the frequency at which the neurons synchronize (cf. Fig 1). Consider a neuronal assembly consisting of neurons which synchronized their activity at 40 Hz. One cycle of this activity has a duration of 25 ms. Thus, a deviation from the rhythm of only 12 ms (half a cycle) results in maximal temporal dissimilarity. Now consider an assembly oscillating at a lower frequency, say 10 Hz (i.e. a cycle duration of 100 ms). Here, a deviation of 12 ms corresponds roughly to a tenth of a cycle. That is to say, the higher the frequency the more critical is the timing.

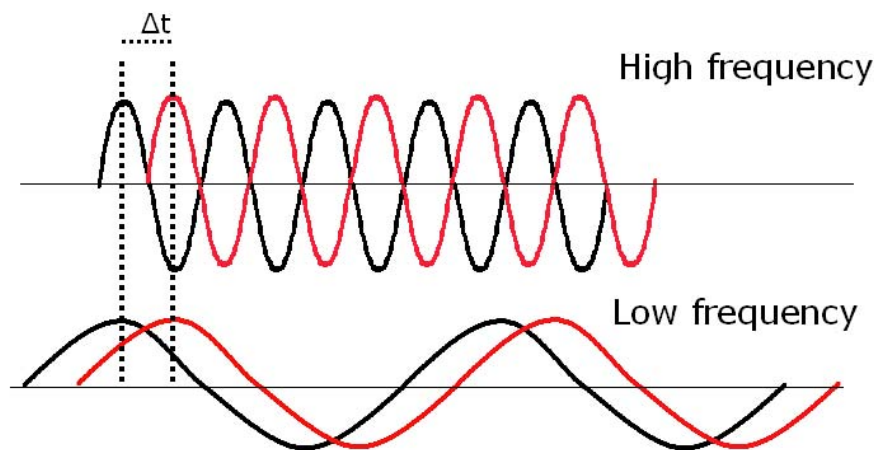


Figure 1: Illustration of the relationship between frequency and temporal precision. A temporal imprecision of Δt results in maximal temporal dissimilarity for a high frequency oscillation while the same amount of imprecision hardly affects the low frequency oscillation.

It is reasonable to assume that the larger a neuronal assembly is the higher the amount of imprecise events could be. Hence, a strategy to circumvent the loss of information due to temporal inaccuracy might be to employ a slower rhythm for larger assemblies. Such a mechanism has been proposed before by Singer (1993) based on animal studies. In a recent study we sought to find evidence for such a relationship between assembly size and neuronal frequency in human EEG. Parts of this experiment have been published in (Busch, Debener, Kranczioch, Engel & Herrmann, 2004)

Methods

16 subjects participated in the study. They performed a simple choice-reaction task that required the

discrimination of circles and squares. Three different stimulus sizes were employed: 1.5°, 4° and 8° visual angle. Stimuli were presented for 250 ms. The rationale of the size variation was the assumption that larger stimuli activate larger neuronal assemblies in retinotopic visual areas. EEG was recorded with 64 Ag–AgCl electrodes mounted in an elastic cap. All electrodes were referenced to the nose. EEG was sampled at 500 Hz. In order to analyze gamma activity a wavelet transform was applied (Herrmann, Mecklinger & Pfeifer, 1999). For each subject and each condition the frequency of the maximum activation in the frequency range between 30 Hz and 80 Hz in a time window from 70 ms to 110 ms was determined.

Results

Wavelet analysis of the EEG signal revealed that stimulus presentations evoked a prominent gamma-band response (GBR). This GBR manifested in an increase of oscillatory activity in the frequency range between 30 Hz and 80 Hz at about 80 ms after stimulus onset (Fig. 2). The GBR was maximal at centro-parietal sites. Individual frequencies varied considerably between subjects. Moreover, the amplitude of this GBR increased with increasing stimulus size.

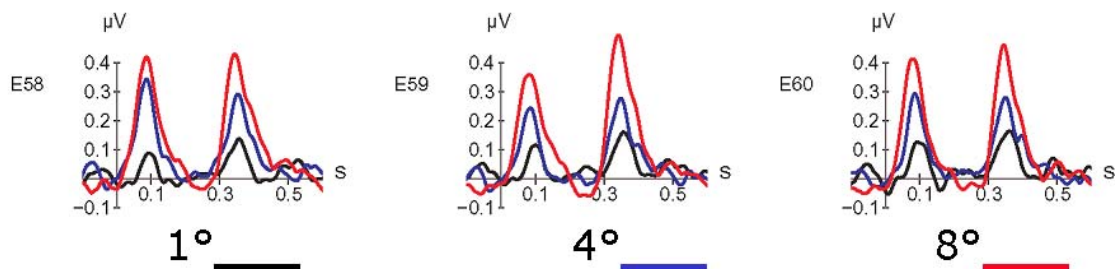


Figure 2: Increase of GBR peak amplitudes with stimulus size (1° - black; 4° - blue; 8° - red). Wavelet transforms are shown for electrodes E58, E59 and E60, corresponding to O1, OZ and O2, respectively. Both onset (~ 80 ms) and offset responses (~ 330 ms; 80 ms + 250 ms stimulus duration) are shown.

Most importantly, we found a significant covariance between stimulus size and frequency of evoked gamma activity. As predicted, GBRs evoked by larger stimuli were of lower frequency than GBRs evoked by smaller stimuli (cf. Fig. 3). GBR peak frequencies were 54 Hz for small, 43 Hz for medium and 41 Hz for big stimuli.

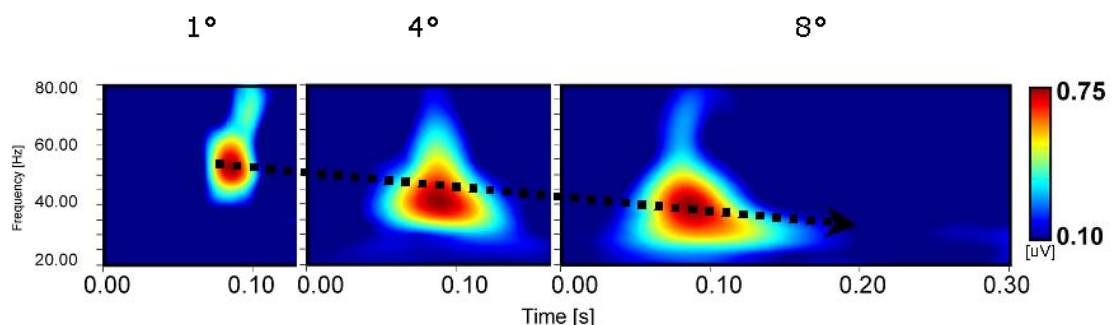


Figure 3: Decrease of GBR frequency with stimulus size

Discussion

Our results seem to indicate that binding processes in the visual system operate in a flexible way.

Bottom-up processes appear to modulate the frequency at which neurons bound to the same assembly synchronize their activity. This idea has been expressed before by Singer (1993): “As the rhythm slows down, the temporal window during which events can be distinguished as synchronous or asynchronous broadens ... and binding by synchrony can be achieved over larger distances and between more cells“. This describes exactly the situation found in our study. Larger stimuli activated larger regions in retinotopic visual areas requiring a lower frequency but evoked GBRs with higher amplitudes. An inverse relationship between frequency and amplitude is actually a well known phenomenon: lower EEG frequencies are of much higher amplitude than higher frequencies. A similar situation has been found with movement-related beta oscillations. Pfurtscheller, Neuper, Pichler-Zalaudek, Edlinger, & Lopes da Silva (2000) found beta oscillations related to hand movements to be of lower frequency than oscillations related to foot movements. The authors speculated that this difference in frequency was due to the larger size of the hand area in the motor-cortex. Furthermore, local oscillations have been found to be of higher frequency than oscillations representing long-range interactions between cortical areas (Chen & Herrmann, 2001; von Stein & Sarnthein, 2000). Taken together, our data complement previous findings that binding of object parts can be accomplished by forming transient neuronal assemblies. The “glue” which keeps these assemblies together is provided by the synchronous activity of cells belonging to the same assembly. Our study demonstrated that this synchronization acts in a highly flexible and adaptive way. In a subsequent study we asked if oscillatory activity might be involved in “glueing” also object features, such as color and shape, in addition to its role in binding object parts.

Feature binding in visual short-term memory

Introduction

According to feature integration theory (FIT), visual information is processed in at least two successive stages (Treisman & Gelade, 1980). In a first stage the presence of elementary stimulus attributes (or features) such as color, spatial orientation or shape is detected and coded in so called feature maps. The theory hypothesizes separate maps for different stimulus dimensions. This idea receives support from neurophysiological studies which show that visual information is processed in a network of different brain areas specialized in the processing of separate stimulus attributes (Livingstone & Hubel, 1988). If a stimulus is defined by more than one feature the problem of integrating the separate features arises (Robertson, 2003). This is accomplished in a second step in which an attentional resource is needed to bind coherent features together. This theory has been tested in visual search paradigms (Treisman & Gelade, 1980; Wolfe, 2003; Wolfe, Cave & Franzel, 1989). In a typical experiment subjects have to search a display for a target stimulus that is hidden among distractors. If the target is defined by only one feature (e.g. a red stimulus among green distractors) search times usually do not increase with the number of distractors. If the target is defined by a conjunction of two features (e.g. a red X among green Xs and red Os) search times increase linearly with the number of distractors (Treisman & Gelade, 1980). Taken together, visual search experiments suggest that processing multi-featured stimuli is more effortful than processing single-featured stimuli. A different pattern of results emerges when a stimulus display does not have to be searched but memorized in visual short term memory (VSTM). The capacity of VSTM is known to be limited to only a few items (Cowan, 2001). In an influential study, Luck and Vogel used multi-featured stimuli in a series of behavioral experiments and demonstrated that capacity is limited only by the number of objects held in VSTM (object-load). Capacity was not limited by the number of object features (feature-load) that had to be memorized (Luck & Vogel, 1997). For instance, performance did not decrease when subjects had to memorize an object that was defined by four features (orientation, size, color and the presence or absence of a black gap) compared to memorizing an object defined by only a single feature (Vogel, Woodman & Luck, 2001). Therefore, the authors concluded that VSTM stores integrated objects rather than a set of individual features (e.g. a red square rather than red and square). Thus, unlike visual perception, the retention of objects in VSTM does not seem to be more effortful for

multi-featured stimuli than for single-featured stimuli. One severe limitation of behavioral measures is that they usually represent the combined output of multiple subprocesses. Thus, it cannot be excluded from the behavioral studies done so far that some subprocesses of VSTM work quite similar to visual perception while others may not. Therefore, electrophysiological measures might be better suited to resolve the apparent divergence between findings from VSTM and visual perception because of their better temporal resolution. Previous studies investigated the effect of memory load on event-related potentials (ERPs) and event-related oscillations (EROs). A common finding is a reduction of P3 amplitude with increasing memory load (Klaver, Smid & Heinze, 1999; McEvoy, Smith & Gevins, 1998; Schack & Klimesch, 2002). An interpretation given by Kok (2001) is that increasing the cognitive demands by increasing memory load leaves fewer resources for stimulus evaluation which is reflected by the P3. In addition, EROs in the alpha band (~10 Hz) were found to increase with memory load during the delay interval in a working memory task (Jensen, Gelfand, Kounios & Lisman, 2002; Schack & Klimesch, 2002). This increase in 10 Hz activity has been interpreted as a correlate of a cortical inhibition of task-irrelevant neural processes (Cooper, Croft, Dominey, Burgess & Gruzelier, 2003; Foxe, Simpson & Ahlfors, 1998; Klimesch, Doppelmayr, Schwaiger, Auinger & Winkler, 1999). While most of these studies employed only single-featured objects, Klaver et al. (1999) used multi-featured objects to investigate the effect of feature- and object-load on ERPs during encoding and retention and failed to find an effect of feature-load. The present study aimed at extending previous results by investigating the effect of both object-load and feature-load. For the first time we investigated the effect of both load factors on ERPs as well as on EROs during all stages of a delayed-matching-to-sample task (encoding, retention and retrieval). Since behavioral measures were not influenced by feature-load in the studies conducted by Luck & Vogel (1997) one could expect electrophysiological measures to be also modulated by object-load only. This study has been published in (Busch & Herrmann, 2003).

Methods

The experiment consisted of four blocks with 100 trials each. A trial always started with a display of three objects (S1; duration 1000 ms; see Fig. 4) that were presented centrally. During the delay interval a blank screen was shown for 3000 ms followed by a probe display containing a single object (S2; duration 1000 ms). Subjects were instructed to indicate with a button press whether S2 was included in S1 or not. Stimuli were defined by shape, color and texture. The order of the four blocks was counterbalanced across subjects. The probability of a new item was always 50%. The amount of features and objects which had to be remembered (feature-load and object-load, respectively) was varied between blocks. Either one or three features (1-feature-conditions and 3-features-conditions, respectively) of one or three objects (1-object-conditions and 3-objects-conditions, respectively) had to be retained in memory. This resulted in a total of four blocks: 1-object/1-feature, 3objects/1-feature, 1-object/3-features, and 3-objects/3-features. It should be noted that in the last of these four conditions not only a total of nine separate features had to be remembered but also the correct combination of them. The rationale behind this paradigm is that different accounts of feature binding make different predictions for variations of feature-load and object-load. For instance, consider the 1-object/1-feature and the 1-object/3-features conditions. If information in VSTM was coded feature-wise an increase in electrophysiological markers of VSTM activity would be expected in the latter condition due to the triplication of feature-load. In contrast, if coding in VSTM was object-based no difference in EEG markers would be expected because object-load does not change.

EEG was recorded using 19 electrodes at the standard 10/20 positions. 10 Hz activity was computed as the sum of phase-locked and non-phase-locked oscillatory activity with a wavelet-based time-frequency analysis (Herrmann & Mecklinger, 2000; Herrmann et al., 1999). ERP components were defined as mean amplitudes in the time intervals 200–500 ms after S1 stimulus onset (encoding-P3) and 400–700 ms after S2 stimulus onset (retrieval-P3). Induced 10 Hz oscillations in the delay interval were analyzed in a time window from S1 offset until S2 onset (3000 ms).

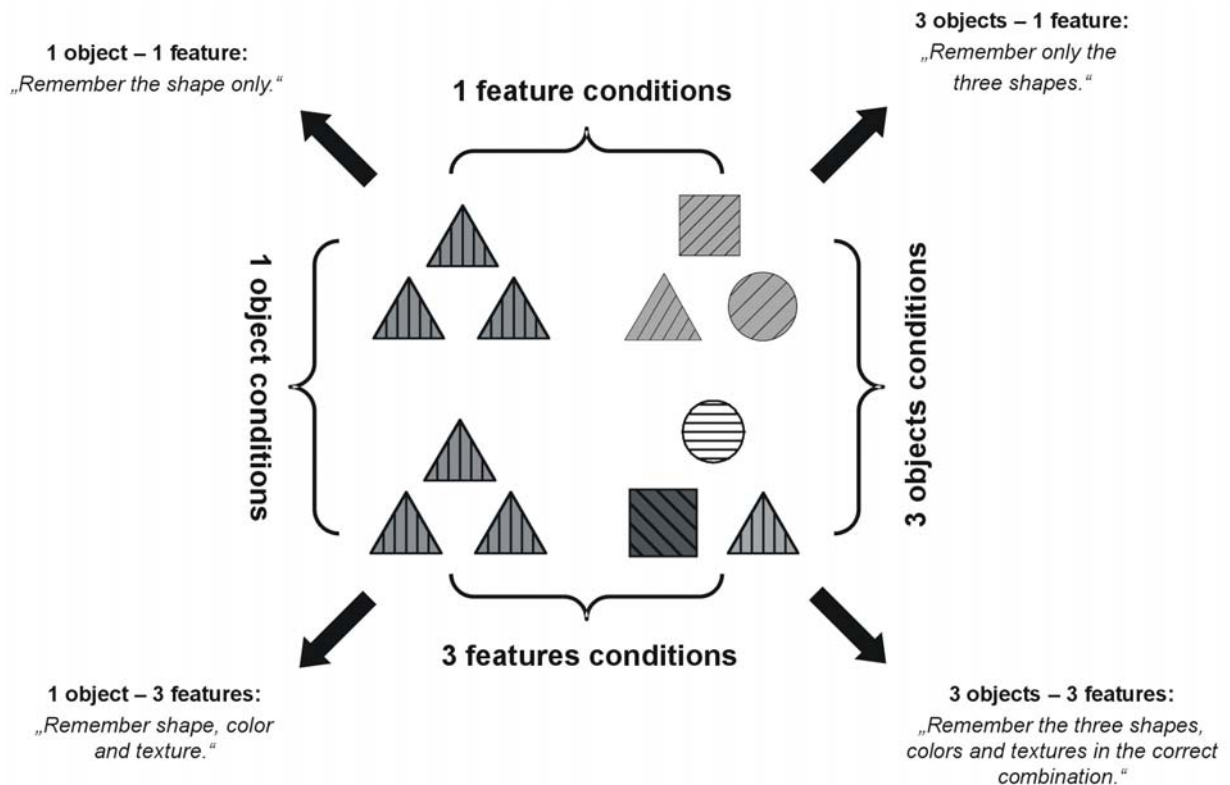


Figure 4: Example of S1 stimulus displays used in the four conditions together with the corresponding instructions. Colors are displayed as different shades of grey. Adapted from Busch & Herrmann (2003).

Results

Figure 5 shows the ERPs in response to S1 and S2 stimuli and induced 10 Hz oscillations during the delay interval. The amplitude of the encoding-P3 was only modulated by object-load with smaller amplitudes for high object-load.

Similarly, the amplitude of induced 10 Hz activity was only modulated by object-load with higher activity for high object-load. Retrieval-P3 amplitudes were modulated by both object-load and feature-load. This interaction was due to an amplitude decrease in the 3-objects/3-features condition.

Discussion

Our study revealed a significant modulation by object-load of encoding-P3 and 10 Hz oscillations during the retention interval but failed to show an effect of feature-load. This is in line with previous results from behavioral (Luck & Vogel, 1997) as well as electrophysiological studies (Jensen et al., 2002; Klaver et al., 1999; Kok, 2001). The smaller amplitude of encoding-P3 in the 3-objects conditions irrespective of feature-load indicates that processing multiple features of a stimulus does not require more resources when that stimulus is transferred into VSTM as compared to when only a single feature is encoded (Kok, 2001). This supports the view that VSTM stores integrated object representations rather than several individual features. The stronger increase in 10 Hz oscillations for high object-load during the retention interval replicates results from previous studies (Jensen et al., 2002; Schack & Klimesch, 2002). For instance, Jensen et al. (2002) found a positive correlation between memory-load and alpha-band

power. In a different paradigm Cooper et al. (2003) found an increase in alpha oscillations in a mental imagery task compared to an externally directed attention task. This increase has been interpreted as a correlate of inhibition of task irrelevant cortical areas. Thus, our results seem to add to the growing evidence that the

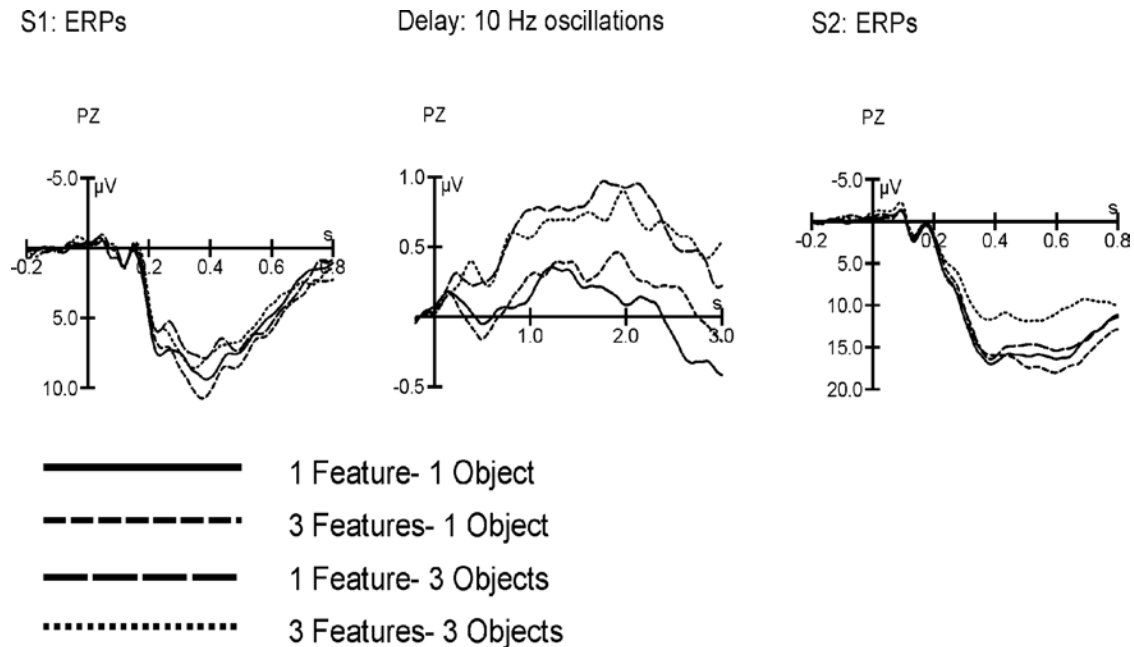


Figure 5: ERPs during encoding (S1, left) are modulated by object-load. P3 amplitude is reduced in the 3-objects conditions. Induced 10 Hz oscillations during retention (delay, middle) are also modulated by object-load only. The 3-objects conditions induce larger 10 Hz amplitudes. At the time of retrieval (S2, right) both factors interact. P3 amplitude is smallest for the most difficult condition (3-features/3-objects). Adapted from Busch & Herrmann (2003).

alpha rhythm represents more than just a state of cortical inactivity (cortical idling). An oscillatory process as the basis of VSTM maintenance was also suggested by Luck & Vogel (1997). If multi-featured objects were stored as separate features in VSTM an increase in feature-load should increase the demand for cortical inhibition of task irrelevant cortical areas. Therefore, one would expect a modulation of 10 Hz activity by both feature-load and object-load. However, a modulation was found for object-load only, supporting the idea of integrated object representations in VSTM. During retrieval, when subjects had to compare the content of their memory with the S2 stimulus, retrieval-P3 was significantly smaller in the 3-objects/3-features condition compared to the other conditions. This condition differed from the others in so far as the probe stimulus had to be scanned not only for new features but also for a new combination of old features. In this case FIT predicts a larger effort for feature integration in order to avoid miscombinations of features from different objects, so called illusory conjunctions (Treisman & Schmidt, 1982). Why is this larger effort only present during retrieval? One possible interpretation is that integrated object representations (as seem to occur in VSTM) are less well suited for comparison with a probe stimulus. Therefore, memory representations would have to be recoded to a representational format that requires additional feature binding, especially in the 3-objects/3-features condition in which illusory conjunctions can occur. Such a representation could be compared with the probe stimulus for each feature dimension separately (and maybe for feature conjunctions) rather than comparing the memory template as a whole. A feature wise comparison process is also known from stimulus classification tasks (Herrmann & Mecklinger, 2000; Herrmann et al., 1999). For instance, in the experiment by Herrmann et al. (1999) a target was defined as an illusory figure (feature one) consisting of four inducer discs (feature two). Reaction times were fastest for stimuli which shared no feature with the target (a nonillusory figure consisting of three inducer discs), intermediate for stimuli sharing one feature with the target and slowest

for target stimuli which, by definition, shared both features. Hence, the authors concluded that stimulus and memory template were compared feature by feature. Taken together, our results confirm that storage and retention work with integrated objects in VSTM but suggest that retrieving and comparing the stored memory content relies on the single features of objects. This also explains why visual search yields effects of feature-load while VSTM experiments often fail to do so. In a visual search experiment the items of the search display have to be compared to a target which was previously encoded and which needs to be retrieved from memory. Thus, the process of retrieval and comparison which yields effects of feature-load is one of the major processes involved in this task. A VSTM experiment, however, is a combination of three subsequent tasks, two of which rely on object-based representations. Thus, it is plausible that feature-load is not as crucial since it is involved only in the last of the three processes.

The present study required subjects to maintain a stimulus representation in working memory and to compare a subsequently presented stimulus to that representation. Of course, the process of comparing an object of perception to a representation in memory also operates on long-term memories. Moreover, it is plausible to assume that these comparisons can take place automatically even when the experimental task does not require this comparison explicitly. In a subsequent study we asked if oscillatory activity might be involved in the comparison and binding of perception and long-term memory representations.

Binding between perception and long-term memory

Introduction

Human and animal brain activity frequently shows oscillations in the gamma frequency range (approx. 30-80 Hz) (Engel et al., 2001; Varela, Lachaux, Rodriguez & Martinerie, 2001). These oscillations have been shown to be correlates of numerous cognitive functions. Among the first functions to be associated with gamma activity was visual feature binding, coherent visual objects inducing more gamma oscillations than others (Gray et al., 1989; Muller et al., 1996). Also tones evoke such gamma responses (Pantev et al., 1991) and attention was associated with auditory gamma activity, attended tones evoking larger auditory gamma peaks than unattended ones (Tiitinen et al., 1993). In addition, it has been shown that object recognition seems to be a crucial factor for the presence of gamma activity (Basar, Basar-Eroglu, Karakas & Schurmann, 2000). For example, faces induced more gamma activity than rotated faces which were not recognizable (Keil, Müller, Ray, Gruber & Elbert, 1999) leading to more synchronization among brain areas within the gamma band (Rodriguez et al., 1999). In addition, gamma activity can be found when subjects suddenly see a meaningful picture in random-dot patterns (autostereoscopic pictures) (Revonsuo, Wilenius-Emet, Kuusela & Lehto, 1997). Also, language comprehension has been associated with gamma activity: words evoke more gamma oscillations in human cortex than do pseudo-words (Pulvermüller, Lutzenberger, Preissl & Birbaumer, 1995) and language-related gamma activity is most prominent over the language-specific left hemisphere (Eulitz et al., 1996). It has even been argued that human gamma activity may be a correlate of consciousness, since it was found to be higher during waking and REM sleep than during deep sleep (Llinas & Ribary, 1993) and anaesthesia (Keller, Madler, Schwender & Poppel, 1990). One mechanism which underlies many of these cognitive functions is access to memory. It has been demonstrated that access to working memory induces gamma activity: when subjects have to actively maintain visual stimuli in working memory the stimuli induced more gamma oscillations as compared to not memorizing them (Tallon-Baudry, Bertrand, Peronnet & Pernier, 1998). Also other publications have positively correlated gamma activity with learning and memory (Fell et al., 2001; Fries, Fernandez & Jensen, 2003; Gruber, Muller & Keil, 2002; Miltner, Braun, Arnold, Witte & Taub, 1999). In a series of previous experiments we tried to reveal which of the mentioned cognitive functions are more important for human gamma activity and which others might be less important. We used four different stimuli to directly contrast visual feature binding and attention. Two of the stimuli were Kanizsa figures for which the constituting parts can be bound together while for the remaining two stimuli this was not

possible. One out of the four stimuli was defined as a target and had to be detected. The experiments revealed that the attended target evoked significantly more gamma oscillations as compared to three the standards (Herrmann et al., 1999). Even when stimuli were used as targets which consisted of features that could not be bound together to coherent objects those targets evoked larger gamma responses than non-target stimuli which could be bound together (Herrmann & Mecklinger, 2001). This indicated that attention towards a target stimulus is more important for the modulation of gamma activity than the feature binding required to bind together coherent objects. Of course, target detection also requires access to working memory. Every stimulus has to be compared to a template of the target which was previously stored in short-term memory. Therefore, in a subsequent experiment, we explicitly tested whether comparing stimuli to memory templates increased gamma activity. When subjects had to identify targets by discriminating multiple stimulus features via comparison with a template in short-term memory (STM) all stimuli evoked significantly more gamma activity than stimuli which could be discriminated by a single feature (their color) (Herrmann & Mecklinger, 2000). We recently obtained similar results for auditory stimuli depending on whether targets match a template in working memory or whether novel stimuli do not match (Debener, Herrmann, Kranczioch, Gembris & Engel, 2003). Targets evoked significantly more gamma oscillations than novel stimuli even though both types of stimuli attract attention and evoke strong P3 components in human EEG. This lead us to the hypothesis that memory access may be crucial for the generation of gamma activity. It might be assumed that not only access to STM but also to long-term memory (LTM) shows a similar effect. Thus, we set out to test whether access to LTM modulates human gamma responses. We investigated whether simple visual stimuli evoke more gamma activity when subjects already have a memory representation of the presented objects as compared to when they perceive novel visual stimuli which do not match LTM. The data of this experiment has been published in (Herrmann, Lenz, Junge, Busch & Maess, 2004).

Methods

The stimulus material consisted of two different types of black and white drawings (210 total). The first type of figures were line drawings of objects for which subjects already had a representation in LTM because they were well-known real-world objects. The second type of stimuli were non-objects. In order to keep the two stimulus types comparable, the non-objects were composed of the same components as the objects but were newly arranged. Thus, each nonobject stimulus comprised the parts of one object stimulus (cf. Fig. 6). Subjects were instructed to judge whether the stimuli appeared to be either edgy or curvy by pressing one of two buttons. Thus, subjects were naive about the purpose of the experiment. This was important, since we did not want subjects to be influenced by the stimulus type which we investigated. We conducted a pre-experiment with another 10 subjects to select the stimuli and to ensure that each stimulus is consistently perceived as a known object or an unknown non-object. Only those stimulus-pairs were used, for which both figures were consistently judged as objects and non-objects, respectively.

EEG was recorded with 52 electrodes mounted in an elastic cap according to the international 10–10 system. In order to analyze gamma activity a wavelet transform was applied (Herrmann et al., 1999).

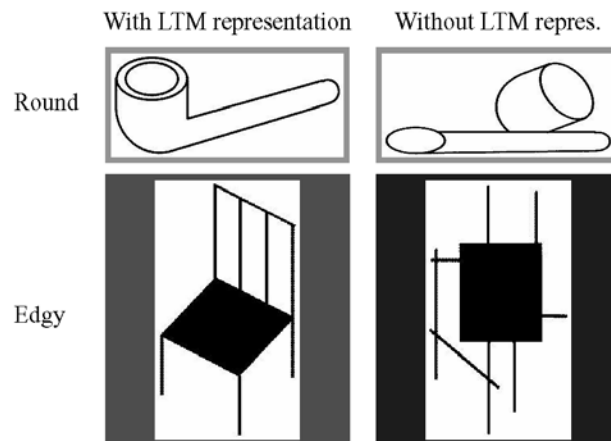


Figure 6: Examples of the stimuli used in the experiment. Two objects with a representation in LTM (left) and the corresponding non-objects which are composed of the same parts but have no such representation in LTM (right). Subjects were to differentiate round (top row) from edgy figures (bottom row) in order to keep the results free of confounds.

Results

A comparison of gamma responses evoked by objects and non-objects revealed a stronger gamma response for stimuli with memory representations (cf. Fig. 7) at a latency of 80 ms. No effect was found for object shape (curvy vs. edgy). The topographic distribution of the evoked gamma peak revealed that the amplitude was largest over occipital cortex indicating that the activity might stem from visual brain areas.

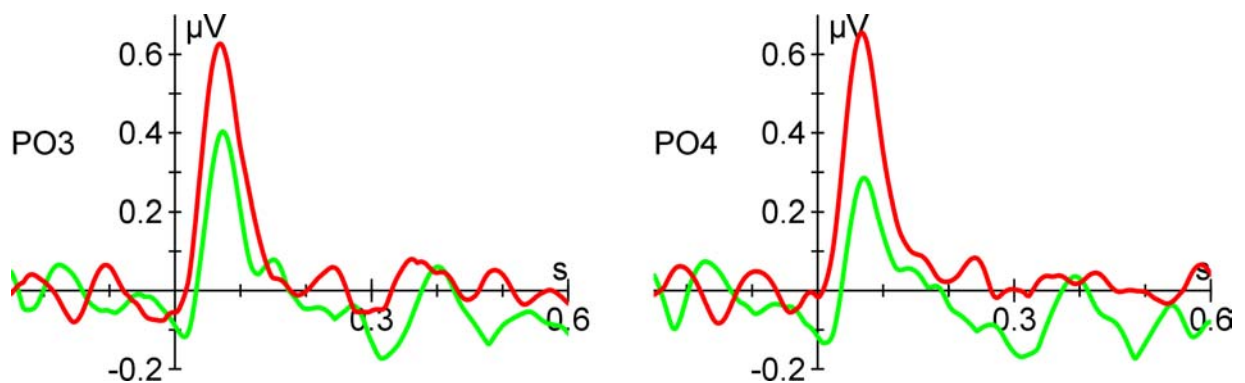


Figure 7: The evoked peak of gamma activity shows a clear difference between known objects (red) and non-objects (green).

Discussion

Our data show that visual stimuli evoke enhanced gamma responses if they match with contents of LTM. We assume that feedback loops from the memory system to perception mechanisms are responsible for this phenomenon. It has been demonstrated that neurons in medial temporal cortex fire in synchrony and at approx. 40 Hz when stimuli are subsequently remembered (Fell et al., 2001). In our experiment the topography of the gamma oscillations was over occipital areas indicating that they were generated by

neurons of visual cortex. However, since stimuli for which subjects had a memory representation evoked larger oscillatory responses, we argue that the feedback from memory systems enhances gamma activity in visual areas. The memory processes which modulate the visual gamma response do not seem to elicit gamma activity themselves, since only occipital responses were found. Such memory processes would, however, be expected to reside in frontal or temporal cortex where no gamma activity was found. A similar phenomenon has been observed for event-related potentials (ERPs). Patients with frontal lobe damage show altered early auditory and visual ERPs which indicates that frontal cortex modulates temporal and occipital cortex in the generation of electrophysiological responses (Barcelo, Suwazono & Knight, 2000; Knight, Staines, Swick & Chao, 1999). However, no frontal ERP component has been identified which represents this modulatory process. The notion that memory access modulates human gamma responses is supported by a great number of experimental findings on evoked gamma activity in the human EEG. For instance, words probably evoke more gamma activity as compared to pseudo-words (Pulvermüller et al., 1995) because we have memory representations of words but not of pseudo-words. Language-specific gamma activity could be lateralized to the left hemisphere (Eulitz et al., 1996) since the mental lexicon where words are stored resides in the left hemisphere. Attended objects reach STM more easily than unattended ones and thus lead to more gamma oscillations (Tiitinen et al., 1993). A target is defined by matching a template stored in STM for all criteria while a standard stimulus will represent a mismatch for at least one criterion. Thus, auditory as well as visual target stimuli receive more positive feedback from STM than standards (Herrmann & Mecklinger, 2001; Herrmann et al., 1999; Yordanova, Kolev & Demiralp, 1997). Due to the similar topographical distributions of our evoked response and induced gamma responses (Gruber et al., 2002; Tallon-Baudry et al., 1998), it seems plausible to assume that evoked and induced gamma activity are generated by the same neural systems only varying in their degree of phase-locking. Under this assumption our memory-explanation might even hold for the induced gamma band responses. We would argue that objects induce more gamma activity than non-objects (Tallon-Baudry & Bertrand, 1999) because we have only objects stored in LTM but no non-objects. This is not to claim that gamma activity is not related to binding processes. Our main argumentation is that a memory comparison must occur in order to initiate a binding process in case of a match. The same would be true for faces versus rotated faces (Keil et al., 1999) and meaningful pictures versus random-dot patterns (Revonsuo et al., 1997). However, it is probably not the aspect of meaningfulness per se that enhances early gamma band activity. In the experiment by Debener et al. (2003) target tones evoked more gamma activity than novel stimuli. In this experiment targets were simple sine waves while novels were real world (meaningful) sounds. Thus, the effect should have been reversed if meaningful stimuli should evoke more gamma activity. Also, behavioral relevance is probably not a crucial factor involved in the modulation of gamma activity. In the present study the factor of interest (memory vs. non-memory) was totally irrelevant for the subjects' task. Although subjects did not have to perform an explicit memory task the main distinction between the two conditions was related to extent of the memory representation since stimuli were similar in all other aspects. Although this procedure may not be common practice in memory experiments it circumvents the possible confound of putative memory effects by response or task effects. Even the notion that gamma activity might reflect aspects of consciousness (Keller et al., 1990; Llinas & Ribary, 1993) is supported by our data: During conscious states we always compare every perception to the contents of LTM (Rock, 1984) which yields the observed gamma activity. During unconscious states of sleep or anaesthesia this comparison is no longer carried out. Taken together, we propose that gamma activity is modulated by access to STM and LTM. Of course also other cognitive processes without explicit memory access may modulate human gamma activity. It is known, for example, that task-difficulty (Senkowski & Herrmann, 2002) and the speed of manual reaction (Haig, De Pascalis & Gordon, 1999) covary with gamma activity. Multiple modulatory mechanisms of gamma responses are very probable, since multiple oscillatory responses can be found in the human EEG at different frequencies in the gamma range with different topographies and time-courses.

Conclusion

In a series of experiments we investigated binding processes at several levels of information processing. Furthermore, we were able to show that oscillatory activity is a valuable source of information for the investigation of binding processes. Clearly, the three experiments reported here show that the oscillations involved in the diverse binding processes under investigation span over a wide range of frequencies. In line with earlier proposals (von Stein & Sarnthein, 2000) we found binding mechanisms which modulate local processes to be related to high frequency oscillations in the gamma frequency range (experiment 1 & 3). In experiment 2 in which a more distributed representation had to be processed oscillations of lower frequencies in the alpha range were found.

It is evident that binding is required from low-level perceptual processes up to top-down cognition in stimulus recognition. At the lowest level of perceptual processing neuronal assemblies belonging to the same object have to be bound together. Moreover, these assemblies need to be distinguished from assemblies coding different objects. Current theories of binding in the visual system assume that these functions are achieved by oscillatory activity (Singer, 1993). At this level of analysis we found the frequency of neuronal oscillations to be related to the size of the neuronal ensemble. Thus, we were able to confirm an important prediction made by the „temporal correlation hypothesis“ (Singer & Gray, 1995). At a subsequent stage of processing stimulus features belonging to the same object have to be integrated. This feature binding is required since feature dimensions as color, location or shape are processed separately in different areas of the visual system. The binding of object features has to be maintained when an object representation is held in short-term memory. Neuronal oscillations have been proposed to be the mechanism underlying this maintenance process (Jensen & Lisman, 1998). Our data indicate that binding processes in visual short-term memory are coded differently compared to binding in visual search tasks. Thus, by means of an electrophysiological investigation our results may explain the apparent divergence between these two paradigms which have been used to investigate feature binding behaviorally. Usually, visual processing is not restricted to perception and maintenance of a stimulus. At a higher level of processing perception needs to be integrated with information acquired in past experience. Our results show that this integration is reflected in an enhancement of oscillatory activity during earliest stages of visual processing.

References

- Adrian, E. D. (1942). Olfactory reactions in the brain of the hedgehog. *Journal of Physiology*, 100, 459-473.
- Barcelo, F., Suwazono, S. & Knight, R. T. (2000). Prefrontal modulation of visual processing in humans. *Nat Neurosci*, 3(4), 399-403.
- Basar, E., Basar-Eroglu, C., Karakas, S. & Schurmann, M. (2000). Brain oscillations in perception and memory. *Int J Psychophysiol*, 35(2-3), 95-124.
- Busch, N. A., Debener, S., Kranczioch, C., Engel, A. K. & Herrmann, C. S. (2004). Size matters: Effects of stimulus size, duration and eccentricity on the visual gamma-band response. *Clinical Neurophysiology*, Accepted for publication.
- Busch, N. A. & Herrmann, C. S. (2003). Object-load and feature-load modulate EEG in a short-term memory task. *Neuroreport*, 14(13), 1721-1724.
- Chen, A. C. & Herrmann, C. S. (2001). Perception of pain coincides with the spatial expansion of electroencephalographic dynamics in human subjects. *Neurosci Lett*, 297(3), 183-186.
- Cooper, N. R., Croft, R. J., Dominey, S. J., Burgess, A. P. & Gruzelier, J. H. (2003). Paradox lost? Exploring the role of alpha oscillations during externally vs. internally directed attention and the implications for idling and inhibition hypotheses. *Int J Psychophysiol*, 47(1), 65-74.

- Cowan, N. (2001). The magical number 4 in short-term memory: a reconsideration of mental storage capacity. *Behav Brain Sci*, 24(1), 87-114; discussion 114-185.
- Debener, S., Herrmann, C. S., Kranczioch, C., Gembris, D. & Engel, A. K. (2003). Top-down attentional processing enhances auditory evoked gamma band activity. *Neuroreport*, 14(5), 683-686.
- Eckhorn, R., Bauer, R., Jordan, W., Brosch, M., Kruse, W., Munk, M., et al. (1988). Coherent oscillations: a mechanism of feature linking in the visual cortex? Multiple electrode and correlation analyses in the cat. *Biol Cybern*, 60(2), 121-130.
- Engel, A. K., Fries, P. & Singer, W. (2001). Dynamic predictions: oscillations and synchrony in top-down processing. *Nat Rev Neurosci*, 2(10), 704-716.
- Eulitz, C., Maess, B., Pantev, C., Friederici, A. D., Feige, B. & Elbert, T. (1996). Oscillatory neuromagnetic activity induced by language and non-language stimuli. *Brain Res Cogn Brain Res*, 4(2), 121-132.
- Fell, J., Klaver, P., Lehnertz, K., Grunwald, T., Schaller, C., Elger, C. E., et al. (2001). Human memory formation is accompanied by rhinal-hippocampal coupling and decoupling. *Nat Neurosci*, 4(12), 1259-1264.
- Foxe, J. J., Simpson, G. V. & Ahlfors, S. P. (1998). Parieto-occipital approximately 10 Hz activity reflects anticipatory state of visual attention mechanisms. *Neuroreport*, 9(17), 3929-3933.
- Fries, P., Fernandez, G. & Jensen, O. (2003). When neurons form memories. *Trends Neurosci*, 26(3), 123-124.
- Gray, C. M., König, P., Engel, A. K. & Singer, W. (1989). Oscillatory responses in cat visual cortex exhibit inter-columnar synchronization which reflects global stimulus properties. *Nature*, 338(6213), 334-337.
- Gruber, T., Muller, M. M. & Keil, A. (2002). Modulation of induced gamma band responses in a perceptual learning task in the human EEG. *J Cogn Neurosci*, 14(5), 732-744.
- Haig, A. R., De Pascalis, V. & Gordon, E. (1999). Peak gamma latency correlated with reaction time in a conventional oddball paradigm. *Clin Neurophysiol*, 110(1), 158-165.
- Herrmann, C. S., Lenz, D., Junge, S., Busch, N. A. & Maess, B. (2004). Memory-matches evoke human gamma-responses. *BMC Neuroscience*, 5(13).
- Herrmann, C. S. & Mecklinger, A. (2000). Magnetoencephalographic responses to illusory figures: early evoked gamma is affected by processing of stimulus features. *Int J Psychophysiol*, 38(3), 265-281.
- Herrmann, C. S. & Mecklinger, A. (2001). Gamma activity in human EEG is related to high-speed memory comparisons during object selective attention. *Visual Cognition*, 8(3/4), 593-608.
- Herrmann, C. S., Mecklinger, A. & Pfeifer, E. (1999). Gamma responses and ERPs in a visual classification task. *Clin Neurophysiol*, 110(4), 636-642.
- Jensen, O., Gelfand, J., Kounios, J. & Lisman, J. E. (2002). Oscillations in the alpha band (9-12 Hz) increase with memory load during retention in a short-term memory task. *Cereb Cortex*, 12(8), 877-882.
- Jensen, O. & Lisman, J. E. (1998). An oscillatory short-term memory buffer model can account for data on the Sternberg task. *J Neurosci*, 18(24), 10688-10699.
- Jung, T. P., Makeig, S., McKeown, M. J., Bell, A. J., Lee, T. W. & Sejnowski, T. J. (2001). Imaging brain dynamics using independent component analysis. *Proceedings of the IEEE*, 89(7), 1107-1122.

- Keil, A., Gruber, T. & Müller, M. M. (2001). Functional correlates of macroscopic high-frequency brain activity in the human visual system. *Neurosci Biobehav Rev*, 25(6), 527-534.
- Keil, A., Müller, M. M., Ray, W. J., Gruber, T. & Elbert, T. (1999). Human gamma band activity and perception of a gestalt. *J Neurosci*, 19(16), 7152-7161.
- Keller, I., Madler, C., Schwender, D. & Poppel, E. (1990). Analysis of oscillatory components in perioperative AEP-recordings: a nonparametric procedure for frequency measurement. *Clin Electroencephalogr*, 21(2), 88-92.
- Klaver, P., Smid, H. G. & Heinze, H. J. (1999). Representations in human visual short-term memory: an event-related brain potential study. *Neurosci Lett*, 268(2), 65-68.
- Klimesch, W., Doppelmayr, M., Schwaiger, J., Auinger, P. & Winkler, T. (1999). 'Paradoxical' alpha synchronization in a memory task. *Brain Res Cogn Brain Res*, 7(4), 493-501.
- Knight, R. T., Staines, W. R., Swick, D. & Chao, L. L. (1999). Prefrontal cortex regulates inhibition and excitation in distributed neural networks. *Acta Psychol (Amst)*, 101(2-3), 159-178.
- Kok, A. (2001). On the utility of P3 amplitude as a measure of processing capacity. *Psychophysiology*, 38(3), 557-577.
- Livingstone, M. & Hubel, D. (1988). Segregation of form, color, movement, and depth: anatomy, physiology, and perception. *Science*, 240(4853), 740-749.
- Llinas, R. & Ribary, U. (1993). Coherent 40-Hz oscillation characterizes dream state in humans. *Proc Natl Acad Sci U S A*, 90(5), 2078-2081.
- Luck, S. J. & Vogel, E. K. (1997). The capacity of visual working memory for features and conjunctions. *Nature*, 390(6657), 279-281.
- McEvoy, L. K., Smith, M. E. & Gevins, A. (1998). Dynamic cortical networks of verbal and spatial working memory: effects of memory load and task practice. *Cereb Cortex*, 8(7), 563-574.
- Miltner, W. H., Braun, C., Arnold, M., Witte, H. & Taub, E. (1999). Coherence of gamma-band EEG activity as a basis for associative learning. *Nature*, 397(6718), 434-436.
- Muller, M. M., Bosch, J., Elbert, T., Kreiter, A., Sosa, M. V., Sosa, P. V., et al. (1996). Visually induced gamma-band responses in human electroencephalographic activity--a link to animal studies. *Exp Brain Res*, 112(1), 96-102.
- Nelson, J. I. (1995). Binding in the visual system. In M. Arbib (Ed.), *Handbook of Brain Theory and Neural Networks* (pp. 157-159): MIT Press.
- Pantev, C., Makeig, S., Hoke, M., Galambos, R., Hampson, S. & Gallen, C. (1991). Human auditory evoked gamma-band magnetic fields. *Proc Natl Acad Sci U S A*, 88(20), 8996-9000.
- Pfurtscheller, G. & Lopes da Silva, F. H. (1999). Event-related EEG/MEG synchronization and desynchronization: basic principles. *Clin Neurophysiol*, 110(11), 1842-1857.
- Pfurtscheller, G., Neuper, C., Pichler-Zalaudek, K., Edlinger, G. & Lopes da Silva, F. H. (2000). Do brain oscillations of different frequencies indicate interaction between cortical areas in humans? *Neurosci Lett*, 286(1), 66-68.
- Pulvermüller, F., Lutzenberger, W., Preissl, H. & Birbaumer, N. (1995). Spectral responses in the gamma-band: physiological signs of higher cognitive processes? *Neuroreport*, 6(15), 2059-2064.
- Revonsuo, A., Wilenius-Emet, M., Kuusela, J. & Lehto, M. (1997). The neural generation of a unified illusion in human vision. *Neuroreport*, 8(18), 3867-3870.
- Robertson, L. C. (2003). Binding, spatial attention and perceptual awareness. *Nat Rev Neurosci*, 4(2), 93-102.

- Rock, I. (1984). *Perception*. New York: Scientific American Books.
- Rodriguez, E., George, N., Lachaux, J. P., Martinerie, J., Renault, B. & Varela, F. J. (1999). Perception's shadow: long-distance synchronization of human brain activity. *Nature*, 397(6718), 430-433.
- Sannita, W. G. (2000). Stimulus-specific oscillatory responses of the brain: a time/frequency-related coding process. *Clin Neurophysiol*, 111(4), 565-583.
- Schack, B. & Klimesch, W. (2002). Frequency characteristics of evoked and oscillatory electroencephalic activity in a human memory scanning task. *Neurosci Lett*, 331(2), 107-110.
- Senkowski, D. & Herrmann, C. S. (2002). Effects of task difficulty on evoked gamma activity and ERPs in a visual discrimination task. *Clin Neurophysiol*, 113(11), 1742-1753.
- Singer, W. (1993). Synchronization of cortical activity and its putative role in information processing and learning. *Annu Rev Physiol*, 55, 349-374.
- Singer, W. & Gray, C. M. (1995). Visual feature integration and the temporal correlation hypothesis. *Annu Rev Neurosci*, 18, 555-586.
- Tallon-Baudry, C. & Bertrand, O. (1999). Oscillatory gamma activity in humans and its role in object representation. *Trends Cogn Sci*, 3(4), 151-162.
- Tallon-Baudry, C., Bertrand, O., Peronnet, F. & Pernier, J. (1998). Induced gamma-band activity during the delay of a visual short-term memory task in humans. *J Neurosci*, 18(11), 4244-4254.
- Tiitinen, H., Sinkkonen, J., Reinikainen, K., Alho, K., Lavikainen, J. & Näätänen, R. (1993). Selective attention enhances the auditory 40-Hz transient response in humans. *Nature*, 364(6432), 59-60.
- Treisman, A. M. & Gelade, G. (1980). A feature-integration theory of attention. *Cognit Psychol*, 12(1), 97-136.
- Treisman, A. M. & Schmidt, H. (1982). Illusory conjunctions in the perception of objects. *Cognit Psychol*, 14(1), 107-141.
- Varela, F., Lachaux, J. P., Rodriguez, E. & Martinerie, J. (2001). The brainweb: phase synchronization and large-scale integration. *Nat Rev Neurosci*, 2(4), 229-239.
- Vogel, E. K., Woodman, G. F. & Luck, S. J. (2001). Storage of features, conjunctions and objects in visual working memory. *J Exp Psychol Hum Percept Perform*, 27(1), 92-114.
- von Stein, A. & Sarnthein, J. (2000). Different frequencies for different scales of cortical integration: from local gamma to long range alpha/theta synchronization. *Int J Psychophysiol*, 38(3), 301-313.
- Wolfe, J. M. (2003). Moving towards solutions to some enduring controversies in visual search. *Trends Cogn Sci*, 7(2), 70-76.
- Wolfe, J. M., Cave, K. R. & Franzel, S. L. (1989). Guided search: an alternative to the feature integration model for visual search. *J Exp Psychol Hum Percept Perform*, 15(3), 419-433.
- Yordanova, J., Kolev, V. & Demiralp, T. (1997). The phase-locking of auditory gamma band responses in humans is sensitive to task processing. *Neuroreport*, 8(18), 3999-4004.