

THE NEURONAL CORRELATE OF CONSCIOUSNESS: UNITY IN TIME RATHER THAN SPACE?

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The state of the art and explanatory gaps

For many decades the search for the neuronal underpinnings of cognitive and executive functions has been guided by the behaviorist view that the brain is essentially a highly complex and versatile stimulus response machine. Consequently, neuroscientists set out to study the responses of neurons to sensory stimulations across the various stages of the processing hierarchy, and analyzed activation patterns associated with motor output, hoping that these strategies would eventually lead to reductionist explanations of the neuronal mechanisms that support cognition, memory, decision making, planning and motor behavior. The strategy to follow the transformation of activity from the sensory surfaces over the numerous levels of hierarchically-organized processing structures to the respective effector organs proved to be extremely fruitful. Comparison of brains from different species provided compelling evidence that basic principles according to which neurons function and exchange signals have been preserved throughout evolution with only minor modifications. For the comparatively simple nervous systems of certain invertebrates this behaviorist approach allowed for near complete descriptions of the neuronal mechanisms underlying particular behavioral manifestations. This nurtured the expectation that pursuing this research strategy would sooner or later allow us to explain in the same way the more complex behavior of mammals and ultimately also the highly differentiated cognitive functions of primates and human subjects. However, over the last decades, the pursuit of the behaviorist approach accumulated evidence that requires a revision of the classical hypothesis that emphasizes serial feed-forward processing of sensory information within hierarchically organized architectures. Although the existence of processing streams devoted to the various sensory modalities is undisputed, comprehensive analysis of the brain's connectome revealed as the prevailing principles distributedness of functions and reciprocity of interactions. It has also become clear that the brain is by no means a stimulus driven system. Rather, it is self-active, permanently generating highly structured, high dimensional spatio-temporal activity patterns. These patterns are far from being random

but seem to reflect the specificities of the functional architecture that is determined by the genes, modified by experience throughout post-natal development and further shaped by learning. These self-generated activity patterns in turn seem to serve as priors with which incoming sensory signals are compared. Perception is now understood as an active, reconstructive process in which self-generated expectancies are compared with incoming sensory signals. The development of methods that allow simultaneous registration of the activity of large numbers of spatially distributed neurons revealed a mind-boggling complexity of interaction dynamics that eludes the capacity of conventional analytical tools and because of its non-linearity challenges hypotheses derived from intuition. These new and fascinating insights impose revision of concepts and unravel explanatory gaps that were not visible a few decades ago.

The rather detailed knowledge about the response properties of individual neurons in different brain structures is in harsh contrast to our ignorance of the complex and highly dynamic processes through which these neurons interact in order to produce specific behaviors. In-depth analysis of the brain's connectome revealed complex, nested small world architectures in which the principles of re-entry and distributedness prevail (Van den Heuvel and Sporns, 2011). Evidence from invasive and non-invasive multi-site recordings indicates that most higher brain functions result from the coordinated interaction of large numbers of neurons that become associated in a context and goal dependent way into ad-hoc formed functional networks that are dynamically configured on the backbone of the anatomical connections (for review see von der Malsburg *et al.*, 2010). Evidence also indicates that these interactions give rise to extremely complex spatio-temporal patterns that are characterized by oscillations in a large number of different frequency bands that can synchronize, exhibit phase shifts and even cross frequency coupling (Uhlhaas *et al.*, 2009). In the light of these novel data, the brain and in particular the neocortex appears as a self-active, self-organizing "complex system" that exhibits non-linear dynamics, is capable of utilizing multiple dimensions for coding (space, amplitude, phase), operates in a tightly controlled range of self-organized criticality (Shew *et al.*, 2009), (edge of chaos) and constantly generates highly structured, high dimensional activity patterns that are likely to represent stored information. However, how exactly information is encoded in the trajectories of these high dimensional and non-stationary time series is largely unknown and the subject of increasingly intense research. Moreover, with the exception of a few studies in which selective manipulation of the activity of defined neuron groups were shown to affect behavior in a particular way (Salzman

et al., 1992; Houweling and Brecht, 2008; Han *et al.*, 2011) most of the available evidence on the relations between neuronal responses and behavior is still correlative in nature. This makes it difficult to determine whether an observed variable is an epiphenomenon of a hidden underlying process or is causally involved in accomplishing a particular function. Thus, systems neuroscience now faces the tremendous challenge to analyze the principles of distributed dynamic coding and to obtain causal evidence for the functional role of specific activation patterns in order to distinguish between functionally relevant variables and epiphenomena. In conclusion, we have to abandon classical notions on the neuronal representation of perceptual objects. The consequence is that it became again unclear how the distributed processes that deal with the various properties of a perceptual object, its visual, haptic, acoustic, olfactory and gustatory features, are bound together in order to give rise to a coherent representation or percept. Given this, it may appear more than bold to attempt to identify the neuronal correlates of consciousness, the probably highest and most mysterious of our cognitive functions.

An attempt to define the explanandum

Most languages have coined a term for consciousness. Thus, it must be a robust phenomenon on which human beings can agree. However, while it is easy to use the term, it is virtually impossible to give a formal definition of what exactly it means. Nevertheless, the implicit understanding of what it is to be conscious seems to be sufficiently clear and widely accepted to justify search for its neuronal correlates and ultimately, to identify the neuronal mechanisms that enable a subject to be conscious of something. In their seminal paper, (Crick & Koch, 1990) proposed that consciousness is a specific cognitive function and as such must have neuronal correlates that can be analyzed with tools of the natural sciences. With the development of non-invasive imaging technologies, the tools became available to actually pursue this project and the search for the neuronal correlates of consciousness (NCC) has become a mainstream endeavor.

Before discussing some of the proposed theories for NCC, I shall attempt to give an operational definition of what I mean when referring to awareness and consciousness or in other terms what it means to be aware of something or to be conscious. Subjects will be considered as aware of something if they are able to report the presence or absence of the content of a cognitive process irrespective of whether this content is made available by recall from stored memories or drawn from actual sensory experience. Thus,

the criterion for awareness is the reportability of the presence of a cognitive content. These reports can in principle consist of any motor response but to be on the safe side, it is requested that the report be verbal. The reason is that behavioral responses can be obtained under forced choice conditions, that clearly indicate that the brain has processed and recognized the respective sensory material and produced a correct response even though the subject may not have been aware of having perceived the stimulus. There is thus an inherent ambiguity in non-verbal responses. They can but need not necessarily signal awareness which constrains research on the NCC in animal experiments. Since consciousness is so difficult to define an attempt will be made to avoid this term and rather use the adverb “consciously” and the adjective “conscious” in order to further specify particular brain states or aspects of a perceptual process. Also, no attempt will be made to address the hard problem of consciousness research, the problem to explain the phase transition from neuronal processes to the qualia of subjective experience (Chalmers, 2000).

The search for NCC needs to take into account a number of distinct properties that characterize the state of being aware of something. One important feature is unity or relatedness: Contents that one is aware of are experienced as simultaneously present and related with each other. Because of the distributed organization of brain processes, mechanisms supporting phenomenal awareness must be able to bind together computational results obtained in multiple specialized and widely distributed processing areas. Another feature of awareness is that the contents that one is aware of change continuously but are bound together in time, appearing as a seamless flow that is coherent in space and time. Finally, subjects are only aware of a small fraction of ongoing cognitive operations. Thus, there must be a mechanism that determines which signals subjects actually become aware of. As signals that subjects are not aware of are also readily processed and impact behavior (Dehaene *et al.*, 1998; Van Gaal *et al.*, 2008), these gating mechanisms must have a more subtle effect on neuronal interactions than simply blocking information processing. Therefore, the identification of the NCC requires analysis of the mechanisms that gate access to awareness.

Some competing hypotheses

One class of theories focuses on the philosophical implications of the hard problem without attempting to provide detailed descriptions of putative neuronal mechanisms (Searle, 1997; Metzinger, 2000; Dennett 1992; Chalmers, 2000). Solutions to the hard problem have also been sought for by transcending current concepts on neuronal processes and incorporating

theories borrowed from other scientific disciplines. The most prominent of these approaches assumes that phenomena unraveled by quantum physics also play a role in neuronal processes and might be able to account for the emergence of consciousness from the material interactions in the brain (Hameroff, 2006; Penrose, 1994). As none of the predictions of these theories are at present amenable to experimental verification, these will not be discussed further. Another class of theories pursues more modest goals and attempts to examine neuronal mechanisms potentially capable of supporting awareness of cognitive contents. Their aim is to define neuronal mechanisms supporting the unitary character of awareness, its coherence in space and time and the control of states distinguishing between conscious and unconscious processing.

The intuitively most plausible solution for the unity of awareness is convergence of the results obtained in distributed processing areas to a singular structure at the top of the processing hierarchy. Theories derived from this intuition predict the activation of specific cortical areas when subjects are aware of stimuli. Consequently, these regions should remain inactive during unconscious processing of the same material. Likewise, lesions of these putative areas should abolish the ability to become aware of perceptual objects. So far a region with such “observer functions” has not been identified and this option is considered theoretically implausible (Denet, 1992). There is also little if any experimental evidence for such a scenario. Behavioral and brain imaging studies have shown that unconscious processing engages very much the same areas as conscious processing, including frontal and prefrontal cortex (Lau and Passingham, 2007; van Gaal *et al.*, 2008). Thus, there is no compelling evidence for specific areas supporting conscious processing. Lesions of the processing structures proper lead to a selective elimination from conscious perception of those aspects of the stimulus material that are processed in these regions but access to awareness is unimpaired for other contents. A prominent example for such conditions are agnosia and blindsight (Covey & Stoerig, 1991). There are projection systems in the brain whose destruction abolishes all conscious experience but these cannot be considered as NCC. Rather, these systems adjust the activation level of the brain and are necessary for the maintenance of the state during which conscious processing of stimulus material is possible.

Another class of theories favors the notion that the mechanisms supporting awareness of stimulation material are distributed and do not require anatomical convergence. Baars (1997) and Dehaene *et al.* (2006) proposed that there is a work space of consciousness whose neuronal correlate is a widely distributed network of neurons located in the superficial layers of

the cortical mantle. As mentioned above, these neurons are reciprocally coupled through a dense network of cortico-cortical connections that have features of small-world networks. The proposal is that subjects become aware of signals if these are sufficiently salient to ignite coordinated activity within this workspace of consciousness. This is assumed to be the case for signals that either have high saliency because of high physical energy of the stimuli or because they are made salient due to attentional selection.

Yet another and related proposal is that subjects become aware of contents, irrespective of whether they are triggered by sensory events or recalled by imagery from stored memories, if the distributed neurons coding for these contents get organized into assemblies characterized by coherent, temporally structured activity patterns. In this case, the critical state variable distinguishing conscious from non-conscious processing would be the spatial extent and the precision of coherence of temporally structured neuronal responses (Rodriguez *et al.*, 1999; Metzinger, 2000; Varela *et al.*, 2001).

In the following evidence will be reviewed in support of the latter hypothesis. However, before discussing this evidence it is required to briefly recall the reasons why temporal coherence should matter in neuronal processing.

The formation of functional networks by temporal coordination

Because of the small world architecture of the cortical connectome any neuron can communicate with any other neuron either directly or via only a few interposed nodes. Thus, efficient and highly flexible mechanisms are required that permit selective routing of signals and assure that only those neurons effectively communicate with one another that need to interact in order to accomplish a particular task. Evidence from multisite invasive recordings and from non-invasive registration of global activity patterns with magneto-encephalography or functional magnetic resonance imaging indicates that indeed functional sub-networks are configured on the fly on the backbone of fixed anatomical connections in a task and goal dependent way. A mechanism that can accomplish such fast and selective association of neurons and gate neuronal interaction is the temporal coordination of oscillatory activity (Gray *et al.*, 1989; Fries, 2005). Since the discovery (Gray & Singer, 1989) that spatially distributed neurons in the primary visual cortex tend to engage in oscillatory responses in the beta and gamma frequency band when activated by appropriately configured contours and that these oscillatory responses can synchronize over large distances within and across cortical areas and even hemispheres, numerous studies have confirmed that oscillations and their synchronization in different frequency bands are an ubiquitous phenomenon in the mammalian brain. Pacemakers of these os-

cillations are reciprocal interactions in local networks of inhibitory and excitatory neurons. The long distance synchronization of this oscillatory activity appears to be achieved by several mechanisms operating in parallel: Long range excitatory cortico-cortical connections, long range inhibitory projections and pathways ascending from nuclei in the thalamus and the basal forebrain (for review see Uhlhaas *et al.*, 2009). When neurons engage in oscillatory activity, they pass through alternating cycles of high and low excitability. At the peak of an oscillation cycle neurons are depolarized, highly susceptible to excitatory input and capable of emitting action potentials. In the subsequent trough of the cycle the membrane potential is hyperpolarized and membrane conductance is high because of strong GABAergic inhibition generated by the rhythmically active inhibitory interneurons. During this phase neurons are little susceptible to excitatory inputs because EPSPs are shunted and because the membrane potential is far from threshold. Hence, neurons are unlikely to respond to pre-synaptic excitatory drive. These periodic modulations of excitability can be exploited to gate communication among neurons. By adjusting oscillation frequency and phase of coupled neuronal populations communication among those neurons can either be facilitated or blocked. To form a functional network of distributed neurons it suffices to coordinate their oscillatory activity in a way that assures that signals emitted by neurons of this network are timed such that they impinge on other members of the network at times when these are highly susceptible to input. One way to achieve this is to entrain the neurons that should be bound into a functional network to engage in oscillations of the same frequency, to synchronize these oscillations and to adjust the phases such that neurons that ought to be able to communicate can communicate.

Evidence from multi-site recordings indicate that neurons are indeed bound together into sometimes widespread functional networks by synchronization of their oscillatory activity in a task dependent way (Salazar *et al.*, 2012; Buschman *et al.*, 2012). This supports the hypothesis (Gray *et al.*, 1989; Singer, 1999) that synchronization of oscillatory neuronal activity is a versatile mechanism for the temporary association of distributed neurons and the binding of their responses into functionally coherent assemblies which as a whole represent a particular cognitive content. Such a dynamic binding mechanism appears as an economical and highly flexible strategy to cope with the representation of the virtually unlimited variety of feature constellation characterizing perceptual objects. Taking the unified nature of conscious experience and the virtually infinite diversity of possible contents that can be represented, the formation of distributed representations by re-

response synchronization offers itself as a mechanism allowing for the encoding of ever changing constellations of contents in a unifying format. Synchronization is also ideally suited to contribute to the selection of contents for access to consciousness. Synchronization enhances the saliency of signals by concentrating spike discharges to a narrow temporal window. This increases the coincidence of EPSPs in target cells receiving input from synchronized cell groups. Because coincident EPSPs summate much more effectively than temporally dispersed EPSPs, synchronized inputs are particularly effective in driving post-synaptic target cells. It is thus not unexpected that entrainment of neuronal populations in synchronized gamma oscillation is used for attention dependent selection of input configurations (Fries *et al.*, 2001a; Fries, 2009).

If activation patterns that subjects can become aware of are indeed characterized by globally coherent states of those cortical regions that process the contents actually appearing as unified, one does expect that these states of awareness are associated with large scale synchronization of neuronal activity. Candidate frequency bands are the gamma and beta oscillations as these have been shown to serve the temporal coordination of cortical networks. By contrast, if subjects are not aware of the presented stimulus material, processing should remain confined to smaller subnetworks that operate in relative isolation and do not get integrated into globally coherent states. In this case one should observe only local synchronization of more circumscribed neuronal populations.

Finally, adjustments of oscillation frequency and phase fulfill the requirement that assemblies representing consciously processed contents need to be reconfigured at an extremely fast rate. The contents that subjects are aware of can change at a rapid pace, at least four times a second, if one considers that this is the frequency with which the direction of gaze changes during the scanning of natural scenes. Thus, assemblies representing contents that are consciously perceived must be reconfigurable at similarly fast time scales. Evidence suggests that cortical networks operate in a regime of self-organized criticality close to the edge of chaos (Shew *et al.*, 2009). Dynamical systems operating in this range can undergo very rapid state changes characterized by shifts in oscillation frequencies, synchronization and phase.

Methodological caveats

The most frequently used strategy for the identification of the NCC is the contrastive analysis. One creates perceptual conditions in which targets are consciously perceived only in a subset of trials while making sure that physical conditions are kept as constant as possible. This strategy implies that

detection tasks are designed that operate close to perceptual threshold. This can be achieved by reducing the physical energy of the stimuli or by masking them. While subjects are engaged in such detection tasks, neuronal responses are measured and then are sorted depending on whether the subjects did or did not perceive the stimulus. By subtracting the average responses obtained in the two conditions from one another, those neuronal responses can be isolated that occur only in the condition of successful detection and these are then commonly interpreted as neuronal correlate of conscious perception. This seemingly simple approach is not without ambiguity. Thus, noise fluctuations in afferent pathways are likely to lead to significant differences in the available sensory evidence, especially since experiments are performed at perceptual threshold. Therefore, those aspects of neuronal responses that truly reflect the NCC may be contaminated by signals resulting from noise fluctuations at processing stages preceding those actually mediating awareness. Also, once subjects have become aware of stimuli, there are a number of subsequent processing steps that need not necessarily be linked to the NCC. These comprise the covert verbalization of stimulus material, the engagement of working memory, the transfer of information into declarative memory and perhaps also the preparation of covert motor responses. The distinction between these various confounding factors is difficult because all these processes are intimately related to each other. A detailed discussion of this problem is given in Aru *et al.* (2012a). One distinguishing feature could be the latency of the electrographic signatures of these various processing steps. Noise dependent fluctuations in sensory evidence should be manifest early on, responses related to the NCC proper should have some intermediate latencies and the consequences of having become aware of a stimulus should have the longest latencies. In order to use these latencies as distinguishing criterion, it is of course required to estimate the precise latency at which the mechanisms leading to conscious perception are likely to be engaged. Assuming that the time required to prepare and execute simple motor responses is rather constant, the interval of interest can be constrained and has been proposed to be somewhere between 180 and a few hundred milliseconds, depending on the sensory modality and the difficulty of the detection task. Attempts to use latency criteria for the elimination of confounds is of course restricted to electroencephalographic and magneto-encephalographic data and cannot be applied to results obtained with functional magnetic resonance imaging because of the limited temporal resolution of this technique.

Another option for the reduction of confounds is to combine manipulations that influence the conscious perception of a stimulus through dif-

ferent mechanisms and to compare the electrographic responses between conditions (Aru *et al.*, 2012b). We applied this strategy in investigations of patients with subdurally implanted recording electrodes located over the visual cortex. In one set of trials the visibility of stimuli, in this case faces, was manipulated by changing the sensory evidence of the stimulus material. In another set of trials visibility of the same stimuli was influenced by allowing the subjects to familiarize themselves with some of the stimuli. This also facilitates detectability but now because of an expectancy driven top-down process. The reasoning was that neuronal responses reflecting the NCC proper should be the same irrespective of whether stimuli were consciously perceived because of enhanced sensory evidence or because of top-down facilitation. As electrographic signature of interest we analyzed the neuronal activity in the gamma band. In a previous study (Fisch *et al.*, 2009) had shown that category specific gamma band responses in the visual cortex correlate with conscious perception. Conscious recognition led to a phasic enhancement of the gamma band response supporting the notion that conscious perception arises locally within sensory cortices which is in line with previous conclusions (Zeki, 2001; Malach, 2007). In our study we found that the reports of the subject were clearly modulated both by changing sensory evidence and by prior knowledge of the stimuli, as expected, but the gamma band responses were solely reflecting sensory evidence. This suggests that the differential activation of specific areas of the visual cortex, in our case mainly the fusiform face area, reflect processes that prepare access to conscious perception but are not its substrate proper.

Another frequently used paradigm in the search for the NCC is interocular rivalry. If the two eyes are presented with stimuli that cannot be fused into one coherent percept, subjects perceive only one of the two stimuli at a time and these percepts alternate. There are various ways to label the stimuli presented to the two eyes, to trace the responses related to their processing in the brain and then to see which brain structures need to get involved in order to support conscious perception. Again, these studies have led to inconclusive results. Some claim that suppression of signals corresponding to the non-perceived stimulus occurs only at very high levels of visual processing as for example the temporal cortex, the highest stage of the ventral processing stream. The conclusion from these studies is that activation of this particular cortical network is a necessary prerequisite for conscious processing (Logothetis *et al.*, 1996; Silver & Logothetis, 2004). Others, by contrast, found diverging activity patterns already at the level of the thalamus and the primary visual cortex (Haynes *et al.*, 2005; Fries *et al.*, 1997). Recent correlations between the dynamics characterizing binocular

rivalry and anatomical features of the primary visual cortex actually provide compelling evidence, that the rivalry phenomenon is based on processes occurring within V1 (Genc *et al.*, 2013, under revision). However, none of these studies allows one to unambiguously locate the processes that lead to conscious perception. They only contribute to the identification of the earliest levels of processing in which changes are detectable that correlate with conscious perception.

Interesting and of potential relevance for interpretations given in the next chapter is the observation that the access of sensory signals to conscious processing does not seem to be gated by modulation of the neurons' discharge rate but rather by changes of the synchronization of their activity – at least at early stages of processing. What mattered was the degree of synchronicity of oscillatory activity in the gamma frequency range. Signals conveyed by well-synchronized neuronal assemblies had access to conscious processing while signals conveyed by similarly active but purely synchronized neurons failed to do so (Fries *et al.*, 2001b). Of interest in this context is also that stimuli access conscious perception more easily if they are attended to and that attention enhances synchronization of neuronal responses in the gamma frequency band in early visual areas. Again, however, this local increase in synchrony is likely to just enhance the saliency of the neuronal responses, facilitating their propagation across the cortical networks and cannot per se be considered as a neuronal correlate of consciousness.

Evidence relating long-range synchronization and consciousness

The results described in the following were obtained in a study where we presented words that could be perceived in some trials and not in others (by adjusting the luminance of masking stimuli) and simultaneously performed electroencephalographic (EEG) recordings (Melloni *et al.*, 2007). Several measures were analyzed: Time-resolved power changes of local signals, the precision of phase synchronization across recording sites over a wide frequency range, and event-related potentials (ERPs). A brief burst of long distance synchronization in the gamma frequency range between occipital, parietal and frontal sensors was the first event that distinguished seen from unseen words at about 180ms poststimulus. In contrast local synchronization was similar between conditions. Interestingly, after this transient period of synchronization, several other measures differed between seen and unseen words: We observed an increase in amplitude of the P300 ERP for visible words which most likely corresponds to the transfer of information to working memory. In addition, during the interval period in which visible words had to be maintained in memory, we observed increases in

frontal theta oscillations. Theta oscillations have been related to maintenance of items in short-term memory (Jensen & Tesche, 2002; Schack *et al.*, 2005).

To test whether the increase in long-distance synchronization relates to awareness or depth of processing, we further manipulated the depth of processing of invisible words. It has previously been shown that invisible words can be processed up to the semantic and motor level (Dehaene *et al.*, 1998). In a subliminal semantic priming experiment we briefly presented words (invisible) that could either be semantically related or not related with a second visible word on which subjects had to carry out a semantic classification task. Invisible words were processed up to semantic levels as revealed by modulation of the reaction times depending on the congruency between invisible and visible words: Congruent pairs exhibited shorter reaction times than incongruent ones. We observed increases in power in the gamma frequency range for unseen but processed words. For visible words we additionally observed increases in long-distance synchronization in the gamma frequency range (Melloni & Rodriguez, 2007). Thus, local processing of stimuli is reflected in increases in gamma power, whereas long-distance synchronization seems to be related to awareness of the stimuli. This suggests that conscious processing requires a particular dynamical state of the cortical network. The large-scale synchronization that we observed in our study could reflect the transfer of contents into awareness and/or their maintenance. We favor the first possibility given the transient nature of the effect and argue that the subsequent theta oscillations might support maintenance. It is conceivable that short periods of long-distance synchronization in the gamma band reflect the update of new contents, while the slower pace of theta oscillations might relate to sustained integration and maintenance of local results in the workspace of consciousness. The interplay between these two frequency bands might underlie the phenomenon of continuous but ever changing conscious experience (see below).

More recently, Gaillard *et al.* (2009) revisited the question of processing of visible and invisible words. In intracranial recordings in epileptic patients they observed that invisible words elicited activity in multiple cortical areas which quickly vanished after 300 ms. In contrast, visible words elicited sustained voltage changes, increases in power in the gamma band, as well as long-distance synchronization in the beta band and long-range Granger causality. In contrast to our study, Gaillard *et al.* observed a rather late (300–500 ms) rise of long-distance synchronization. However, it is important to note that in the study of Gaillard *et al.*, phase-synchrony was analyzed mostly over electrodes within a given cortical area or at most between hemispheres. It is thus conceivable that earlier synchronization events passed undetected

because of incomplete electrode coverage. Despite these restrictions, this study provides one of the most compelling pieces of evidence for a relation between long-distance synchronization and consciousness.

Some results of the experiments on binocular rivalry point in the same direction. Several studies have shown increased synchronization and phase locking of oscillatory responses to the stimulus that was consciously perceived and controlled behavior (Cosmelli *et al.*, 2004; Doesburg *et al.*, 2005; Fries *et al.*, 1997; Srinivasan *et al.*, 1999). Cosmelli *et al.* (2004) extended the findings obtained in human subjects by performing source reconstruction and analyzing phase-synchrony in source space. These authors observed that perceptual dominance was accompanied by co-activation of occipital and frontal regions, including anterior cingulate and medial frontal areas. Recently, Doesburg *et al.* (2009) provided evidence for a relation between perceptual switches in binocular rivalry and theta and gamma band synchronization. Perceptual switches were related to increments in long-distance synchronization in the gamma band between several cortical areas (frontal and parietal) that repeated at the rate of theta oscillations. The authors suggested that transient gamma-band synchronization supports discrete moments of perceptual experience while theta oscillations structure their succession in time, pacing the formation and dissolution of distributed neuronal assemblies. Thus, long-range gamma synchronization locked to ongoing theta oscillations could serve to structure the flow of conscious experience allowing for changes in content every few hundred millisecond. Further research is required to clarify the exact relation between the two frequency bands and their respective role in the generation of percepts and the pacing of changes in perception.

Another paradigm in consciousness research exploits the attentional blink phenomenon. When two stimuli are presented at short intervals among a set of distractors, subjects usually detect the first (S1) but miss the second (S2) when it is presented 200-500 ms after S1. Increases in long-range neuronal synchrony in the beta and gamma frequency ranges have been observed when the S2 is successfully detected (Gross *et al.*, 2004; Nakatani *et al.*, 2005). Furthermore, Gross *et al.* (2004) observed that successful detection of both S1 and S2 was related to increased long-distance synchronization in the beta range to both stimuli, and this enhanced synchrony was accompanied by higher de-synchronization in the inter-stimulus-interval. Thus, de-synchronization might have facilitated the segregation of the two targets, allowing for identification of the second stimulus (also see Rodriguez *et al.*, 1999). Source analysis revealed, as in the case of binocular rivalry, dynamical coordination between frontal, parietal,

and temporal regions for detected targets (Gross *et al.*, 2004).

In summary, studies of masking, binocular rivalry, and the attentional blink support the involvement of long-range synchronization in conscious perception. Recent investigations have suggested further that a nesting of different frequencies, in particular of theta and gamma oscillations, could play a role in pacing the flow of consciousness. Furthermore, the study of Gross *et al.* (2004) suggests that de-synchronization could serve to segregate representations when stimuli follow at short intervals. These results are encouraging and should motivate further search for relations between oscillatory activity in different frequency bands and consciousness, whereby attention should be focused not only on the formation of dynamically configured networks but also on their dissolution.

Conclusions and outlook

Large-scale synchronization of oscillatory activity has been identified as one candidate for the NCC. This variable has the advantage that it can be measured relatively directly in humans, who are able to give detailed descriptions about their conscious experience. However, oscillations and synchrony seem to be mechanisms that are as intimately and inseparably related to neuronal processing in general just as the modulation of neuronal discharge rates. Thus, without further specification these phenomena cannot stand up as NCC apart from the triviality that consciousness does not exist without them. We propose that the spatial scale and the precision and stability of neuronal synchrony might be taken as more specific indicators of whether the communication of information in the brain is accompanied by conscious experience or not. In this framework, conscious experience arises only if information that is widely distributed within or across subsystems is not only processed and passed on to executive structures but bound together into a coherent, all-encompassing, non-local but distributed meta-representation. This interpretation is compatible with views considering consciousness as the result of the dynamic interplay of brain subsystems that allows for a rapid and highly flexible integration of information provided by the numerous distributed subsystems that operate in parallel. This view resembles the proposal of Sherrington formulated in his book *The Integrative Action of the Nervous System* (Sherrington, 1904): “Pure conjunction in time without necessarily cerebral conjunction in space lies at the root of the solution of the problem of the unity of mind”. The additive value of conscious processing would then be the possibility to establish in a unified data format ever changing relations between cognitive contents irrespective of whether they are read out from memory or induced by sensory signals. By virtue of

this dynamic definition of novel relations, non-local meta-representations of specific constellations could be established that have the status of cognitive objects. Just as any other distributed representation of contents these could then be stored as distributed engrams by use dependent modification of synaptic connections and influence future behavior. Thus, conscious processing would differ from non-conscious processing because it allows for the versatile binding of the previously unbound into higher order representations. If so, “conscious” processing would be functionally relevant and not merely an epiphenomenon.

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