Rhythmic neuronal synchronization subserves selective attentional processing

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Abstract
Selective attention relies on dynamic restructuring of cortical information flow in order to prioritize neuronal communication between those neuronal groups conveying information about behaviorally relevant information, while reducing the influence from groups encoding irrelevant and distracting information. Electrophysiological evidence suggests that such selective neuronal communication is instantiated and sustained through selective neuronal synchronization of rhythmic gamma band activity within and between neuronal groups: Attentionally modulated synchronization patterns evolve rapidly, are evident even before sensory inputs arrive, follow closely subjective readiness to process information in time, can be sustained for prolonged time periods, and convey specific information about perceptually selected sensory features and motor plans. These functional implications of selective synchronization patterns are complemented by recent insights about the mechanistic origins of rhythmic synchronization at micro- and macro- scales of cortical neuronal processing, suggesting that selective attention is subserved by precise neuronal synchronization that is selective in space, time and frequency.

Introduction

Top-down attention is the key mechanism to restructure cortical information flow in order to prioritize processing of behaviorally relevant over irrelevant and distracting information (Gilbert and Sigman, 2007). The behavioral consequences of attentional restructuring of information flow are manifold. Attended sensory inputs are processed more rapidly and accurately and with higher spatial resolution and sensitivity for fine changes, while non-attended information appears lower in contrast and is sometimes not perceived at all (Carrasco, et al. 2004; Simons and Rensink, 2005).

These functional consequences of attention require temporally dynamic and selective changes of neuronal interactions spanning multiple levels of neuronal information processing: Attentional selection modulates (i) interactions among single neurons within cortical microcircuits, (ii) it modulates the impact of selective local neuronal groups conveying relevant information within functionally specialized brain areas, and (iii) it controls long-range interactions among neuronal groups from distant brain areas (Maunsell and Treue, 2006; Mitchell et al. 2007, 2009; Reynolds and Chelazzi, 2004; Womelsdorf and Fries, 2007, Cohen and Maunsell, 2009).

For all these levels of neuronal interactions, converging evidence suggests that the selective modulation of interactions is critically built on selective synchronization. Neuronal synchronization is typically of oscillatory nature, i.e. neurons fire and pause together in a common rhythm. When synchronization is rhythmic, it is often addressed as coherence and we will use these terms interchangeably. This rhythmic synchronization can influence neuronal interactions in several ways: 1) Spikes that are synchronized will have a larger impact on a target neuron than spikes that are not synchronized (Azouz and Gray, 2003; Salinas and Sejnowski, 2001). 2.) Local inhibition that is rhythmically synchronized leaves periods without inhibition, while non-synchronized inhibition will prevent local network activity continuously (Tiesinga et al. 2004). 3.) Rhythmic synchronization of a local group of neurons will modulate the impact of input to that group, and therefore, the impact of rhythmic input will depend on the synchronization between input and target (Womelsdorf et al. 2007). These mechanisms are at work on all levels of attentional selection: At the level of microcircuits, inhibitory interneuron networks have been shown to impose rhythmic synchronization capable of effectively controlling the gain of the neuronal spiking output (Bartos et al. 2007; Tiesinga et al. 2008; Tiesinga and Buia 2009; Cardin et al., 2009). At the level of local neuronal groups, attention selectively synchronizes the responses of those neurons conveying information about the attended feature or location (Womelsdorf and Fries, 2007). And the coherent output from these local neuronal groups has been shown to selectively synchronize over long-range connections with task-relevant neuronal groups in distant brain regions (Buschman and Miller 2007; Saalmann et al. 2007; Schoffelen et al. 2005; Sejnowski and Paulsen 2006; Pesaran et al. 2009; Gregoriou et al. 2009).

These empirical insights suggest that mechanisms underlying neuronal synchronization could be primary mechanisms behind selective attention. In particular, top-down attention may act by biasing rhythmic synchronization to establish and sustain a selective neuronal communication structure (Fries, 2005). In the following, we begin by outlining this conceptual framework for selective attention through selective synchronization. We then survey basic insights from empirical and theoretical studies suggesting that rhythmic synchronization is

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particularly suited to control the selective routing of neuronal information flow, and review how attention recruits these mechanisms across all levels of cortical processing.

Attentional selection as a dynamic instantiation of a selective neuronal communication structure

During natural sensation, top-down control is dynamically established during ongoing processing. Experimentally, top-down signals are set by task instructions, and by instructional cues defining relevant and irrelevant sensory features of the input stream during task performance. In typical paradigms of selective attention, the sensory input is kept identical across trials with variations only in covert attention to different aspects of that input. In such tasks, neuronal responses are modulated with rapid temporal dynamics and high spatial selectivity throughout the cerebral cortex (Fig. 1A).

The temporal dynamics of attentional selection are illustrated by recent evidence of a rapid onset of selective neuronal response modulation in cortical areas as far apart as frontal cortex and primary visual cortices in the macaque brain (Khayat et al. 2006; Monosov et al. 2008; see also Gregoriou et al., 2009). In these studies, monkeys were instructed to detect a predefined target stimulus in visual displays to guide saccadic eye movement. In frontal and parietal cortex, attentional selection occurred within the first 120 ms following the sensory onset of target and distracter stimuli, allowing to predict the spatial focus of attention (Gottlieb, 2002; Monosov et al. 2008). Already about 30 ms later, top-down information changes neuronal responses at the earliest visual cortical processing stage in primary visual cortex (Khayat et al. 2006; Roelfsema, et al. 2007) evident in a response enhancement for neurons with receptive fields overlapping the attentional target stimulus. These findings demonstrate that top-down control restructures cortical activity to sensory inputs across distant cortical sites on a rapid time scale. Attention amplifies almost instantaneously (i.e. with the sensory response latency) the influence of local groups of neurons conveying behavioral relevant information, and attenuates the influence of neuronal groups coding for irrelevant inputs. This finding suggests that those distributed groups processing 'attended' inputs also interact effectively, establishing a selective neuronal communication structures on top of the existing infrastructure of anatomical connections (Fries 2005) (Fig 1A): Interactions among neurons conveying information about attended locations or features are rendered effective, while anatomical connections between neuronal groups activated by distracting information are rendered ineffective.

Beyond the temporal dynamics of attentional selection, its spatial selectivity in restructuring cortical information flow is particularly evident across successive processing stages in visual cortex. Neurons at the highest visual processing stage in IT cortex have receptive fields that span much of a visual field and respond selectively to complex objects composed of simpler visual features. Part of this selectivity arises from their broad and convergent anatomical input from neurons at earlier processing stages having smaller receptive fields and simpler tuning properties. During natural vision, the large receptive field of an IT neuron will typically contain multiple objects. However, when attention is directed to only one of those objects, the IT neuron's response is biased towards the response that would be obtained if only the attended object were presented (Chelazzi et al. 1993; Moran and Desimone 1985; Sejnowski and Paulsen 2006; Sheinberg and Logothetis 2001).

Such dynamic biasing of responses in IT cortex could be achieved by selective enhancement (suppression) of the impact of those afferent inputs from neurons in earlier visual areas coding for the attended (non-attended) input (Reynolds et al. 1999). However, the mechanisms underlying this up- and down- modulation of input gain for subsets of converging connections are only poorly understood, but likely entail a selective increase of temporally precise and coincident inputs from those neurons activated by an attended stimulus in earlier areas. This relevance of spike timing is suggested by fine grained attentional modulation of precise neuronal synchronization within area V4 (Fries et al. 2001; Bichot et al. 2005; Taylor et al. 2005; Womelsdorf et al. 2006; Chalk et al. 2009). Enhanced synchronization of the spiking output among those neuronal groups activated by attended sensory input (Fries et al. 2008) is resulting in enhanced coincident arrival of their spikes at their postsynaptic target neurons in area IT. Temporally coincident input is highly effective in driving neuronal activity (Azouz and Gray 2003; Salinas and Sejnowski 2001; Tiesinga et al. 2008). It is therefore likely that selective synchronization within area V4 underlies attentional biasing within IT cortex and could thus underlie effective spatial routing of information flow within visual cortex.

Note that neuronal synchronization is in principle independent of firing rate, both in terms of metrics and physiology. The different metrics used for quantifying synchronization are typically normalized for firing rate. Physiologically, there are examples where enhanced firing rates are associated with strongly reduced synchronization, e.g. the stimulus induced alpha-band desynchronization in the superficial layers of monkey V4 (Fries et al. 2008). Neuronal gamma-band synchronization typically emerges when neuronal groups are activated and therefore, it is in most cases associated with increased firing rates. However, firing rates and gamma-band synchronization can also be dissociated from each other and this can be found primarily when firing rate changes are not driven by changes in bottom-up input (e.g. stimulus changes), but rather by changes in top-down input (e.g. attention or stimulus selection) (Fries et al. 2002; Womelsdorf et al. 2006).

Synchronization is a neuronal population phenomenon and it is often very difficult to assess it with recordings from isolated single units. Correspondingly, many studies of neuronal synchronization use recordings of multi-unit activity and/or of the local field potential (LFP). The LFP reflects the summed trans-membrane currents of neurons within few hundred micrometers of tissue. Since synchronized currents sum up much more efficiently than unsynchronized currents, the LFP reflects primarily synchronized synaptic activity. Changes in LFP power typically correlate very well with changes in direct measures of neuronal synchronization.

Rhythmic synchronization within a neuronal group does not only increase its impact on postsynaptic target neurons in a feedforward manner. It also rhythmically modulates the group's ability to communicate, such that rhythmic synchronization between two neuronal groups likely subserves their interaction, because rhythmic inhibition within the two groups is coordinated and mutual inputs are optimally timed. We capture these implications in the framework of selective attention through selective synchronization (Fries, 2005).

Selective attention through selective synchronization

Local neuronal groups frequently engage in periods of rhythmic synchronization. During activated states, rhythmic synchronization is typically evident in the gamma frequency band (30 - 90 Hz) (Engel et al. 1990; Gray et al. 1989; Hoogenboom et al. 2005). In-vitro experiments and computational studies suggest that gamma-band synchronization emerges from the interplay of excitatory drive and rhythmic inhibition imposed by interneuron networks (Bartos et al. 2007; Börgers et al. 2005; Börgers and Kopell 2003; Buia and Tiesinga 2006). Interneurons impose synchronized inhibition onto the local network (Bartos et al. 2007; Hasenstaub et al. 2005; Vida et al. 2006). The brief time periods between inhibition provide time windows for effective neuronal interactions with other neuronal groups, because they reflect enhanced postsynaptic sensitivity to input from other neuronal groups, as well as maximal excitability for generating spiking output to other neuronal groups (Azouz 2005; Azouz and Gray 2003; Fries et al. 2007; Tiesinga et al. 2008). As a consequence, when two neuronal groups open their temporal windows for interaction at the same time, they will be more likely to mutually influence each other (Womelsdorf et al. 2007). The consequences for selective neuronal communication are illustrated in Fig. 1B: If the rhythmic synchronization within neuronal groups is precisely synchronized between the two groups, they are maximally likely to interact. By the same token, if rhythmic activity within neuronal groups is uncorrelated between groups or synchronizes consistently out of phase, their interaction is curtailed (Fig. 1B).

This scenario entails that the pattern of synchronization between neuronal groups flexibly structures the pattern of interactions between neuronal groups (Fig. 1C). Consistent with this hypothesis, the interaction pattern of one neuronal group (A) with two other groups (B and C) can be predicted by their pattern of precise synchronization (Fig. 1C). This has recently been demonstrated for interactions of triplets of neuronal groups from within and between areas in awake cat and monkey visual cortex (Womelsdorf et al. 2007). This study measured the trial-by-trial changes in correlated amplitude fluctuation and changes in precise synchronization between pair AB and pair AC, using the spontaneous variation of neuronal activity during constant visual stimulation. The strength of amplitude covariation, i.e. the covariation of power in the LFP and/or multiunit spiking responses, was considered the measure of mutual interaction strength. The results showed that the interaction strength of AB could be inferred from the phase of gamma band synchronization between group A with group B, being rather unaffected by the phase of synchronization of group A with group C (Fig. 1C). This finding was evident for triplets of neuronal groups spatially separated by as little as 650 µm illustrating a high spatial resolution and specificity of the influence of precise phase synchronization between neuronal groups on the efficacy of neuronal interaction. Importantly, additional analysis supported a mechanistic role for the phase of synchronization between rhythmic activities to modulate the effective interaction strength (Womelsdorf et al. 2007). In particular, precise phase synchronization preceded higher amplitude covariations in time by few milliseconds arguing for a causal influence of precise phase synchronization to trigger neuronal interactions. Taken together, these results provide the most direct evidence available so far to suggest a critical mechanistic role of selective synchronization for neuronal interactions. They demonstrate that synchronization patterns can shape neuronal interactions with high specificity in time, space, and frequency.

Importantly, these same characteristics of selective neuronal interactions are the key elements underlying selective attention. Attentional selection dynamically evolves at a rapid time scale and with high spatial resolution by enhancing (reducing) the effective connectivity among neuronal groups conveying task relevant (irrelevant) information. Such dynamic restructuring of neuronal interactions could be accomplished through mechanisms evoking selective synchronization patterns within interneuron networks. Selective changes of precise synchronization in local neuronal groups are capable of modulating in a self-emergent manner selective interaction patterns across neuronal groups (Börgers and Kopell 2008; Mishra et al. 2006; Tiesinga et al. 2008; Tiesinga and Buia, 2009).

The outlined scheme of selective attention implemented as selective neuronal synchronization comprises explicit assumptions that selective attention affects interneuron networks and synchronization patterns during task performance. The following surveys the available insights on interneuron networks and review the emerging signatures of attentional modulation of selective synchronization patterns in macaque cortex.

Synchronization in interneuron networks and their attentional modulation

Interneurons comprise about a fifth of the neuron population, but despite their ubiquitous presence, their functional roles underlying cortical computations or cognitive processes are far from understood (Markram et al. 2004). However, a central role for the control of local cortical network activity has been suggested for the large class of interneurons of the basket cell type (Buzsaki, 2006). These neurons target perisomatic regions of principal cells and are thereby capable of determining the impact of synaptic inputs arriving at sites distal to a cell's soma. Such perisomatic connectivity critically controls the input gain of principal cells across a large population of principal cells (Cardin et al. 2009; Tiesinga and Sejnowski, 2009; Buzsaki et al. 2007; Cobb et al. 1995; Markram et al. 1998; Rudolph et al. 2007; Tiesinga et al. 2004). As described above, the inhibitory synaptic influence is inherently rhythmic at high frequencies, carrying stronger gamma band power than pyramidal cells (Cardin et al. 2009; Bartos et al. 2007; Hasenstaub et al. 2005).

The prominent role of these high frequency inputs in shaping the spiking output of principal cells has recently been demonstrated directly in cat and rodent visual cortex. It was shown that the spiking of principal cells is indeed preceded by brief periods of reduced inhibition (Rudolph et al. 2007; see also Fig. 8 of Hasenstaub et al. 2005 and Fig. 4 of Cardin et al. 2009). Taken together, these findings suggest that interneurons are the source of rhythmic inhibition onto a local group of neurons synchronizing the discharge of pyramidal cells to the time windows between inhibition.

In the context of selective attention, interneuron networks could be activated by various possible sources. They may be activated by transient, and spatially specific neuromodulatory inputs (Lin et al. 2006; Rodriguez et al. 2004). Alternatively, selective attention could target local interneuron networks directly via top-down inputs from neurons in upstream areas (Buia and Tiesinga 2008, 2009; Mishra et al. 2006; Tiesinga et al. 2008). In these models, selective synchronization emerges either by depolarizing selective subsets of interneurons (Buia and Tiesinga 2008; Tiesinga and Sejnowski 2004), or by biasing the phase of rhythmic activity in a more global inhibitory interneuron pool (Mishra et al. 2006). In either case, rhythmic inhibition controls the spiking responses of groups of excitatory neurons, enhancing

the impact of those neurons spiking synchronously within the periods of disinhibition, while actively reducing the impact of neurons spiking asynchronous to this rhythm. This suppressive influence on excitatory neurons, which are activated by distracting feedforward input, reflects the critical ingredient for the concept of selective attention through selective synchronization: Attention not only enhances synchronization of already more coherent activity representing attended stimuli, but actively suppresses the synchronization and impact of groups of neurons receiving strong, albeit distracting inputs, because they arrive at non-optimal phase relations to the non-inhibited periods in the target group. The computational feasibility of both facilitatory and suppressive aspects, and the critical role of the timing of inhibitory circuits, have recently received direct support (Börgers and Kopell 2008; Tiesinga and Buia 2009).

Despite the prominent computational role of interneuron activity for selective communication, there are only sparse insights into their implications in selective information processing during cognitive task performance. The basic prediction from the above models is that interneurons are attentionally modulated. Consistent with this presupposition, a recent study by Mitchell, Sundberg and Reynolds reports a clear attentional modulation of putative interneurons in visual area V4 during a selective attention task requiring monkeys to track moving grating stimuli (Mitchell et al. 2007). Putative interneurons showed similar relative increases in firing rate and greater increases in reliability compared to putative pyramidal neurons. However, tests of more refined predictions about the relative modulation of synchronization and the phase relation of spiking responses of inhibitory and excitatory neuron types still need to be conducted (Buia and Tiesinga 2008).

Selective modulation of synchronization during attentional processing.

Direct evidence for the functional significance of selective synchronization within local neuronal groups for attentional selection has been obtained from recordings in macaque visual cortical area V4 (Fries et al. 2001; Taylor et al. 2005; Womelsdorf et al. 2006; Chalk et al. 2010; Gregoriou et al. 2009). One consistent result across studies in V4 is that spatial attention enhances gamma-band synchronization within those neuronal groups with receptive fields overlapping the attended location. The enhanced rhythmic synchronization is strongly evident within the LFP signal and in more precise synchronization of neuronal spiking responses to the LFP. Importantly, the synchronization among the spiking output from neurons coding for the attended location is also enhanced compared to the spiking output of neurons activated by a non-attended distractor stimulus (Fig. 2) (Fries et al. 2008). These attentional effects on spike-to-spike synchronization imply that the postsynaptic targets receive more coherent input from those neuronal groups conveying behaviorally relevant information.

Functional implications of selective gamma band synchronization.

In addition to the described attentional effect, recent studies demonstrated that the precision of local synchronization in visual area V4 is closely related to task performance, including behavioral accuracy and the reaction time to detect behaviorally relevant stimulus changes (Taylor et al. 2005; Womelsdorf et al. 2006). The relation to behavioral accuracy was derived from an error analysis of the pattern of synchronization in area V4 (Taylor et al. 2005). In this study, the spatial focus of attention could be inferred from the pattern of synchronization measured through epidural electrodes. Gamma band synchronization was not

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only stronger for correct trials than for miss trials, but additionally, the degree of synchronization predicted whether the monkey was paying attention to the distracter. Thus, this study demonstrated that gamma-band synchronization reflects the actual allocation of attention rather than merely the attentional cueing itself. The link to reaction time was made in a recent study, which demonstrated that the precision of stimulus induced gamma-band synchronization predicts how rapidly a stimulus change can be reported behaviorally. When monkeys were spatially cued to select one of two stimuli in order to detect a color change of the attended stimulus, the speed of change detection could be partly predicted by the strength of gamma band synchronization shortly before the stimulus change actually occurred (Womelsdorf et al. 2006). Importantly, the reaction times to the stimulus change could not be predicted at times before the stimulus change by overall firing rates, nor by synchronization outside of the gamma band. Notably, the correlation of gamma band synchronization with the speed of change detection showed high spatial selectivity: Neurons activated by an unattended stimulus engaged in lower synchronization when the monkeys were particularly fast in responding to the stimulus change at locations outside their receptive field. This finding rules out a possible influence of globally increased synchronization during states of enhanced alertness and arousal (Herculano-Houzel et al. 1999; Munk et al. 1996; Rodriguez et al. 2004). And it argues for a fine-grained influence of synchronization to modulate the effective transmission of information about the stimulus change to postsynaptic target areas concerned with the planning and execution of responses.

These behavioral correlates of gamma band synchronization during selective attention tasks are complemented by a variety of correlational results linking enhanced gamma band synchronization to efficient task performance in various attention-demanding paradigms. For example, in memory-related structures, the strength of gamma band synchronization has been linked to the successful encoding and retrieval of information (Montgomery and Buzsaki, 2007; Sederberg et al. 2003, 2006; Jutras et al. 2009).

Selective gamma band coherence beyond visual cortex.
These results of selective gamma band synchronization with selective spatial attention are supported by a growing number of converging findings from human EEG and MEG studies (Doesburg et al. 2007; Fan et al. 2007; Wyart and Tallon-Baudry, 2008; Siegel et al. 2008). Importantly, attention modulates gamma band synchronization beyond sensory visual cortex. It has been reported for auditory cortex (Kaiser et al. 2006; Tiitinen et al. 1993) and more recently in somatosensory cortex (Bauer et al. 2006; Hauck et al. 2007). Spatial attention for tactile discrimination at either the right or left index finger in humans enhanced stimulus induced gamma band synchronization in primary somatosensory cortex when measured with MEG. Similar topographies and dynamics of gamma band synchronization correlate with the actual perception of somatosensory induced pain (Gross et al. 2007). Importantly, enhanced oscillatory dynamics in the gamma band during tactile perception is not restricted to the somatosenroy cortex (Ohara et al. 2006). In recent intracranial recordings in humans, synchronization was modulated across somatosensory cortex, medial prefrontal and insular regions when subjects had to direct attention to painful tactile stimulation (Ohara et al. 2006).

Spatially specific synchronization patterns during preparatory attentional states.

The described gamma band modulation of rhythmic activity is most prominent during activated states. However, attentional top-down control biases neuronal responses in sensory cortices already before sensory inputs impinge on the neuronal network (Fries et al. 2001; Fries et al. 2008; Luck et al. 1997; Siegel et al. 2008; Schroeder et al. 2010). In many attention studies, the instructional cue period is followed by a temporal delay void of sensory stimulation. During these preparatory periods, top-down signals set the stage for efficient processing of expected stimulus information, rendering local neuronal groups ready to enhance the representation of attended sensory inputs. Intriguingly, the described preparatory bias is evident in selective synchronization patterns in the gamma band.

In macaque visual cortical area V4, neurons gamma synchronize their spiking responses to the LFP more precisely when monkeys expected a target stimulus at the receptive field location of the respective neuronal group (Fig. 2B). This modulation was evident even though rhythmic activity proceeded at far lower levels in the absence of sensory stimulation compared to synchronization strength during high contrast sensory drive. Lower overall strength, and correspondingly lower signal-to-noise ratio, may account for the lack of significant gamma band modulation of LFP power or spike-to-spike synchronization during the pre-stimulus period when compared to attentional modulation during stimulation (Fig. 2).

During preparatory periods, and thus in the absence of strong excitatory drive to the local network, rhythmic activity is dominated by frequencies lower than the gamma band. In the described study from macaque V4, pre-stimulus periods were characterized by alpha band peaks of local rhythmic synchronization when monkeys attended away from the receptive field of the neuronal group. Fig. 2B,C demonstrates reduced locking of neuronal spiking in the alpha band to the LFP and to spiking output of nearby neurons (Fig. 2B,C). This finding agrees with various studies reporting reduced alpha band activity during attentional processing (Bauer et al. 2006; Pesaran et al. 2002; Rihs et al. 2007; Worden et al. 2000; Wyart and Tallon-Baudry 2008; Siegel et al. 2008). Interestingly, human EEG studies extend this finding by showing that the degree of alpha frequency desynchronization during prestimulus intervals of visuo-spatial attention tasks indicate how fast a forthcoming target stimulus is processed (Jin et al. 2006; Sauseng et al. 2006; Thut et al. 2006). For example, reaction times to a peripherally cued target stimulus are partially predicted by the lateralization of alpha activity in a one second period before target appearance (Thut et al. 2006). While this predictive effect was based predominantly on reduced alpha band responses over the hemisphere processing the attended position, recent studies suggest that alpha band oscillations are selectively enhanced within local neuronal groups processing distracting information, i.e. at unattended locations (Kelly et al. 2006; Rihs et al. 2007; Yamagishi et al. 2003). These findings suggest that rhythmic alpha band synchronization may play an active role in preventing the signaling of stimulus information. According to this hypothesis, attention up-regulates alpha band activity of neuronal groups expected to process distracting stimulus information, rather than to down-regulate local alpha band synchronization for neuronal groups processing attended stimulus features and locations.

Synchronization patterns reflecting temporal expectancies of target processing.

The previous paragraph surveyed evidence for an influence of spatially specific expectancy of target and distracter stimuli on synchronization patterns in visual cortex. In addition

to spatially selective expectancy, the expectation of the occurrence of behaviorally relevant target events is known to influence neuronal synchronization patterns and firing rates in parietal and frontal cortex (Ghose and Maunsell, 2002; Janssen and Shadlen, 2005; Riehle 2005; Schoffelen et al. 2005; Pesaran et al. 2008; Gregoriou et al. 2009; Schroeder and Lakatos 2009). Attentional modulation of neuronal firing rates in extrastriate visual area MT is strongest around the time point at which the subjective anticipation for a target change, given that it had not occurred before in the trial (i.e. the hazard rate), is maximal (Ghose and Maunsell 2002). In premotor and motor cortex, the hazard rate is smoothly reflected in the strength of synchronization (Riehle, 2005; Schoffelen et al. 2005). Importantly, enhanced readiness to respond to attended sensory changes is thereby functionally closely linked to long-range synchronization of motor cortex with spinal motor units suggesting a direct mechanistic influence of synchronization on the speed to respond to behaviorally relevant sensory events (Schoffelen et al. 2005).

An influence of temporal expectancy on synchronization in early sensory cortices has recently been demonstrated in recordings in primary visual cortex of macaques (Lakatos et al. 2008). In this study, monkeys were cued to detect deviant sensory stimuli in either an auditory or visual input stream to receive reward. Auditory and visual stimuli alternated, and both stimulus streams followed a noisy 1.55 Hz rhythm. This low frequency rhythm of sensory inputs entrained neuronal responses in early visual cortex, such that responses to individual stimuli in the visual stream added to the entrained response. Attention to the visual stream amplified the entrainment (Fig. 3A), but the most prominent attentional effect was evident in the phase of the 1.55 Hz entrainment in the superficial layers of visual cortex: This entrainment was always determined by the stimulus stream that was attended, i.e. it switched by half a cycle when attention switched from the visual to the auditory stream (Fig. 3B), which had a phase opposite to the visual stream. Importantly, low frequency fluctuations in the LFP likely reflect fluctuations in neuronal excitability. With attention to the visual (auditory) input stream, the phase corresponding to maximal (minimal) neuronal excitability occurred around the average time when the target information was most likely to reach visual cortex. Consistent with a functional role of the entrained delta phase, the authors reported the strongest attentional enhancement of gamma band synchronization in the LFP and spiking activity around this time (Fig. 3C,D), and showed that the detection of deviant visual stimuli was fastest (slowest) when the delta phase at stimulus onset corresponded to maximal (minimal) neuronal excitability (Fig. 3E).

The described results suggest that top-down information selectively modulates excitability in early sensory cortices through changes in the phase of rhythmic entrainment in these areas (Lakatos et al. 2009). The exact frequency band underlying excitability modulations may extend from the low delta band, directly imposed by the stimulus structure in the described study, to the theta band around 4–8 Hz. This suggestion may be derived from the time-frequency evolution of LFP power in the theta band and its attentional modulation, shown in Fig. 3A. Intriguingly, similar to the effect of delta phase on the gamma band response demonstrated directly in the discussed study (Figure 3B), previous studies have linked the phase of rhythmic activity in the theta band to the strength of high frequency gamma band synchronization in rodent hippocampus and over large regions in the human cortex (Canolty et al. 2006; Csicsvari et al. 2003). An additional hint suggesting a functional relevance of low

frequency phase fluctuations can be found in a recent study demonstrating that spiking responses in rodent prefrontal cortex phase lock to theta band activity in the hippocampus during task epochs requiring spatial decisions in a working memory context (Jones and Wilson 2005). In macaque visual cortex, the phase of theta band synchronization has been directly linked to selective maintenance of task related information (Lee et al. 2005). Taken together, the emerging evidence demonstrates (i) that top-down, task-related information modulates low frequency rhythmic activity, (ii) that the phase of this rhythmic activity can be functionally related to task performance, and (iii) that the phase of low frequency activity shapes the strength of gamma band synchronization in response to sensory inputs. As such, the pattern of selective synchronization in the gamma band described in the previous paragraphs could be tightly linked to underlying, selective low frequency activity modulations. Whether both are coupled in an obligatory way, or whether the co-modulation may be triggered by specific task demands, will be an interesting subject for future research (Schroeder et al. 2010).

Feature-selective modulation of rhythmic synchronization.

The preceding sections discussed evidence for selective neuronal synchronization patterns evolving with space-based attentional selection of sensory inputs. However, in addition to spatial selection, attention frequently proceeds only on top-down information about the behaviorally relevant sensory feature and independent of the exact spatial location at which input impinges on sensory cortices. Such feature-based attention is known to modulate the responses of neurons tuned to the attended feature such as a particular motion direction, or the color of a visual stimulus (Maunsell and Treue 2006).

Importantly, a recent study demonstrated that attention to a particular feature selectively synchronizes the responses of neurons tuned to the attended stimulus feature (Bichot et al. 2005). In this study, spiking responses and LFPs were recorded in macaque visual area V4 while monkeys searched in multi-stimulus displays for a target stimulus defined either by color, shape, or both. When monkeys searched e.g. for a red stimulus by shifting their gaze across stimuli on the display, the non-foveal receptive fields of the recorded neurons could either encompass non-target stimuli (e.g. of blue color), or the (red) target stimulus prior to the time when the monkey detected the target. The authors found that neurons synchronized to the LFP stronger in response to their preferred stimulus feature when it was the attended search target feature rather than a distracter feature.

Thus, attention enhanced synchronization of the responses of those neurons sharing a preference for the attended target feature - and irrespective of the spatial location of attention (Bichot et al. 2005). This feature-based modulation was also evident during a conjunction search task involving targets defined by two features: When monkeys searched for a target stimulus with a particular orientation and color (e.g. a red horizontal bar), neurons with preference to one of these features enhanced their neuronal synchronization (Bichot et al. 2005). This enhancement was observed not only in response to the color-shape defined conjunction target, but also in response to distracters sharing one feature with the target (e.g. red color). This latter finding corresponds well with the behavioral consequences of increased difficulty and search time needed for conjunction defined targets.

This study shows that feature salience is indexed not only by changes in firing rates (Martinez-Trujillo and Treue, 2004; Treue and Martinez Trujillo, 1999; Wannig et al. 2007),

but also by selectively synchronizing neuronal responses depending on the similarity between neuronal feature preferences and the attended stimulus feature. The mechanisms behind this selective influence of featural top-down information could be based on a similar spatial weighting of interneuron network activity as implicated for spatial selection. Neuronal tuning to many basic sensory features is organized in regularly arranged local maps. Correspondingly, the tuning of groups of neurons measured with the LFP is locally highly selective. Importantly, neuronal stimulus preference is systematically related to the strength of neuronal synchronization in the gamma frequency band. This has been demonstrated for stimulus orientation and spatial frequency (Frien et al. 2000; Gray et al. 1990; Kayser and König 2004; Kreiter and Singer 1996; Siegel and König 2003), the speed and direction of visual motion (Liu and Newsome, 2006), and the spatial motor intentions and movement directions (Scherberger and Andersen 2007; Scherberger et al. 2005). These findings show that rhythmic synchronization conveys feature selective information. Feature-based attention appears to recruit this property with high spatial resolution by modulating which neurons synchronize to the local rhythmic activity.

Taken together, the previous subsections surveyed the accumulating evidence demonstrating selective neuronal synchronization patterns that evolve with selective spatial and feature-based attention within sensory cortices. Only few studies have extended these insights to investigate how selective attention modulates selective neuronal interaction patterns between different visual areas and between visual and higher-order cortical areas during task performance. Recent evidence shows that such dynamic inter-areal interaction patterns are evident in long-range synchronization patterns between cortical areas.

Selective inter-areal synchronization during attentional processing

In the preceding sections, selective synchronization patterns evolved for local neuronal groups in sensory cortices supporting a functional role for gamma band synchronization for the selective restructuring of neuronal communication during attentional processing (Fig. 1). However, attentional processing relies on effective interactions *between* local subsets of neuronal groups from distant cortical regions. So far, only few studies have investigated these inter-areal interaction patterns during task epochs with selective attention (Engel et al. 2001; Varela et al. 2001; Womelsdorf and Fries 2007). The emerging evidence from these studies points towards a critical role of rhythmic long-range synchronization in the gamma band (Gregoriou et al. 2009; see Fig. 4) and at lower frequencies, most prominently at beta frequencies ranging from 15 Hz to 30 Hz.

Early studies in awake cats demonstrated transiently enhanced beta frequency synchronization among visual cortical and premotor regions, and between visual cortex and thalamus during non-selective states of expectancy of a behaviorally relevant stimulus (in e.g. 'Go/No-Go tasks') (Roelfsema et al. 1997; von Stein et al. 2000; Wrobel et al. 2007). Recent studies in the macaque monkey have extended these findings by showing that fronto-parietal and intra-parietal interactions between areas are accompanied by synchronization at beta frequencies (15-35 Hz) during task epochs requiring searching for and selecting behaviorally relevant visual stimuli (Buschman and Miller 2007; Saalmann et al. 2007; Pesaran et al. 2008). Fig. 5 illustrates findings from a visual search task requiring monkeys to detect a search target that is either salient and pops out among distracting stimuli ("bottom-up

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search"), or that is non-salient by sharing features with distracting stimuli (Buschman and Miller, 2007). In contrast to bottom-up salient targets, the non-salient target stimuli were detected more slowly, indicating that they require attentive search through the stimuli in the display before they are successfully detected ("top-down search"). Paralleling the difference in behavioral demands, the authors found a selective synchronization pattern among the LFPs in frontal and parietal cortex. While attentive "top-down search" enhanced specifically rhythmic synchronization at 20-35 Hz compared to the "bottom-up" search, the stimulus driven "bottom-up" search resulted in stronger inter-areal synchronization in the gamma-frequency band (Fig. 5b). The pattern of results is most likely due to relative differences in task demands in both search modes and was unaffected by differences in reaction times. Therefore these findings suggest that inter-areal communication during attentional top-down control is conveyed particularly through rhythmic synchronization in a high beta band, either in addition to, or separate from the frequency of rhythmic interactions underlying bottom-up feedforward signaling (Engel and Fries 2010).

Consistent with a functional role for top-down mediated long-range neuronal communication, various experimental paradigms demanding attentive processing have shown long range synchronization in a broad beta band, although mostly at frequencies below 25 Hz. The following provide a few examples of beta band modulation in recent studies using very different task paradigms: Choosing freely a sequence of target stimuli for arm movements induces 15 Hz coherence among neurons in premotor cortex and the parietal reach region when compared to instructed searches (Pesaran et al. 2008). Notably, during periods of enhanced inter-areal coherence, spiking activity in premotor cortex was more predictive of the direction of forthcoming arm movements compared to periods of lower coherence (Pesaran et al. 2008). Variations in reaction times and readiness to respond to a sensory change event induced corresponding fine-grained variations of motor-spinal coherence in the beta band (Schoffelen et al. 2005). Somatosensory and motor cortex synchronize in the beta band during sensorimotor integration (Brovelli et al. 2004). Selective working memory maintenance in a delayed match-to-sample task results in stronger coherence in the beta band between higher visual areas in humans (Tallon-Baudry et al. 2001) and locally predicts performance in a similar task in the monkey (Tallon-Baudry et al. 2004). The failure to detect a target stimulus in a rapid stream of stimuli in the attentional blink paradigm is associated with reduced fronto-parietal and fronto-temporal beta band synchronization (Gross et al. 2004). And as a last example for a potential functional role of beta band activity, the perception of coherent objects from fragmented visual scenes goes along with transiently enhanced beta band synchronization of the LFP among prefrontal, hippocampal and lateral occipital sites (Sehatpour et al. 2008).

Taken together, these diverse findings agree to suggest that inter-areal synchronization critically subserves neuronal interactions during attentive processing. In the surveyed studies, synchronization in a broadly defined beta band occurred selectively during task epochs requiring effective neuronal integration of information across distributed cortical areas. However, further studies need to elucidate the properties of particular frequency bands and their characteristic recruitment during specific tasks (Kopell et al. 2000).

Concluding Remarks

Selective attention describes a central top-down process that restructures neuronal activity patterns to establish a selective representation of behavioral relevance. The surveyed evidence suggests that attention achieves this functional role by selectively synchronizing those neuronal groups conveying task relevant information. Attentionally modulated synchronization patterns evolve rapidly, are evident even before sensory inputs arrive, follow closely subjective readiness to process information in time, can be sustained for prolonged time periods, and carry specific information about top-down selected sensory features and motor aspects.

In addition to these functional characteristics, insights into the physiological origins of synchronization have begun to shed light on the mechanistic underpinning of selective neuronal interaction patterns at all spatial scales of cortical processing: At the level of single neurons and local microcircuits, studies are deciphering the role of inhibitory interneuron networks, how precise timing information is conveyed and sustained even at high oscillation frequencies, and how rhythmic synchronization among interneurons is actively made robust against external influences (Bartos et al. 2007; Vida et al. 2006). These insights are integrated at the network level in models demonstrating how selective synchronization patterns evolve in a self-organized way (Börgers and Kopell, 2008; Tiesinga et al. 2008). Acknowledging those basic physiological processes underlying the dynamic generation of selective synchronization seems to be pivotal to elucidate further the mechanistic working principles of selective attention in the brain.
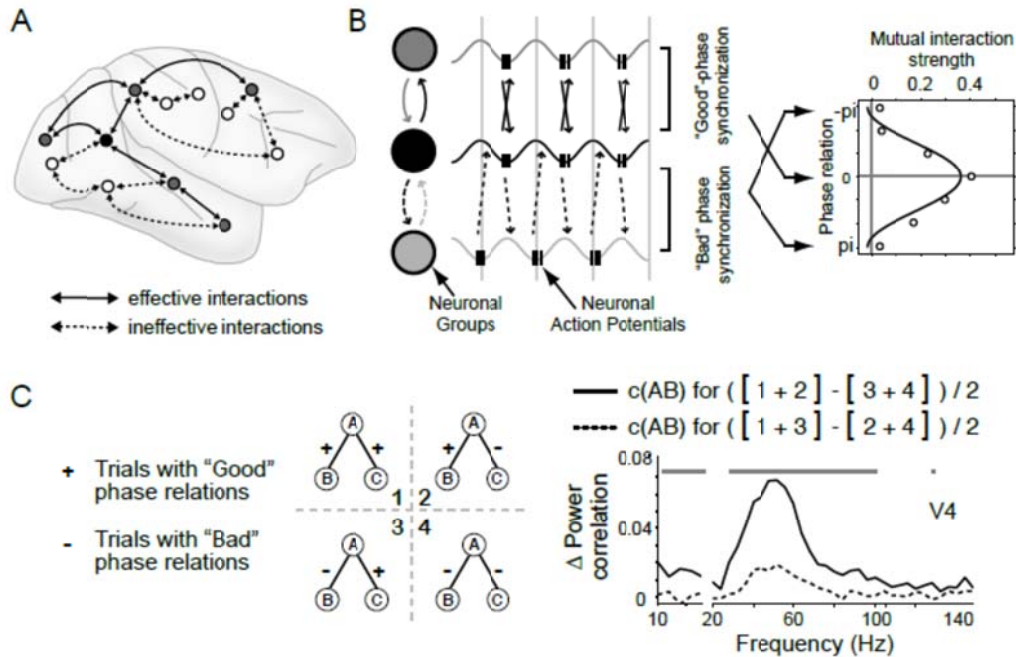
Figure 1 Selective synchronization renders neuronal interactions among subsets of neuronal groups effective. **(A)** Anatomical connectivity (sketched as lines) provides a rich infrastructure for neuronal communication among neuronal groups (circles) throughout the cortex. With selective attention, only a small subset of these connections are rendered effective (solid lines). Interactions among groups conveying irrelevant information (light grey circles) for the task at hand are rendered less effective (dashed lines). **(B)** Illustration of the hypothesized role of selective synchronization for selective communication among three neuronal groups (circles). Rhythmic activity (LFP oscillations with spikes in troughs) provide briefly reoccurring time windows of maximum excitability (LFP troughs), which are either in-phase (black and dark grey groups), or in anti-phase (black and light grey groups). The plot on the right shows that mutual interactions (upper axis, correlation of the power of the LFP and the neuronal spiking response between neuronal groups) are high during periods of in-phase synchronization and lower otherwise. **(C)** The trial-by-trial interaction pattern between neuronal groups (A-to-B, and A-to-C) is predicted by the pattern of synchronization: If AB synchronizes at a good phase, their interaction is strongest, irrespective of whether A synchronizes with C at good or bad phase relations in the same trials. Thus, the spatial pattern of mutual interactions can be predicted by the phase of synchronization among rhythmically activated neuronal groups. Panels in (B) and (C) adapted from (Womelsdorf et al. 2007).
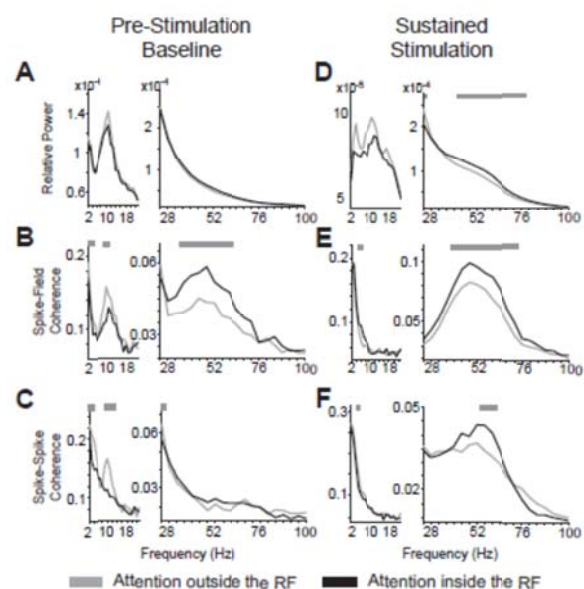
Figure 2 The pattern of attentional modulation of synchronization in macaque visual area V4 before and during sensory stimulation (A-C) Attentional modulation of relative LFP power (A), spike-to-LFP coherence (B) and spike-to-spike coherence (C) across low and high frequencies during the baseline period of a spatial attention task. Monkeys either attended (dark lines) or ignored (grey lines) the receptive field location of the recorded neuronal groups in blocks of trials. (D-F) Attentional modulation of the neuronal response during stimulation with an attended/ignored moving grating. Same format as in (A-C). Horizontal grey bars denote frequencies with significant attentional effects. Adapted from (Fries et al. 2008).
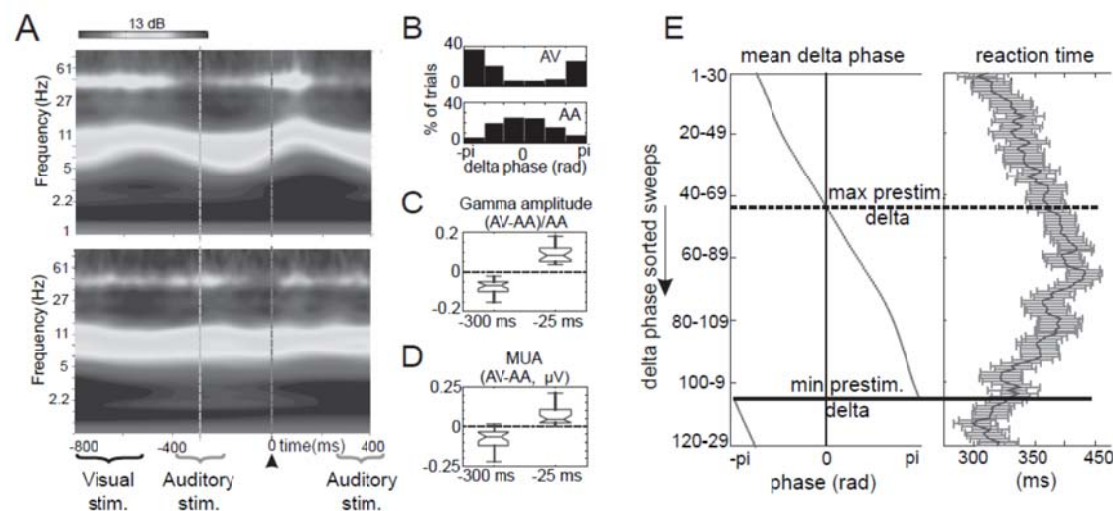

Figure 3 Entrainment of synchronization from delta- to gamma- band frequencies in supragranular layers of the primary visual cortex during an auditory-visual change detection task. (B) Time-frequency spectrograms during attention to the visual (upper panel) and auditory (bottom panel) input stream, aligned to the onset time of the visual stimulus. The task cued monkeys to detect infrequent deviant stimuli in either the auditory (white noise tones), or visual (red light flashes) input stream. Visual (auditory) stimuli were onset at a regular interval of 650ms ± 150ms indicated below the time axis (mean stimulus rate = 1.55 Hz). (C) Entrainment of delta frequency phase in visual cortex measured as the delta (1.55 Hz) phase at the time of visual stimulus onset when attention was directed to the visual (upper panel) and auditory (lower panel) modality across recording sessions. (D, E) Modulation of gamma band amplitude of the LFP (D) and multiunit activity (E) before and at visual stimulus onset. Positive values indicate enhancement with visual versus auditory attention. (F) Reaction times (x-axis) to the visual target stimulus sorted into groups of trials according to the pre-stimulus delta phase (at

0ms to stimulus onset) (y-axis). Solid/ dashed horizontal lines indicate the group of trials corresponding to maximum/minimum delta amplitudes. Adapted from (Lakatos et al. 2008).
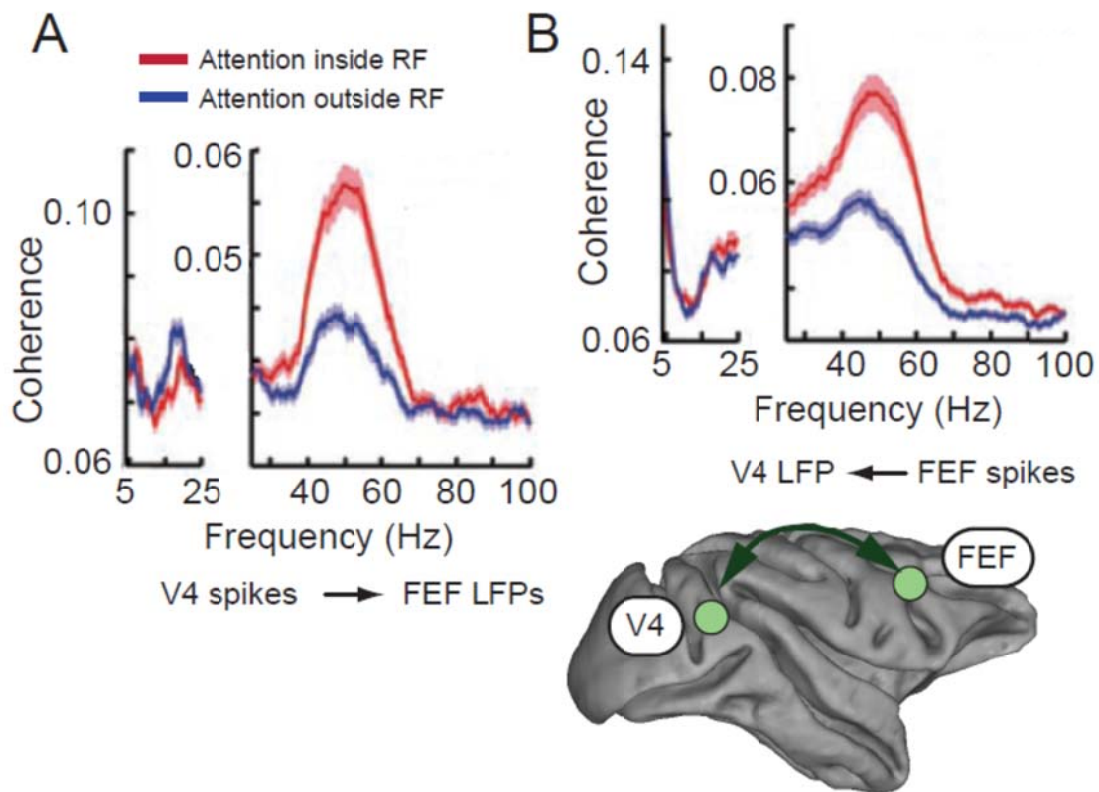

Figure 4 Selective modulation of long-range synchronization between the frontal eye field (FEF) and visual area V4 during states of selective visual attention (Gregoriou et al., 2007). (A) Coherence (*y-axis*) of spike trains in V4 to the local field potential (LFP) in FEF, across frequency (*x-axis*), when attention was directed to a stimulus inside (red) and outside (blue) the receptive field (V4) and response field (FEF). Recording areas are indicated in the macaque brain outline below the panel. (B) Same as in A, but depicting the coherence between spiketrains in FEF and the LFP in V4. Adapted from (Gregoriou et al., 2007).
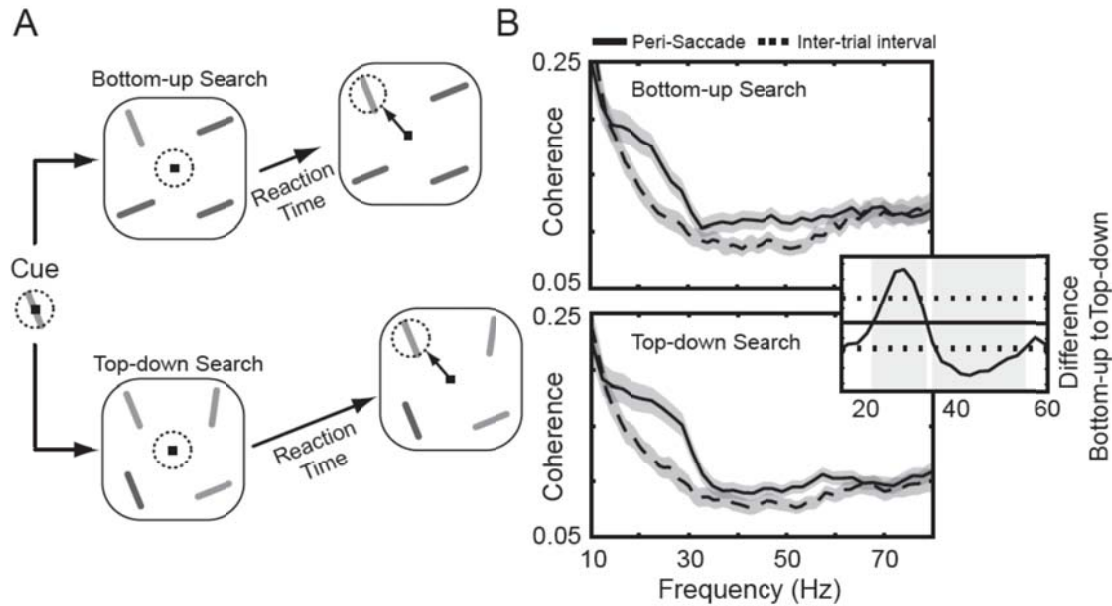
Figure 5 Selective modulation of long-range synchronization between frontal and parietal cortex during visual search. (**A**) Sketch of two visual search tasks used by (Buschman and Miller, 2007). A cue instructed monkeys about the orientation and color of a bar that was the later search target in a multi-stimulus display during a bottom-up search task (both, target color and orientation was unique, upper panels) and during a a top-down search task (target shared color or orientation with distracting stimuli, bottom panels). Monkeys covertly attended the multi-stimulus array and made a saccade to the target stimulus position as soon as they found it. The authors measured the coherence of the LFP activity of neuronal groups in the frontal eye field and dorso-lateral prefrontal cortex) and parietal area LIP. The line plots on the right show the coherence (y-axis) for different frequency bands (x-axis) in the bottom-up and top-down tasks, along with the coherence difference across tasks (solid line in inlet). The results show that attentional demand modulated long-range fronto-parietal coherence at different frequency bands. Adapted from (Buschman and Miller, 2007).

References

Azouz R (2005) Dynamic spatiotemporal synaptic integration in cortical neurons: neuronal gain, revisited. J Neurophysiol, 94(4):2785-2796

Azouz R, Gray CM (2003) Adaptive coincidence detection and dynamic gain control in visual cortical neurons in vivo. Neuron, 37(3):513-523

Bartos M, Vida I, Jonas P (2007) Synaptic mechanisms of synchronized gamma oscillations in inhibitory interneuron networks. Nat Rev Neurosci, 8(1):45-56

Bauer M, Oostenveld R, Peeters M, Fries P (2006) Tactile spatial attention enhances gamma-band activity in somatosensory cortex and reduces low-frequency activity in parieto-occipital areas. J Neurosci, 26(2):490-501

Bichot NP, Rossi AF, Desimone R (2005) Parallel and serial neural mechanisms for visual search in macaque area V4. Science, 308(5721):529-534

Börgers C, Epstein S, Kopell NJ (2005) Background gamma rhythmicity and attention in cortical local circuits: A computational study. Proc Natl Acad Sci U S A, 102(19):7002-7007

Börgers C, Kopell NJ (2003) Synchronization in networks of excitatory and inhibitory neurons with sparse, random connectivity. Neural Comput, 15(3):509-538

Börgers C, Kopell NJ (2008) Gamma oscillations and stimulus selection. Neural Comput, 20(2):383-414

Brovelli A, Ding M, Ledberg A, Chen Y, Nakamura R, Bressler SL (2004) Beta oscillations in a large-scale sensorimotor cortical network: directional influences revealed by Granger causality. Proc Natl Acad Sci U S A, 101(26):9849-9854

Buia C, Tiesinga P (2006) Attentional modulation of firing rate and synchrony in a model cortical network. J Comput Neurosci.

Buia CI, Tiesinga PH (2008) The role of interneuron diversity in the cortical microcircuit for attention. J Neurophysiol.

Buschman TJ, Miller EK (2007) Top-down versus bottom-up control of attention in the prefrontal and posterior parietal cortices. Science, 315(5820):1860-1862

Buzsaki G (2006) Rhythms of the Brain. Oxford New York: Oxford University Press Inc.

Buzsaki G, Kaila K, Raichle M (2007) Inhibition and brain work. Neuron, 56(5):771-783

Canolty RT, Edwards E, Dalal SS, Soltani M, Nagarajan SS, Kirsch HE, Berger MS, Barbaro NM, Knight RT (2006) High gamma power is phase-locked to theta oscillations in human neocortex. Science, 313(5793):1626-1628

Cardin JA, Carlen M, Meletis K, Knoblich U, Zhang F, Deisseroth K, Tsai LH, Moore CI (2009) Driving fast-spiking cells induces gamma rhythm and controls sensory responses. Nature 459:663-667

Carrasco M, Ling S, Read S (2004) Attention alters appearance. Nat Neurosci, 7(3):308-313

Chalk M, Herrero JL, Gieselmann MA, Delicato LS, Gotthardt S, Thiele A Attention reduces stimulus-driven gamma frequency oscillations and spike field coherence in V1. Neuron 66:114-125

Chelazzi L, Miller EK, Duncan J, Desimone R (1993) A neural basis for visual search in inferior temporal cortex. Nature, 363(6427):345-347

Cobb SR, Buhl, EH, Halasy K, Paulsen O, Somogyi P (1995) Synchronization of neuronal activity in hippocampus by individual GABAergic interneurons. Nature, 378(6552):75-78

Cohen MR, Maunsell JH (2009) Attention improves performance primarily by reducing inter-neuronal correlations. Nat Neurosci 12:1594-1600

Csicsvari J, Jamieson B, Wise KD, Buzsaki G (2003) Mechanisms of gamma oscillations in the hippocampus of the behaving rat. Neuron, 37(2):311-322

Doesburg SM, Roggeveen AB, Kitajo K, Ward LM (2007) Large-Scale Gamma-Band Phase Synchronization and Selective Attention. Cereb Cortex.

Engel AK, Fries P, Singer W (2001) Dynamic predictions: oscillations and synchrony in top-down processing. Nat Rev Neurosci, 2(10):704-716

Engel AK, Konig P, Gray CM, Singer W (1990) Stimulus-Dependent Neuronal Oscillations in Cat Visual Cortex: Inter-Columnar Interaction as Determined by Cross-Correlation Analysis. Eur J Neurosci, 2(7), 588-606.

Engel AK, Fries P (2010) Beta-band oscillations--signalling the status quo? Curr Opin Neurobiol 20:156-165.

Fan J, Byrne J, Worden MS, Guise KG, McCandlissa BD, Fossella J, Posner MI (2007) The relation of brain oscillations to attentional networks. J Neurosci, 27(23):6197-6206

Frien A, Eckhorn R, Bauer R, Woelbern T, Gabriel A (2000) Fast oscillations display sharper orientation tuning than slower components of the same recordings in striate cortex of the awake monkey. Eur J Neurosci, 12(4):1453-1465

Fries P (2005) A mechanism for cognitive dynamics: neuronal communication through neuronal coherence. Trends Cogn Sci, 9(10):474-480

Fries P, Neuenschwander S, Engel AK, Goebel R, Singer W (2001) Rapid feature selective neuronal synchronization through correlated latency shifting. Nat Neurosci, 4(2):194-200

Fries P, Nikolic D, Singer W (2007) The gamma cycle. Trends Neurosci, 30(7):309-316

Fries P, Reynolds JH, Rorie AE, Desimone R (2001) Modulation of oscillatory neuronal synchronization by selective visual attention. Science, 291(5508):1560-1563

Fries P, Schröder JH, Roelfsema PR, Singer W, Engel AK (2002) Oscillatory neuronal synchronization in primary visual cortex as a correlate of stimulus selection. J Neurosci, 22(9):3739-3754

Fries P, Womelsdorf T, Oostenveld R, Desimone R (2008) The effects of visual stimulation and selective visual attention on rhythmic neuronal synchronization in macaque area V4. J Neurosci, 28(18):4823-4835

Ghose GM, Maunsell JH (2002) Attentional modulation in visual cortex depends on task timing. Nature, 419(6907):616-620

Gilbert CD, Sigman M (2007) Brain states: top-down influences in sensory processing. Neuron, 54(5):677-696

Gottlieb J (2002) Parietal mechanisms of target representation. Curr Opin Neurobiol, 12(2):134-140

Gray CM, Engel AK, Konig P, Singer W (1990) Stimulus-Dependent Neuronal Oscillations in Cat Visual Cortex: Receptive Field Properties and Feature Dependence. Eur J Neurosci, 2(7):607-619

Gray CM, Konig P, Engel AK, Singer W (1989) Oscillatory responses in cat visual cortex exhibit inter-columnar synchronization which reflects global stimulus properties. Nature, 338(6213):334-337

Gregoriou GG, Gotts SJ, Zhou H, Desimone R (2009) High-frequency, long-range coupling between prefrontal and visual cortex during attention. Science 324:1207-1210

Gross J, Schmitz F, Schnitzler I, Kessler K, Shapiro K, Hommel B, Schnitzler A (2004) Modulation of long-range neural synchrony reflects temporal limitations of visual attention in humans. Proc Natl Acad Sci U S A, 101(35):13050-13055

Gross J, Schnitzler A, Timmermann L, Ploner M (2007) Gamma oscillations in human primary somatosensory cortex reflect pain perception. PLoS Biol, 5(5):e133

Hasenstaub A, Shu Y, Haider B, Kraushaar U, Duque A, McCormick DA (2005) Inhibitory postsynaptic potentials carry synchronized frequency information in active cortical networks. Neuron, 47(3):423-435

Hauck M, Lorenz J, Engel AK (2007) Attention to painful stimulation enhances gamma-band activity and synchronization in human sensorimotor cortex. J Neurosci, 27(35):9270-9277

Herculano-Houzel S, Munk MH, Neuenschwander S, Singer W (1999) Precisely synchronized oscillatory firing patterns require electroencephalographic activation. J Neurosci, 19(10):3992-4010

Hoogenboom N, Schoffelen JM, Oostenveld R, Parkes LM, Fries P (2005) Localizing human visual gamma-band activity in frequency, time and space. Neuroimage.

Janssen P, Shadlen MN (2005) A representation of the hazard rate of elapsed time in macaque area LIP. Nat Neurosci, 8(2):234-241

Jin Y, O'Halloran JP, Plon L, Sandman CA, Potkin SG (2006) Alpha EEG predicts visual reaction time. Int J Neurosci, 116(9):1035-1044

Jones MW, Wilson MA (2005) Theta rhythms coordinate hippocampal-prefrontal interactions in a spatial memory task. PLoS Biol, 3(12):e402

Jutras MJ, Fries P, Buffalo EA (2009) Gamma-band synchronization in the macaque hippocampus and memory formation. J Neurosci 29:12521-12531.

Kaiser J, Hertrich I, Ackermann H, Lutzenberger W (2006) Gamma-band activity over early sensory areas predicts detection of changes in audiovisual speech stimuli. Neuroimage, 30(4):1376-1382

Kayser C, König P (2004) Stimulus locking and feature selectivity prevail in complementary frequency ranges of V1 local field potentials. Eur J Neurosci, 19(2):485-489

Kelly SP, Lalor EC, Reilly RB, Foxe JJ (2006) Increases in alpha oscillatory power reflect an active retinotopic mechanism for distracter suppression during sustained visuospatial attention. J Neurophysiol, 95(6):3844-3851

Khayat PS, Spekreijse H, Roelfsema PR (2006) Attention lights up new object representations before the old ones fade away. J Neurosci, 26(1):138-142

Kopell N, Ermentrout GB, Whittington MA, Traub RD (2000) Gamma rhythms and beta rhythms have different synchronization properties. Proc Natl Acad Sci U S A, 97(4):1867-1872

Kreiter AK, Singer W (1996) Stimulus-dependent synchronization of neuronal responses in the visual cortex of the awake macaque monkey. J Neurosci, 16(7):2381-2396

Lakatos P, Karmos G, Metha AD, Ulbert I, Schroeder CE (2008) Entrainment of Neuronal Oscillations as a Mechanism of Attentional Selection. Science, 320(5872):110-113

Lakatos P, O'Connell MN, Barczak A, Mills A, Javitt DC, Schroeder CE (2009) The leading sense: supramodal control of neurophysiological context by attention. Neuron 64:419-430

Lee H, Simpson GV, Logothetis NK, Rainer G (2005) Phase locking of single neuron activity to theta oscillations during working memory in monkey extrastriate visual cortex. Neuron, 45(1):147-156

Lin SC, Gervasoni D, Nicolelis MA (2006) Fast modulation of prefrontal cortex activity by basal forebrain noncholinergic neuronal ensembles. J Neurophysiol, 96(6):3209-3219

Liu J, Newsome WT (2006) Local field potential in cortical area MT: stimulus tuning and behavioral correlations. J Neurosci, 26(30):7779-7790

Luck SJ, Chelazzi L, Hillyard SA, Desimone R (1997) Neural mechanisms of spatial selective attention in areas V1, V2, and V4 of macaque visual cortex. J Neurophysiol, 77(1):24-42

Markram H, Toledo-Rodriguez M, Wang Y, Gupta A, Silberberg G, Wu C (2004) Interneurons of the neocortical inhibitory system. Nat Rev Neurosci, 5(10):793-807

Markram H, Wang Y, Tsodyks M (1998) Differential signaling via the same axon of neocortical pyramidal neurons. Proc Natl Acad Sci U S A, 95(9):5323-5328

Martinez-Trujillo JC, Treue S (2004) Feature-based attention increases the selectivity of population responses in primate visual cortex. Curr Biol, 14(9):744-751

Maunsell JH, Treue S (2006) Feature-based attention in visual cortex. Trends Neurosci, 29(6):317-322

Mishra J, Fellous JM, Sejnowski TJ (2006) Selective attention through phase relationship of excitatory and inhibitory input synchrony in a model cortical neuron. Neural Netw, 19(9):1329-1346

Mitchell JF, Sundberg KA, Reynolds JH (2007) Differential Attention-Dependent Response Modulation across Cell Classes in Macaque Visual Area V4. Neuron, 55(1):131-141

Mitchell JF, Sundberg KA, Reynolds JH (2009) Spatial attention decorrelates intrinsic activity fluctuations in macaque area V4. Neuron 63:879-888

Monosov IE, Trageser JC, Thompson KG (2008) Measurements of Simultaneously Recorded Spiking Activity and Local Field Potentials Suggest that Spatial Selection Emerges in the Frontal Eye Field. Neuron, 57(4):614-625

Montgomery SM, Buzsaki G (2007) Gamma oscillations dynamically couple hippocampal CA3 and CA1 regions during memory task performance. Proc Natl Acad Sci U S A, 104(36):14495-14500

Moran J, Desimone R (1985) Selective attention gates visual processing in the extrastriate cortex. Science, 229(4715):782-784

Munk MH, Roelfsema PR, Konig P, Engel AK, Singer W (1996) Role of reticular activation in the modulation of intracortical synchronization. Science, 272(5259):271-274

Ohara S, Crone NE, Weiss N, Lenz FA (2006) Analysis of synchrony demonstrates 'pain networks' defined by rapidly switching, task-specific, functional connectivity between pain-related cortical structures. Pain, 123(3):244-253

Pesaran B, Pezaris JS, Sahani M, Mitra PP, Andersen RA (2002) Temporal structure in neuronal activity during working memory in macaque parietal cortex. Nat Neurosci, 5(8):805-811

Pesaran B, Nelson MJ, Andersen RA (2008) Free choice activates a decision circuit between frontal and parietal cortex. Nature 453:406-409

Reynolds JH, Chelazzi L (2004) Attentional modulation of visual processing. Annu Rev Neurosci, 27:611-647

Reynolds JH, Chelazzi L, Desimone R (1999) Competitive mechanisms subserve attention in macaque areas V2 and V4. J Neurosci, 19(5):1736-1753

Riehle A (2005) Preparation for action: one of the key functions of motir cortex. In A. Riehle and E. Vaadia (Eds.), Motor Cortex in Voluntary Movements: A dsitributed system for distributed functions (Vol. 1, pp. 213-240) Boca Raton, FL: CDC Press.

Rihs TA, Michel CM, Thut G (2007) Mechanisms of selective inhibition in visual spatial attention are indexed by alpha-band EEG synchronization. Eur J Neurosci, 25(2):603-610

Rodriguez R, Kallenbach U, Singer W, Munk MH (2004) Short- and long-term effects of cholinergic modulation on gamma oscillations and response synchronization in the visual cortex. J Neurosci, 24(46):10369-10378

Roelfsema PR, Engel AK, König P, Singer W (1997) Visuomotor integration is associated with zero time-lag synchronization among cortical areas. Nature, 385(6612):157-161

Roelfsema PR, Tolboom M, Khayat PS (2007) Different processing phases for features, figures, and selective attention in the primary visual cortex. Neuron, 56(5):785-792

Rudolph M, Pospischil M, Timofeev I, Destexhe A (2007) Inhibition determines membrane potential dynamics and controls action potential generation in awake and sleeping cat cortex. J Neurosci, 27(20):5280-5290

Saalmann YB, Pigarev IN, Vidyasagar TR (2007) Neural mechanisms of visual attention: how top-down feedback highlights relevant locations. Science, 316(5831):1612-1615

Salinas E, Sejnowski TJ (2001) Correlated neuronal activity and the flow of neural information. Nat Rev Neurosci, 2(8):539-550

Sauseng P, Klimesch W, Freunberger R, Pecherstorfer T, Hanslmayr S, Doppelmayr M (2006) Relevance of EEG alpha and theta oscillations during task switching. Exp Brain Res, 170(3):295-301

Scherberger H, Andersen RA (2007) Target selection signals for arm reaching in the posterior parietal cortex. J Neurosci, 27(8):2001-2012

Scherberger H, Jarvis MR, Andersen RA (2005) Cortical local field potential encodes movement intentions in the posterior parietal cortex. Neuron, 46(2):347-354

Schoffelen JM, Oostenveld R, Fries P (2005) Neuronal coherence as a mechanism of effective corticospinal interaction. Science, 308(5718):111-113

Schroeder CE, Lakatos P (2009) Low-frequency neuronal oscillations as instruments of sensory selection. Trends Neurosci 32:9-18

Schroeder CE, Wilson DA, Radman T, Scharfman H, Lakatos P (2010) Dynamics of Active Sensing and perceptual selection. Curr Opin Neurobiol 20:172-176

Sederberg PB, Gauthier LV, Terushkin V, Miller JF, Barnathan JA, Kahana MJ (2006) Oscillatory correlates of the primacy effect in episodic memory. Neuroimage, 32(3):1422-1431

Sederberg PB, Kahana MJ, Howard MW, Donner EJ, Madsen JR (2003) Theta and gamma oscillations during encoding predict subsequent recall. J Neurosci, 23(34):10809-10814

Sederberg PB, Schulze-Bonhage A, Madsen JR, Bromfield EB, McCarthy DC, Brandt A, Tully MS, Kahana MJ (2006) Hippocampal and Neocortical Gamma Oscillations Predict Memory Formation in Humans. Cereb Cortex.

Sehatpour P, Molholm S, Schwartz TH, Mahoney JR, Mehta AD, Javitt DC, Stanton PK, Foxe JJ (2008) A human intracranial study of long-range oscillatory coherence across a frontal-occipital-hippocampal brain network during visual object processing. Proc Natl Acad Sci U S A, 105(11):4399-4404

Sejnowski TJ, Paulsen O (2006) Network oscillations: emerging computational principles. J Neurosci, 26(6):1673-1676

Sheinberg DL, Logothetis NK (2001) Noticing familiar objects in real world scenes: the role of temporal cortical neurons in natural vision. J Neurosci, 21(4):1340-1350

Siegel M, König P (2003) A functional gamma-band defined by stimulus-dependent synchronization in area 18 of awake behaving cats. J Neurosci, 23(10):4251-4260

Siegel M, Donner TH, Oostenveld R, Fries P, Engel AK (2008) Neuronal synchronization along the dorsal visual pathway reflects the focus of spatial attention. Neuron 60:709-719

Simons DJ, Rensink RA (2005) Change blindness: past, present, and future. Trends Cogn Sci, 9(1):16-20

Tallon-Baudry C, Bertrand O, Fischer C (2001) Oscillatory synchrony between human extrastriate areas during visual short-term memory maintenance. J Neurosci, 21(20):RC177

Tallon-Baudry C, Mandon S, Freiwald WA, Kreiter AK (2004) Oscillatory synchrony in the monkey temporal lobe correlates with performance in a visual short-term memory task. Cereb Cortex, 14(7):713-720

Taylor K, Mandon S, Freiwald WA, Kreiter AK (2005) Coherent oscillatory activity in monkey area v4 predicts successful allocation of attention. Cereb Cortex, 15(9):1424-1437

Thut G, Nietzel A, Brandt SA, Pascual-Leone A (2006) Alpha-band electroencephalographic activity over occipital cortex indexes visuospatial attention bias and predicts visual target detection. J Neurosci, 26(37):9494-9502

Tiesinga P, Fellous JM, Sejnowski TJ (2008) Regulation of spike timing in visual cortical circuits. Nat Rev Neurosci, 9(2):97-107

Tiesinga PH, Fellous JM, Salinas E, Jose JV, Sejnowski TJ (2004) Inhibitory synchrony as a mechanism for attentional gain modulation. J Physiol Paris, 98(4-6):296-314

Tiesinga P, Sejnowski TJ (2009) Cortical enlightenment: are attentional gamma oscillations driven by ING or PING? Neuron 63:727-732

Tiesinga PH, Buia CI (2009) Spatial attention in area V4 is mediated by circuits in primary visual cortex. Neural Netw 22:1039-1054

Tiesinga PH, Sejnowski TJ (2004) Rapid temporal modulation of synchrony by competition in cortical interneuron networks. Neural Comput, 16(2):251-275

Tiitinen H, Sinkkonen J, Reinikainen K, Alho K, Lavikainen J, Naatanen R (1993) Selective attention enhances the auditory 40-Hz transient response in humans. Nature, 364(6432):59-60

Treue S, Martinez Trujillo JC (1999) Feature-based attention influences motion processing gain in macaque visual cortex. Nature, 399(6736):575-579

Varela F, Lachaux JP, Rodriguez E, Martinerie J (2001) The brainweb: phase synchronization and large-scale integration. Nat Rev Neurosci, 2(4):229-239.

Vida I, Bartos M, Jonas P (2006) Shunting inhibition improves robustness of gamma oscillations in hippocampal interneuron networks by homogenizing firing rates. Neuron, 49(1):107-117

von Stein A, Chiang C, König P (2000) Top-down processing mediated by interareal synchronization. Proc Natl Acad Sci U S A, 97(26):14748-14753

Wannig A, Rodriguez V, Freiwald WA (2007) Attention to Surfaces Modulates Motion Processing in Extrastriate Area MT. Neuron, 54(4):639-651

Womelsdorf T, Fries P (2007) The role of neuronal synchronization in selective attention. Curr Opin Neurobiol, 17(2):154-160

Womelsdorf T, Fries P, Mitra PP, Desimone R (2006) Gamma-band synchronization in visual cortex predicts speed of change detection. Nature, 439(7077):733-736

Womelsdorf T, Schoffelen JM, Oostenveld R, Singer W, Desimone R, Engel AK, Fries P (2007) Modulation of neuronal interactions through neuronal synchronization. Science, 316(5831):1609-1612

Worden MS, Foxe JJ, Wang N, Simpson GV (2000) Anticipatory biasing of visuospatial attention indexed by retinotopically specific alpha-band electroencephalography increases over occipital cortex. J Neurosci, 20(6):RC63

Wrobel A, Ghazaryan A, Bekisz M, Bogdan W, Kaminski J (2007) Two streams of attention-dependent beta activity in the striate recipient zone of cat's lateral posterior-pulvinar complex. J Neurosci, 27(9):2230-2240

Wyart V, Tallon-Baudry C (2008) Neural dissociation between visual awareness and spatial attention. J Neurosci, 28(10):2667-2679

Yamagishi N, Callan DE, Goda N, Anderson SJ, Yoshida Y, Kawato M (2003) Attentional modulation of oscillatory activity in human visual cortex. Neuroimage, 20(1):98-113