Different frequencies for different scales of cortical integration: from local gamma to long range alpha/theta synchronization

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Abstract

Cortical activity and perception are not driven by the external stimulus alone; rather sensory information has to be integrated with various other internal constraints such as expectations, recent memories, planned actions, etc. The question is how large scale integration over many remote and size-varying processes might be performed by the brain. We have conducted a series of EEG recordings during processes thought to involve neuronal assemblies of varying complexity. While local synchronization during visual processing evolved in the gamma frequency range, synchronization between neighboring temporal and parietal cortex during multimodal semantic processing evolved in a lower, the beta (12–18 Hz) frequency range, and long range fronto-parietal interactions during working memory retention and mental imagery evolved in the theta and alpha (4–8 Hz, 8–12 Hz) frequency range. Thus, a relationship seems to exist between the extent of functional integration and the synchronization-frequency. In particular, long-range interactions in the alpha and theta ranges seem specifically involved in processing of internal mental context, i.e. for top-down processing. We propose that large scale integration is performed by synchronization among neurons and neuronal assemblies evolving in different frequency ranges. © 2000 Elsevier Science B.V. All rights reserved.

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1. Introduction

Sensory information is known to be propagated along the various input channels to the cortex. To be used efficiently, however, this information has to be integrated with various other sensory information and, more important, with internal constraints such as the behavioral goal pursued in each particular situation. Evidently, this integration cannot be a sequential processing, as the
behavioral goal substantially influences the selection of stimuli and thus the perceptual process per se (‘top-down’ processes). Rather, the multiple brain processes have to mutually influence each other in any moment in time to produce a coherent and behaviorally adequate outcome. Local stimulus properties have been shown to induce synchronous activity among visual sensory cortical neurons (for review see Singer and Gray, 1995; König and Engel, 1995). Similar processes have been shown in other sensory domains (de Charms and Merzenich, 1996; Murthy and Fetz, 1992). Also, neuronal activity related to motor planning, expectancy and decision making has been established (Riehle et al., 1998; Shadlen and Newsome, 1996). It is, however, not known how the different processes interact to obtain a multiple constraint satisfaction, and in particular, how such large scale integration might be performed by the brain.

We describe a series of EEG recordings during processes thought to involve neuronal assemblies of varying complexity. While local sensory integration evolved with a fast, gamma ($25–70$ Hz) dynamics, multisensory integration evolved with an intermediate, beta ($12–18$ Hz) dynamics, and long-range integration during top-down processing evolved with a temporal dynamics in a low, theta/alpha ($4–12$ Hz) frequency range. Inspired by these results we propose that large-scale integration is performed by synchronization among neurons and neuronal assemblies evolving with varying temporal dynamics.

2. Relationship between scalp EEG and cortical processing

Since synchronization of cortical activity was found to play a role in cortical processing, it seems of great benefit to investigate fast temporal dynamics also in humans. Traces of intracortical potentials can be measured even at distant electrodes, on the scalp (EEG), allowing to investigate processes with fast temporal dynamics — albeit with low spatial resolution — also in human subjects. This allows us to extend the study of synchronization processes onto humans, which is desirable since in particular demanding top-down processes are only accessible in human subjects.

What is the relationship between EEG and cortical processing? The EEG measured at a site on the scalp consists of the summed electrical field potentials from cortical neurons in a certain volume of tissue under the electrode. Cortical field potentials are generated by postsynaptic dendritic currents. If several dendrites are arranged in parallel they generate potentials that can be measured at the scalp, at sites which are perpendicular to these dendrites. Effective contribution comes mostly from the synchronized components of cortical activity (Cooper et al., 1965; Elul, 1972; Nunez, 1995, 2000). Besides synchronous input to the cortical input layers which produces the dipolar field of the evoked potential (e.g. Creutzfeldt et al., 1969), there is a continuous change in cooperativity within the cortical network even without external stimulation (intrinsic potentials, Bullock, 1995; Lopes da Silva, 1991). This changing pattern of synchronization and desynchronization within different neuronal groups of the network generates the macroscopic potentials of the ongoing EEG (Elul, 1972). Since intrinsic potentials stem from the network interactions, they generate low amplitude fields which are effective only in close vicinity, thus influencing the potentials mostly at individual scalp electrodes. It has been estimated that one electrode integrates cortical input under a scalp surface of the order of $10 \text{ cm}^2$ (Nunez, 1995). Changes in the degree of synchronization of this intrinsic activity are reflected in changes in EEG amplitude of different frequencies at the scalp. Investigation of induced changes of EEG spectral parameters (see contributions to this volume), thus, is a suitable method to detect stimulus-induced changes of synchronization of this intrinsic activity (Rappelsberger and Petsche, 1988; Makeig, 1993; von Stein et al., 1993; Tallon et al., 1995; Lutzenberger et al., 1995; Müller et al., 1996).

While EEG amplitude predominantly reflects the amount of synchronized activity in the underlying tissue, the degree of interactions between two signals can be measured by coherence (Rap-
Coherence is a statistical measure: the value of coherence depends on the amount of repeated correlations between events in the frequency domain. The phase relationship between the two signals is irrelevant; however, it must be stable. Since the signal at each electrode-site mostly reflects the network activity under the electrode, coherence between two electrodes should measure interactions between two neuronal populations; while cortico-cortical correlations occupy only a minute part of the power of the EEG-signal at each site, the statistical nature of coherence helps to unravel them from noise if they repeat consistently. Despite the success of cross-correlation analysis in intracortical recording, analysis of inter-areal interactions has only been rarely applied to the human EEG (Sarnthein et al., 1998; von Stein et al., 1999a; Rodriguez et al., 1999). A technical question is whether functional coherence can be distinguished from coherence arising because of volume conduction between two electrodes. As the spatial resolution of EEG has been estimated to be approximately 5 cm (Nunez, 1995; Srinivasan et al., in press), with an electrode spacing of approximately 7 cm as in the 10/20 System volume conduction becomes less likely. Also, in volume conducted coherence, the amplitudes of the signals at the concerned electrodes should increase, and in both electrodes. To consider an increase in coherence as functionally relevant, we always check whether this is the case.

We aimed to investigate synchronization processes in humans using both amplitude and coherence analysis of the EEG.

3. Local, visual feature-dependent synchronization in the gamma frequency range

As a first step in using the scalp EEG for detection of synchronization processes in humans (von Stein et al., 1995), we had to relate to the results that were found in cats. In these experiments (review: Singer and Gray, 1995) it was shown that Gestalt criteria of coherency such as stimulus contingency and common motion are translated into coherent neuronal firing. The difficulty to be dealt with in reproducing these results with scalp recordings was the large amount of averaging that lies between the single neuronal potential and the scalp EEG. The following argument was used to develop an appropriate experimental design: if the coherency within a stimulus is translated into coherent neuronal firing, then by increasing the coherency within a stimulus we should be able to increase the amount of coherent neuronal activity, and in this way neuronal synchronization should become large enough to be macroscopically visible on the scalp. We therefore presented parallel grating stimuli (Fig. 1a) containing an increasing number of bars per texture and expected cortical synchronization to increase. Scalp EEG (Fig. 1b) was recorded during presentation of 16 such grating stimuli (n = 40 each) presented in a randomized order. Average power was determined in five frequency ranges. The hypothesis was that power in the gamma frequency range would increase with the number of bars per grating.

The experiment was performed in four different sessions. A positive correlation was indeed found (Fig. 1d) in all four experiments. The maximum of the correlation was at lateral occipital electrode sites, roughly corresponding to the horizontal median. No correlation was found over temporal cortex electrodes T5rT6. This is compatible with the interpretation that the increased power reflects increased synchrony among the columns of the first stages of visual cortex. In all subjects, two frequency ranges showed such a positive correlation with the number of bars per degree: gamma, and alpha. The increase of alpha was also present at temporal electrodes, indicating the involvement of alpha in spatially extended processes (see below). To control for a simple increase of the number of responding neurons to the higher density of contrasts, we presented a stimulus with the same amount of bars, with, however, disturbed coherency (Fig. 1c). If the increase in EEG power would be due to an increase in the mere number of generators and not their synchrony, then in the case of disturbed coherency, EEG power should remain equal (or increase due to the slight increase of contrast borders). This, however, was not the case. As
predicted by our hypothesis, gamma power during the uncoherent stimulus dropped considerably (Fig. 1e). Thus, the crucial feature playing a role was indeed the coherence in the stimulus and in the neuronal activity. These results indicate that, similar to what has been found in the cat, cortical synchronization in the gamma frequency range can be measured by EEG power in human subjects and reflects visual Gestalt criteria of coherency.

4. Supramodal processing induces temporoparietal interactions that evolve with a lower (12–18 Hz) temporal dynamics than gamma

As a next step to expand the knowledge about cortical synchronization, we wanted to investigate a related but more global process (von Stein et al., 1999a). Objects are more than visual features. Only if sensory experience through all sensory channels is consistent and if sensory–motor interactions lead to repeatedly similar results, then the organism will represent such a sensory constellation as an ‘object’. Thus, objects are multimodal, semantical entities. Until now, synchronization has been found locally, between neurons from different visual areas (Frien, 1994) and across the two visual hemispheres (Engel et al., 1991). Also, the relevance of synchronization has been extended to other sensory domains such as the auditory cortex or the motor cortex (deCharms and Merzenich, 1996; Murthy et al., 1992; Riehle et al., 1997). Few studies have shown perception-
related correlations between neurons from different modality-specific areas. If coherent activity between the different feature-representations is a possible mechanism to guarantee their binding into a unified percept (for review see König et al., 1995), however, then coherent activity should also be observed between neuronal populations from areas serving different modalities, e.g. during representation of multi-modal semantical entities, i.e. objects. Therefore, we investigated cortical

![Diagram](image)

**Fig. 2.** Stimuli: 40 concrete objects of daily life were presented in three modalities, as written word (written presentation), as spoken word (auditory presentation), and as picture (pictorial presentation). Additionally (not shown), non-sense items were presented in the same three modalities (non-sense pictures were line drawings consisting of the same elements as the pictorial presentations of objects, but not denoting known objects). Stimulus presentation 2 s, interstimulus intervals 2–3 s in all conditions. Stimuli of a category were presented in blocks; within each block, stimuli were randomized. As a baseline condition (EO, eyes open) subjects has to relax and fixate a spot on the screen positioned within the same distance as the features of the stimulus conditions. Recording and data analysis: EEG was recorded from 19 electrodes distributed over the scalp according to the 10–20 system sampling rate 128 Hz, time constant of 0.3 s and low-pass filtering at 35 Hz. Averaged power spectra, $C_{xx}$, and cross-power spectra, $C_{xy}$, for all neighboring electrode pairs were computed over the 2 s epochs of stimulus presentation for all six stimulus conditions and the control conditions. Spectral bins were averaged to obtain mean values for the six frequency ranges delta (2–4 Hz), theta (4–8 Hz), alpha (8–12 Hz), beta1 (13–18 Hz), beta2 (18–24 Hz) and gamma (24–32 Hz). Coherence $K_{xy}$ for two signals, $x$ and $y$, is equal to the average cross-power spectrum normalized by the averaged powers of the compared signals: $K_{xy} = (C_{xy})^2/(C_{xx}C_{yy})$. Coherence is the frequency domain equivalent to the cross-covariance function, it estimates the degree to which phases at the frequency of interest are dispersed. Statistically significant differences between the stimulus and the baseline condition were determined using a paired Wilcoxon test and were interpreted as induced power/coherence. (b) Results: Inter-electrode sites where coherence changed significantly with respect to the baseline condition are mapped, for all three presentation modes (written, auditory, pictorial). Solid lines indicate an increase, dashed lines indicate a decrease of coherence. Only changes that where significant with an error probability of $P < 0.05$ or better are depicted ($n = 19$ subjects). For a better anatomical orientation, electrode positions are depicted in relation to cortical structure as determined by an MRI study (Homan et al., 1987). The shaded areas indicate the variance of electrode positions obtained with the 10/20 system with respect to the cortical surface. Common to all three conditions dealing with objects is an increased coherence between electrodes above temporal and above parietal cortex (thick line) in the 13–18 Hz range, bilateral. (c) Same as (b) for the non-sense conditions. Common to the non-sense conditions is a similar increase in coherent activity between temporal and parietal electrodes, however mostly at the right hemisphere (thick line) (from: von Stein et al., 1999).
activity related to supramodal semantical processing of objects.

Our experimental design was to present the same object in three different modalities and to search for a correlate of modality independent processing, i.e. a common electrophysiological pattern underlying all three ways of presentation. In this study we extended the analysis of EEG power to the computation of spectral coherence, a measure for inter-areal cross-correlation. Forty daily life objects were presented as spoken words, as written words, and as pictures (n = 19 subjects) (Fig. 2a). EEG was measured over 19 electrodes covering the scalp (10/20 system). Power and inter-electrode coherence were computed in six different frequency ranges for each condition and for a baseline condition.

The question was whether any induced change of power and coherence appeared consistently in all three presentation modes. Such a consistently induced pattern was a change in inter-areal synchronization between temporal and parietal electrodes (Fig. 2b, black lines). Thus, modality independent processing of objects seems to induce synchronization of activity between temporal cortex and parietal cortex. Interestingly, there was no such consistent change of power at single electrodes, implying that there are no local ensembles that seem to be responsible for supramodal representations. The fact that the increase in coherence was not accompanied by an increase in power might be interpreted as increased phase locking between the neuronal activity of two cortical sites without an increase in the number of active neurons. Thus, what was commonly induced seems not a global activation of one specific area but rather a phase-locking between neurons of different cortical areas, i.e. members of a distributed ensemble. The frequency range of this synchronized activity was not gamma as seen during visually induced synchronization, but the lower beta 1 range (12–18 Hz).

Similar changes of temporo-parietal coherence but with a tendency of right hemisphere lateralization were found during a control condition, the presentation of pronounceable non-sense words (Fig. 2c), not, however, during non-pronounceable letter strings (data not shown). This confirms that the dominant process behind the temporo-parietal synchronization during object perception is the inter-modal binding. Furthermore, it stresses the importance of only the left temporo-parietal cortex for semantic processing. The left/right lateralization fits to common knowledge about hemispheric specialization (Kimura, 1973).

We did not only observe induced coherence in the beta 1 frequency range, but also in the gamma frequency range and other frequencies; the pattern of changes, however, was not attributable to one of the two aspects of processing addressed with this study, semantics or modality. Reasons that no sensory-specific gamma changes were observed might be, on one hand, that the gamma range investigated here was chosen rather low to avoid contamination with muscle artifacts. On the other hand, sensory-specific changes in gamma might occur on a shorter time scale; the window of our analysis, however, was chosen rather long (2 s) in order to detect late, longer lasting semantical components of processing.

A relation of supramodal, semantical processing to brain structures of temporal and parietal cortex is in agreement with early neuropsychological studies. The area of posterior parietal cortex, especially left angular gyrus, is known as a supramodal, integrating area (e.g. Luria, 1973), with lesions in that region leading to failure in cross-modal matching (Butters and Brody, 1968) and to deficits in forming higher integrative concepts (agnosias). Temporal cortex, on the other hand, is part of the ventral stream of visual processing and a higher order visual association cortex (e.g. Tanaka, 1996), and has also been shown to be involved in visual imagery (e.g. Roland and Gulyas, 1994). An increase of correlated activity between both structures, temporal cortex and parietal cortex, during perception of objects might therefore indicate an interaction between visual representations (temporal cortex) and higher order representations (parietal cortex) for multimodal semantic integration in humans. Furthermore, parietal cortex is a highly connected, supramodal center in the cortex, connected with different sensory cortices, association cortices, subcortical structures, etc. (Mesulam, 1990), thus making it a suitable candidate for the proposed
function of multimodal semantic integration. The interactions between temporal and parietal cortex might also be interpreted as indicating an integration of information carried by the dorsal and the ventral stream. It has often been proposed that the two have to be integrated at various levels (DeYoe and Van Essen, 1988).

Taken together, our results indicate that similar processes of binding as in the visual domain are also observable for multi-modal semantic objects; they deviate in the fact that synchronization during supra-modal processing does not evolve with a temporal dynamics in the gamma frequency, but in a lower (beta1, 12–18 Hz) frequency domain.

5. Very long range interactions during working memory processes evolve with a temporal dynamics in the theta (4–8 Hz) frequency range

In a third experiment, we investigated synchronization during a process known to involve a system of largely separated cortical areas (Sarnthein et al., 1998). Working-memory is known to involve at least two separate structures, prefrontal cortex and posterior association cortex. Additionally, during working-memory retention no external stimuli are presented to the brain, which allows us to investigate cortical activity during purely internal mental processes. Working-memory retention might be considered a prototype of ‘top-down’ activity, where the origin of this internal activity is still partly controlled by the previously presented stimulus.

Two subsets of a working memory paradigm were performed (Fig. 3a), both requiring the active retention of a stimulus in short term memory. In Task I (character strings), the stimulus was a string of 6–8 standard keyboard characters. First, the stimulus was presented for 6 s (perception interval). After stimulus offset, subjects actively retained the stimulus in memory for 4 s (retention interval) while fixating the dark screen. Finally, subjects were cued by a white screen onset to reproduce the stimulus with paper and pencil. Although there was no auditory stimulation in Task I, subjects reported transforming the visually-presented characters into phonological equivalents and rehearsing them subvocally during the retention interval. In Task II (visuo-spatial condition), stimuli were abstract line drawings activating visuo-spatial working memory. As a control condition, in the beginning of the session a 2-min period was chosen during which subjects fixated the dark computer screen. EEG was recorded during the 6 s of stimulus presentation, the retention period, and the baseline condition. Power and coherence were investigated for all four different epochs and changes with respect to a baseline condition were determined. Of major interest are the changes in power/coherence induced during the retention epoch; changes here reflect differences between two purely mental states without stimulus presentation, the baseline state and a state of mental rehearsal.

The major pattern of synchronization that was seen in both subsets of the mental rehearsal period was a highly significant interaction between prefrontal cortex and posterior cortex, in the theta frequency range (Fig. 3b). No such interaction was found during perception (Fig. 3c). Although significant interactions were found in other frequency ranges, the interactions in the theta range were the only interactions that were specific for the retention period (Table 1). Thus, our findings are evidence that synchronization of activity plays a role for mediating interactions between prefrontal cortex and posterior association cortex during working memory processes. The importance of these areas for working memory is well established by extensive experiments on humans and non-human primates using a variety of techniques. Single-cell recordings have found prefrontal and parietal neurons most active during delay periods in delayed-response tasks (Goldman-Rakic, 1997; Fuster, 1995). Several imaging studies on working memory in humans have reported increased activity in both prefrontal cortex and posterior regions (e.g. Smith et al., 1996; Tallon-Baudry et al., 1998). Anatomical studies indicate high connectivity between frontal and posterior association cortices (Goldman-Rakic, 1988). A functional interaction was already implied by the fact that cooling parietal cortex reduces the activity of prefrontal neurons in
macaque brain (Fuster, 1995), the interaction itself, however, had remained unclear. Our findings suggest that synchronized neuronal activity in the 4–8 Hz range plays a role in the interaction of posterior association cortex, where sensory information is thought to be stored, and prefrontal cortex, where relevant current information is held and continuously updated.

These findings indicate that very long range cortico-cortical interactions between prefrontal and posterior cortex during working memory retention evolve with a temporal dynamics in a low frequency range (theta, 4–8 Hz). Furthermore, they show that purely mental processes, i.e. processes without sensory input, may cause specific patterns of interactions and in a particular frequency range.

6. Relation between the size of a neuronal assembly and the frequency range of integration

In the set of experiments presented, the tasks were such that the cortical area involved extends over different length scales. During local visual processing, we found evidence for synchronization among members of ensembles reflecting stimulus coherence; in accordance with other reports (Singer and Gray, 1995) this synchronization evolved in the gamma frequency range. During semantical processing of objects, assemblies are multimodal and thus should be more extended. A pattern of synchronization was induced that consists of interactions between temporal cortex and parietal cortex. In contrast to the synchronization between columns in visual cortex, this interaction, however, evolved in a lower, the beta1 (12–18 Hz) frequency range. Finally, synchronous activity could even be found between the largely separated areas of frontal cortex and posterior association cortex during working memory retention. This very long-range interaction was found in the theta (4–8 Hz) frequency range. These results suggest a relation between the size and distance of an interaction and the frequency of synchronization: the larger the neuronal assembly involved, the lower the frequency in which activity in the assembly gets synchronized. Related evidence was found within primary visual cortex: the

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larger the spatial extent of a stimulus, the slower was gamma synchronization (Eckhorn, 1994). A theoretical framework for an inverse relation between frequency of activity and spatial scale of a network has been given by Nunez (1999). According to our results, however, the network is not defined on anatomical grounds but rather is recruited functionally according to the cognitive task. Together, we propose that as a manifestation of cooperative activity in larger neuronal ensemble, inter-areal synchronization during processes extending over more than one area evolve with a slower temporal dynamics than local visual processing.

The finding that gamma synchronization is a local process is further based on several observations from intracortical recordings. Synchronous activity in the gamma range was repeatedly shown to decline with distance, reaching unsynchronized levels at a distance between recording sites > 8–10 mm (Eckhorn, 1994; Bullock, 1995). This, however, raises questions regarding the hypothesis that feature binding is mediated by coherent neuronal activity, as coherency should not be restricted to local features but should also be found between largely separate areas. Our proposal that lower frequencies play a role in mediating long range interactions thus might resolve that question. In agreement with this proposal, simulation studies have shown that gamma synchrony is lost over longer distances and that lower frequency interactions are better suited to sustain long range synchronization (Kopell et al., 2000).

Recent evidence obtained with multiple recordings in area 17 and area 7 further confirmed this...
hypothesis, showing that intra-areal interactions evolved in the gamma range, while long range interactions were mediated by cross-correlations in lower, alpha and theta frequency ranges in cats (von Stein et al., 2000). In contradiction to those results showing gamma synchronization to be locally restricted, there are several reports showing gamma synchrony over longer distances such as between the two hemispheres (Engel et al., 1991) or between distant electrodes in EEG recordings (Rodriguez et al., 1999). The study by von Stein et al. (2000) partly solves this conflict, as it gives evidence that whether two sites show gamma synchronization or not does not depend on the absolute distance between the sites, but rather on the number of synapses involved in an interaction. Indeed, a common feature in most examples showing inter-areal gamma synchronization (e.g. Engel et al., 1991; Frien et al., 1994; Roelfsema et al., 1997; Castelo-Branco et al., 1998) are strong monosynaptic connections between the investigated areas. Similarly, the range of 8 mm where gamma synchronization was found within an area, is the range of the horizontal — monosynaptic — connections. Thus, gamma synchronization seems a local phenomenon in the sense of being restricted to monosynaptic interactions, either within one area or between neurons of different areas that are coupled monosynaptically.

Summarizing, we propose that long range integration during processes extending over more than one area is mediated by correlated activity in lower frequency ranges; a relationship might exist between the extension of the integrating process and the frequency range of synchronization.

7. Examples of complex multiple integration: the role of alpha/theta synchronization in top-down processes

Two of the above described observations concerning integration over largely extended cortical areas may be related: first, very long range integration occurred in a low frequency range (4–8 Hz), and second, long range interactions were dominant in a state without actual sensory input, in the retention period of a working memory paradigm. The mental rehearsal of pictorial items as during retention is a process where a ‘mental’ sensory experience is produced not by an external stimulus but by internal processes. Such a kind of activity is called top-down activity. Is there a general relation between low frequency interactions and top-down processes? Indeed, a similar predominance of low frequency interactions was found during other forms of purely internal mental activity. In a study on mental imagery, the predominant feature was an increased inter-areal coherence in the theta (4–8 Hz) and alpha (8–12 Hz) frequency range (Petsche et al., 1997), and during mentally playing an instrument we found characteristic coherence patterns in the alpha frequency range (unpublished data). This suggests that low frequency interactions in general might be a characteristic feature of top-down activities. During top-down processing the input into the sensory areas is highly convergent from multiple cortical areas. A commonly assumed goal of top-down processing is to produce a ‘summary’ of all momentary activities in the cortex to generate an hypothesis about fruitful future actions that might then guide the selection of new sensory input. The computation performed can thus be considered an integration over activities of most available cortical areas. Given the proposed relationship between the complexity of interaction (the number of elements taking part in the interaction) and the frequency range in which the dynamics in a network evolve, an involvement of low frequencies in the complex interactions of top-down processing seems a plausible generalization.

The described results imply that theta and in particular alpha activity are related to top-down processing. This may seem astonishing since alpha activity is commonly known as an ‘idling rhythm’ of the brain. We view this not as a contradiction but rather as supporting evidence. Our argument is the following: Large amplitude 8–12-Hz alpha activity is prevalent above the visual cortex in states with eyes closed and disappears upon eye opening. Alpha activity is also found with eyes opened, where it is maximal in states of quiet restfulness, i.e. in states without focussed attention, and disappears once attention
is focussed to a specific stimulus (Adrian, 1947). These two observations have led to the notion of alpha activity as reflecting an inactive cortex. Our proposal now is to redefine this notion. We propose that states with maximal alpha activity such as with eyes closed and during rest do not reflect inactive brain states, but rather reflect states with internal mental activity. Rather than reflecting the absence of cortical processing, they reflect the absence of bottom up processing and thus can be classified a pure form of top-down activity. In the light of this reinterpretation, the hypothesis that slow frequency interactions reflect top-down processing has gained further support in the classical alpha rhythm. It is maximal in situations where cortical processes are not determined by external stimuli but are driven by free floating associations, mental imagery, planning, etc. There is evidence that supports the interpretation that alpha is related to top-down processing instead of idling. Strong alpha activity has been found in cat intracortical recordings in states of intense expectancy (Chatila et al., 1992), i.e. in a state that is classically associated with top-down processing and generating hypothesis about the environment. Along similar lines, prestimulus background activity — dominated by activity in the alpha range — has a major influence on processing of sensory stimuli (Arieli et al., 1995, 1996), compatible with the top-down process of stimulus selection. Furthermore, although spindle generation in thalamocortical loops upon unarousal (Steriade et al., 1990) has often been used as a model for alpha generation, it has been shown that alpha may also be generated in cortex itself (Lopes da Silva and van Leeuwen, 1977). Finally, it has been found recently in behaving cats that top-down contexts exert an effect on alpha and theta inter-areal synchronization, with phase lags and a layer specificity compatible with a top-down directed interaction (von Stein et al., 1999b, 2000; Bernasconi and König, 1999). The plausibility of these ideas is also supported by a computer simulation on a cellular level (Siegel et al., 2000).

Top-down related changes in gamma frequency activity or synchronization has been observed in some experiments (e.g. Tallon-Baudry et al., 1998). These results provide no contradiction to the presented hypothesis, as for a useful processing of data, local information has to be integrated with top-down information, and top-down information also should be able to instantiate or maintain local sensory pattern of synchronization, as, e.g. is supposed to be the case during working memory retention.

We therefore propose that low frequency (theta, alpha) cortico-cortical interactions reflect ‘top-down’ processing, suberving the function to integrate over multiple simultaneous brain activities. Low frequency cortico-cortical interactions would allow the local gamma-synchronized processes to be integrated, thus forming a unified mental construction such as a mental image, a hypothesis, a planned action, or a ‘thought’.

8. Conclusions

Our results obtained in several EEG experiments in humans support the hypothesis that cortico-cortical interactions may occur on different scales, and that the complexity of interaction influences the temporal dynamics evolving within the integrating network. It was shown that local interactions during visual processing involve gamma frequency dynamics, semantical interactions between temporal and parietal cortex involve beta frequency dynamics, and very long range interactions during internal mental (top-down) processes such as working-memory-retention or visual imagery involve interactions in a low (theta or alpha) frequency range. Thus, an inverse relation exists between the scale of integration and the frequency of interaction. Additionally, these studies demonstrated the involvement of alpha/theta frequency interactions in processes reflecting internal mental activity, i.e. top-down effects. Both results may be related, and top-down processing may show low-frequency interactions as a reflection of a complex cortical computation, where the information of many cortical areas is massively integrated. In particular, large-scale low frequency interactions might allow an integration with the different local, fast gamma processes, with which sensory information from the periphery seems to be propagated ‘bottom-up’.
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