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Temporal binding and the neural correlates of sensory awareness

Andreas K. Engel and Wolf Singer

Theories of binding have recently come into the focus of the consciousness debate. In this review, we discuss the potential relevance of temporal binding mechanisms for sensory awareness. Specifically, we suggest that neural synchrony with a precision in the millisecond range may be crucial for conscious processing, and may be involved in arousal, perceptual integration, attentional selection and working memory. Recent evidence from both animal and human studies demonstrates that specific changes in neuronal synchrony occur during all of these processes and that they are distinguished by the emergence of fast oscillations with frequencies in the gamma-range.

The goal of the present article is to consider the relevance of binding mechanisms for sensory awareness. A large body of neuropsychological and physiological evidence suggests that consciousness has to be understood as a function of numerous interacting systems, such as sensory areas, memory structures, centres for executive control as well as circuits mediating emotion and motivation[1,2]. Thus, any theory about the neural correlates of consciousness (NCC) must explain how multiple component processes can be integrated and how large-scale coherence can emerge within distributed neural activity patterns. Furthermore, such a theory must specify mechanisms for the dynamic selection of subsets of neuronal responses, because only a fraction of all available information gains access to consciousness. In this article, we suggest that achieving both, cross-systems coherence and dynamic response selection, requires mechanisms for binding of distributed information[3,4].

Our discussion of the relationship between binding and conscious states will be restricted to one particular aspect of consciousness, namely, sensory awareness. With many authors, we share the view that sensory awareness is one of those facets of consciousness that is (probably) most easily accessible both in terms of experimental quantification and theoretical explanation[5]. There seems to be wide agreement[1,2,5–7] that the physiological prerequisites of awareness include: (1) *arousal*: the 'waking up' of the brain by non-specific modulatory systems; (2) *sensory segmentation*: the basic step in sensory processing,

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which comprises both detection and binding of object features; (3) *selection*: that is, processes (including attention) that lead to an enhanced efficacy of subsets of neural signals; and (4) *working memory*: the short-term storage of information about the current situation. The core of our proposal is that all these processes either require or modify the operation of neuronal binding mechanisms. Moreover, we suggest that, in all these cases, the binding processes relevant for the instigation of awareness may be implemented in the temporal domain, that is, by transient and precise synchronization of neuronal discharges[3,4,8].

Binding and consciousness

The notion of binding has been introduced first in the context of feature integration[9] and perceptual segmentation[10]. Subsequently, the concept of binding has been applied to other domains and is now employed in theories on object recognition[11], attention[12], memory formation and recall[13], motor control[14], sensorimotor integration[15], language processing[16] and logical inference[17]. In all these domains, a set of related computational requirements has been identified which, taken together, define what has been termed the 'binding problem'[3,4,8,9]:

(1) Information processing underlying the functions listed above is distributed across many neurons spread out over different areas or subsystems and, thus, neurons need to be 'tagged' that currently participate in the same cognitive process. This, in turn, requires a mechanism for the expression of specific relationships between individual neural signals.

(2) Perception of and action in a complex environment usually requires the parallel processing of information related to different objects or events that have to be kept apart to allow sensory segmentation and goal-directed behaviour. Thus, neuronal activity pertaining, for example, to a particular object needs to be distinguished from unrelated information in order to avoid confusion and erroneous conjunctions[9,10].

(3) It has been claimed that specific yet flexible binding is required within distributed activation patterns to allow the generation of syntactic structures and to account for the systematicity and productivity of cognitive processes[18].

(4) Most cognitive functions imply the context-dependent selection of relevant information from a richer set of available data. It has been suggested that appropriate binding may be a prerequisite for enhancing the saliency of subsets of responses and, thus, for further joint processing of those signals pertaining to some particular contents[4,8].

The central hypothesis we focus on in the following is that these facets of the binding problem also apply to the issue of consciousness[5,8,19] and that, hence, unravelling the mechanisms capable of solving the binding problem may be critical for understanding the NCC. In the current debate, Crick and Koch were among the first to propose that binding may be intimately related to the neural mechanisms of sensory awareness[5]. According to their view, only appropriately bound neuronal activity can trigger short-term memory and, thus, become available for access to phenomenal consciousness. At about the same time, Damasio has suggested that conscious recall of sensory contents requires the binding of distributed information stored in spatially separate cortical areas[13]. More recently, numerous other authors have also advocated, albeit with different emphases, a relationship between binding and consciousness. Thus, Llinas and Ribary have argued that arousal and awareness result from the activation of nonspecific thalamocortical circuits which serve to bind sensory contents encoded by specific thalamocortical loops[20]. Similarly, Newman and Baars have suggested that unspecific and specific thalamocortical systems interact to form a 'global workspace', where bound contents become globally available and, hence, lead to the emergence of conscious states[6]. A related view has been expressed by von der Malsburg who postulates that the degree of consciousness attributable to a whole cognitive system may covary with the degree of coherence, or functional coupling, between different neural subsystems[21]. Recently, Tononi and Edelman have suggested that consciousness requires binding or, in their terms, reentrant interactions between systems performing perceptual categorization and brain structures related to working memory and action planning[7]. Finally, Grossberg has proposed that conscious states result from a resonance, or match, between top-down priming and bottom-up processing of incoming information, which allows learning and binding of information into coherent internal representations[22].

Common assumptions

Taken together, all these authors seem to imply a set of common assumptions, namely: (1) that consciousness results from a cooperative process in a highly distributed network, and is not attributable to a single brain structure or process; (2) that binding is highly relevant for the NCC; and (3) that only coherent activity, resulting from the operation of binding mechanisms, could become functionally salient, causally efficacious and globally available, and, thus could lead to the emergence of conscious mental states and their respective behavioural manifestations. The critical point is that binding may not only serve for achieving the 'unity of consciousness' but, first of all, for 'gating' the access to awareness and, hence, for turning subconscious information into conscious mental content. In what follows, we will discuss one particular candidate mechanism, namely, dynamic binding by transient and precise synchroni zation of neuronal discharges. As we will argue, there is now empirical evidence suggesting that such 'temporal binding' serves to generate coherent internal states and to achieve perceptual selection, both of which may be crucial for controlling the access of information to conscious awareness.

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Temporal binding

The concept of dynamic binding by synchronization of neuronal discharges has been developed mainly in the context of perceptual processing. Clearly, sensory systems (at least those of mammals) provide paradigmatic examples for functional architectures that give rise to binding problems of the kind defined above. The most dramatic case is represented by the primate visual system where anatomical and physiological studies have led to the identification of more than 30 distinct visual cortical areas[23]. This parcellation is assumed to reflect some kind of functional specialization because neurons in each of these visual areas are, at least to some degree, selective for characteristic subsets of object features. As a consequence of this functional specialization, any object present in the field of view is represented by a large distributed set of activate neurons – a so-called cell assembly.

On theoretical grounds, it has been suggested that the binding problem arising in distributed networks may be solved by a mechanism which exploits the temporal aspects of neuronal activity[10]. The prediction is that neurons which represent the same object or event might fire their action potentials in temporal synchrony with a precision in the millisecond range. However, no such synchronization should occur between cells which are part of different representations, or cell assemblies. Such a transient and context-dependent synchrony would provide an elegant solution to the binding problem mentioned above[3,4]. Synchrony would selectively tag the responses of neurons that code for one object and demarcate their responses from those of neurons activated by other objects[10]. This highly selective temporal structure would allow the co-activation of multiple assemblies in the same network which nonetheless remain distinguishable. Moreover, temporal binding could serve as a mechanism for selection of assemblies for further processing, because precisely synchronized spikes constitute highly salient events which can be detected by coincidence-sensitive neurons in other brain areas[24,25]. These selectively activated neurons could in turn become organized into assemblies through binding operations within the respective areas, thus assuring 'read-out' of information, that is the propagation and further processing of selected activation patterns.

Crick and Koch were the first to apply this concept of temporal binding to the issue of consciousness. As mentioned already, they have argued for a close relationship between binding and sensory awareness[5]. Beyond that, they were the first to suggest that a temporal binding mechanism of precisely the kind discussed here could be required for the establishment of awareness. Inspired by the finding that visual stimuli can elicit synchronized activity in the visual cortex , they proposed that an attentional mechanism could induce synchronous discharges in selected neuronal populations, and that this temporal structure would facilitate transfer of the encoded information to working memory. At the time it was published, Crick and Koch's speculative proposal was not supported by experimental evidence. In the following, we will discuss more recent results which suggest that temporal binding may indeed be a prerequisite for the emergence of awareness.

Animal studies on synchrony and awareness

By now, the synchronization phenomena predicted by the temporal binding hypothesis have been documented for a wide variety of neural systems. It is well established that neurons in both cortical and subcortical centers can synchronize their discharges with a precision in the millisecond range. The results available from animal studies show that synchronization of neural discharges occurs with a surprising degree of ubiquity, both across systems and species. Box 1 presents an overview of studies that have applied correlation analysis to data obtained at the cellular level. Characteristic features of the synchronization observed can be summarized as follows: (1) In all systems and species studied, synchrony can be very precise, with a coincidence window of about 10ms (Box 1). (2) Synchrony reflects the topology of feature space and is clearly dependent on, for example, proximity of receptive fields and similarity of neuronal feature preferences. (3) Synchrony can occur both internally generated (non-stimulus-locked) as well as externally imposed (stimulus-locked). The former type occurs predominantly with responses to stimuli lacking a distinct temporal structure or with self-generated activity and is due to interactions mediated by reciprocal intrinsic connections[26]. The latter, in contrast, is characterized by phase-locking to the stimulus, occurs in response to rapid stimulus transients[27] and is due to synchronized sensory input signals. (4) In many studies, the synchrony observed was associated with an oscillatory modulation of the responses at frequencies in the gamma range, i.e., above 20 Hz (Box 1). These oscillations can occur both with internally generated synchrony and in stimulus-locked activity[28].

Functional relevance of synchrony

In the following, we will summarize evidence for a potential role of synchronization in the generation and maintainance of awareness. As these studies indicate, synchrony relates to all four presumed component processes of awareness, namely, arousal, segmentation, selection and working memory. Clearly, precise synchronization of neuronal discharges is more prevalent during states characterized by arousal, and moreover, gamma-oscillations are also particularly prominent during epochs of higher vigilance[29,30]. An example taken from one of these studies is illustrated in Fig. 1. Furthermore, several lines of evidence make it likely that temporal binding is highly relevant for scene segmentation, leading to structured representation of sensory inputs. A key observation supporting this notion is that neuronal synchronization depends on the stimulus configuration. Thus, spatially separate cells show strong synchronization only if they respond to the same object. However, if responding to two independent stimuli moving in different directions, the cells fire in a less correlated manner or even without any fixed temporal relationship. This effect has been documented for cortical[31-35] and subcortical[36] neurons in anesthetized cats as well as for cortical cells in anesthetized[37] and awake, trained[38] monkeys.

The idea that binding of neural activity by synchronization might activate working, or short-term, memory has been a key ingredient of Crick and Koch's awareness model[5]. They speculated that synchronized activity might either reverberate in neural circuits, or trigger short-term changes in synaptic efficacy to express transient memory states in the cortex. As indicated by both experimental studies and computational modelling approaches, volleys of synchronized discharges may be particularly efficient in creating reverberatory activity in cell assemblies, which might be a basis for transient memory[39,40]. Several recent studies also suggest a role of synchronized discharges for synaptic modification. In-vitro studies have demonstrated that temporal relations between pre- and postsynaptic activity are critical for the occurrence of long-term potentiation (LTP) or long-term depression (LTD) with a coincidence window of 10-20ms that is defined by temporal contiguity with the spike backpropagating into the dendrites of the postsynaptic cell[41]. Oscillations may be of particular relevance for memory formation, because they establish 'windows of depolarization' that may be critical for LTP and LTD to occur[42].

Relationship to perceptual selection

Recent evidence also indicates that synchrony may be relevant for the selection of sensory information for access to awareness. This is suggested by a study of Fries *et al.*[43] in which neuronal responses were recorded from cat visual cortex under conditions of binocular rivalry. Binocular rivalry is an interesting case of dynamic response selection because the perceptual shift in conditions of rivalry occurs without any change of the physical stimulus[44]. This experimental situation is particularly revealing for the issue at stake, because neuronal responses to a given stimulus can be studied either with or without awareness and, thus, there is a chance of revealing the mechanisms leading to the selection of perceptual information.

The study by Fries *et al.*[43] investigated the hypothesis that response selection in primary and secondary visual cortex might be achieved by modulation of the synchrony rather than the rate of discharges. Awake cats were presented with dichoptic stimulation, that is, patterns moving in different directions were simultaneously shown to the left and the right eye (Fig. 2). Perceptual dominance was inferred from the direction of eye movements induced by the drifting gratings (so-called optokinetic nystagmus), which in humans is taken to be a reliable indicator of shifts in perceptual awareness[45]. The results showed that neurons representing the perceived stimulus were strongly synchronized, whereas cells processing the suppressed visual pattern showed only weak, if any, temporal correlation (see Fig. 2). In these experiments, synchrony across recording sites was accompanied by prominent gamma-oscillations, which showed the same changes under the rivalry condition: the power in the gamma-band increased for neurons representing the dominant stimulus, although it decreased for cells responding to the suppressed pattern (Fig. 2). Importantly, however, no differences were noted under the rivalry condition for the discharge rates of cells responding to the selected and the suppressed eye, respectively[43]. These results therefore demonstrate that, at least at early processing levels, dynamic selection and suppression of sensory signals are associated with modifications of the synchrony rather than the rate of neuronal discharges. Changes in temporal correlation patterns at early stages of processing should result in changes of discharge rate at later stages, if the saliency of responses depends on their synchronicity. Studies in awake monkeys are in accordance with this prediction, showing that unequivocal rate changes under perceptual rivalry are observed predominantly in higher cortical areas[44].

Additional support for a relationship between temporal binding and perceptual selection comes from recent work on the superior colliculus, a midbrain structure with important integrative functions which mediates orienting responses towards a target of interest. Lesions of the colliculus lead to neglect – a severe impairment of spatial attention and phenomenal awareness for events in the space contralateral to the lesion. In the cat, visual cortical neurons can synchronize - via the corticotectal pathway - with collicular cells, and synchrony occurs within the colliculus itself if the neurons are responding to a coherent visual stimulus[36,46]. These findings suggest that potential targets for orienting behaviour are represented in the colliculus by assemblies of synchronously firing cells. More recent experiments have attempted to test directly the idea that temporal binding plays a role in target selection in the colliculus[47]. These experiments investigated how electrically evoked saccadic eye movements were affected by varying the temporal relationship between microstimulation trains applied at two different sites in the colliculus. As shown in Fig. 3, small temporal phase-shifts led to a motor output radically different from that evoked by synchronous stimulation. These data strongly suggest that synchrony in the millisecond range is an important determinant for target selection in the corticotectal pathway.

Taken together, the results from animal studies suggest that synchronization is involved in the generation and maintenance of awareness. These experiments show that synchrony and gamma-oscillations occur in a state-dependent manner, are related to stimulus coherence, co-vary with perceptual selection, and have relevance for the formation of memory traces. This in turn suggests that temporal binding mechanisms may be important

Box 1. Animal studies of synchrony

It has quite frequently been questioned whether synchrony can provide a valid basis for the implementation of dynamic binding operations. Therefore, it seems worthwhile to consider the surprising degree of ubiquity of synchronization phenomena of the kind discussed in this article, both across neural systems and species. A small subset of the available animal studies that have focussed on synchronization are listed in Table I. This reflects the relative distribution of studies performed on the various systems and species. By far the largest proportion of investigations have been devoted to the visual system of either cat or monkey (e.g. for cat striate cortex more than 35 studies on oscillations and synchrony are available). As the table shows, precise synchronization (i.e. temporal correlation distinguished by a narrow coincidence window) occurs in a large number of different neural systems and across a wide range of species. It has been observed in all sensory systems, in the motor system and in memory/association structures. Species include primates, carnivores, lagomorphs, rodents, birds, reptiles, amphibia and insects. Also shown is the fact that, in many studies, synchrony between separate neurons is accompanied by gamma-band (>20 Hz) oscillations. In most instances where oscillations were not reported it is because this issue has actually not been addressed, and only relatively few studies explicitly provide negative evidence (Refs. i, k, s). It should be noted that, in addition to the studies listed in the table, there are a number of studies demonstrating cross-system interactions; for example, correlations between visual and motor cortices[aa,bb] or across different visual processing levels[cc]. Taken together, the available data suggest that neural synchronization on a time scale of around 10 ms could constitute a fairly universal mechanism for binding of distributed information.

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Table 1. Synopsis of animal correlation studies.

Modality/System	Area/Structure	Species	Preparation	Coincidence window[1]	Oscillation frequency range	Ref.
Visual	V1	Cat	anesthetized	10 ms	40–60 Hz	a
Visual	V1	Cat	awake	10 ms	20–70 Hz	b
Visual	V1	Macaque	anesthetized	10 ms	n.i.	c
Visual	V1	Macaque	awake	6 ms	20–70 Hz	d
Visual	V1	Mouse	anesthetized	10 ms	25–50 Hz	e
Visual	Dorsal cortex	Turtle	anesthetized	n.i.	15–30 Hz	f
Visual	PMLS	Cat	anesthetized	10 ms	40–60 Hz	g
Visual	MT	Macaque	awake	10 ms	30–60 Hz	h
Visual	V1, MT, IT	Macaque	anesthetized	n.i.	neg.	i
Visual	IT	Macaque	awake	50 ms	n.i.	j
Visual	IT	Macaque	awake	n.i.	neg.	k
Visual	LGN, Retina	Cat	anesthetized	10 ms	40–120 Hz	l
Visual	Retina	Salamander	*in vitro*	20 ms	n.i.	m
Visual	Superior colliculus	Cat	awake	20 ms	10–70 Hz	n
Visual	Optic Tectum	Pigeon	awake	20 ms	20–30 Hz	o
Auditory	A1	Cat	anesthetized	30 ms	n.i.	p
Auditory	A1	Macaque	awake	30 ms	n.i.	q
Auditory	A1, A2	Rat	anesthetized	n.i.	20–60 Hz	r
Somatosensory	S1	Cat	anesthetized	5 ms	neg.	s
Somatosensory	S1	Macaque	awake	n.i.	20–50 Hz	t
Somatosensory	S1, Thalamus	Rat	awake	20 ms	10 Hz	u
Olfactory	Olfactory bulb	Rabbit	awake	10 ms	40–80 Hz	v
Olfactory	Antennal lobe	Locust	immobilized	20 ms	20 Hz	w
Motor	M1, S1	Macaque	awake	20 ms	25–35 Hz	x
Motor	M1	Macaque	awake	5 ms	n.i.	y
Memory	Hippocampus	Rat	awake	10 ms	40–100 Hz	z

Abbreviations: n.i., not investigated; neg., negative evidence; V1, primary visual cortex; PMLS, postero-medial lateral suprasylvian area; MT, middle-temporal area; IT, infero-temporal cortex; LGN, lateral geniculate nucleus; A1, primary auditory cortex; A2, secondary auditory cortex; S1, primary somatosensory cortex; M1, primary motor cortex.

[1]Values listed refer to the width of typical cross-correlogram peaks in the respective study.

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cc Castelo-Branco, M. *et al.* (1998) Synchronization of visual responses between the cortex, lateral geniculate nucleus, and retina in the anesthetized cat. *J. Neurosci.* 18, 6395–6410

for the processes of arousal, segmentation, selection and working memory, respectively. Clearly, these results do not imply that synchrony would be the *only* mechanism for binding and selection relevant for the NCC. Changes in firing rates, as the other highly relevant coding dimension, can also contribute to an enhancement of the saliency of neural signals[48].

Human studies on timing and perceptual consciousness

In humans, numerous studies using the technique of electroencephalographic (EEG) or magnetoencephalographic (MEG) recording have provided evidence supporting the conclusions drawn above. An important methodological difference is that the signals recorded in EEG/MEG studies result from spatial averaging across large neuronal assemblies and, thus, at this macroscopic level the cellular processes of synchronization and oscillatory response structure cannot be dissociated. Rather, both phenomena show up in a lumped fashion as changes of power in particular frequency bands. This caveat in mind, the results from human studies can well be compared with the data obtained at the cellular level in other species. Following the discovery of gamma-band synchrony in animals, there has been a revived interest in high-frequency activity in humans, and in recent years, numerous studies have provided evidence for stimulus- and task-related gamma-band activity. In the following, we will briefly discuss a number of human studies that have implications for the issue of awareness.

As other mammals, humans show an enhancement of high-frequency EEG components during states of increased arousal, sleep–waking transitions and REM sleep. Several studies indicate that in the awake state and during REM sleep, gamma-band frequencies are present in the EEG or MEG, which are diminished during deep sleep[20,49]. The similarity of high-frequency activity during REM phases and the awake state has led to the suggestion that, in both cases, synchrony in this frequency band correlates with similar processes leading to consciousness, which are just differently modulated by external stimulation[20]. Moreover, high-frequency components of sensory evoked potentials have been shown to disappear under deep anesthesia[50]. During wakefulness, synchronization in the gamma-band is enhanced in epochs of phasic arousal which may occur in response to alerting stimuli and during orienting or investigatory action[51].

A role of temporal mechanisms for perceptual binding and segmentation is suggested by several studies in humans. Thus, it has been demonstrated that gamma-synchronization is correlated with conscious discrimination of distinct auditory events[52]. Tallon-Baudry, Bertrand and their co-workers[53] were among the first to show in humans that perception of coherent objects is specifically associated with ‘induced’ gamma activity which is not phase-locked to stimulus transients. The relationship between high-frequency activity and perception of object coherence

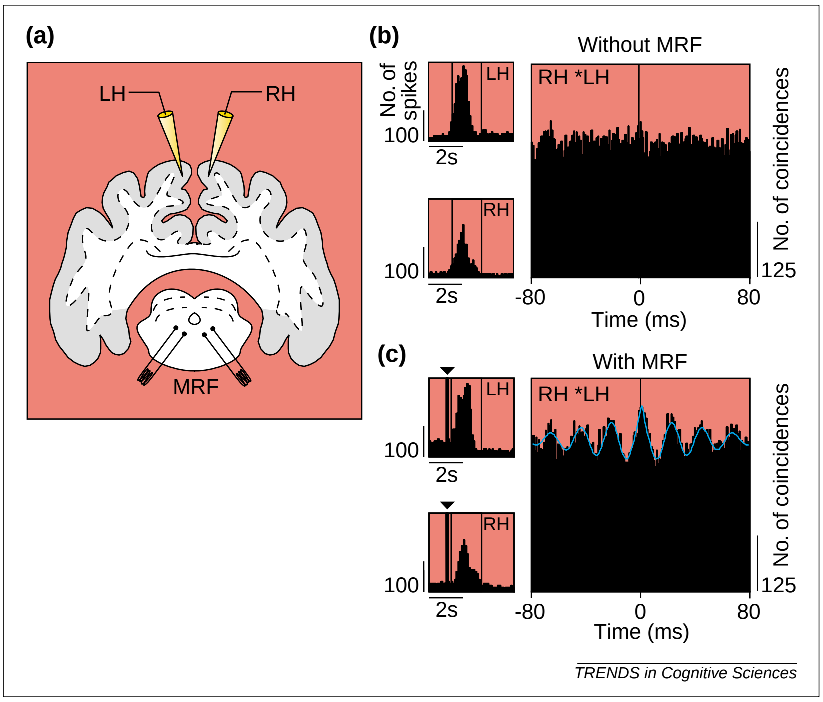

Fig. 1. Central activating systems and cortical gamma-band synchronization. (a) An experiment in the anesthetized cat in which recordings from left and right striate cortex (LH, RH) were performed simultaneously. In addition, stimulation electrodes were placed in the midbrain reticular formation (MRF). Delivery of electrical pulse trains to the MRF has been shown to result in transient desynchronization of the EEG and in activation patterns that closely resemble those observed during wakefulness and during paradoxical sleep. (b) In the case illustrated, visual stimulation yielded strong visual responses (small insets correspond to peri-stimulus–time histograms, vertical lines indicate the time window for which cross-correlation was computed). However, neuronal discharges were not synchronized across recording sites, resulting in a flat cross-correlogram (right). (c) If the visual stimulus was preceded by an electrical MRF stimulus (arrowhead indicates the electrical stimulus in the peri-stimulus–time histograms), a pronounced synchronization became apparent, which was accomanied by an oscillatory modulation of the responses at gamma-band frequencies.The continuous line superimposed on the correlogram represents a damped cosine function fitted to the data to assess the significance of the modulation. Note that the strength of the responses (insets in b and c) is not changed by MRF stimulation. (Modified from Ref. 30.)

has been confirmed by more recent studies using a variety of different paradigms[54,55].

The relationship of synchrony to perceptual selection has been investigated in several recent studies. Electrical[56] and neuromagnetic[57] correlates of binocular rivalry were investigated using the method of 'frequency tagging', that is, the stimuli presented to the two eyes were flickered at different frequencies. Under these conditions, cortical steady-state responses are dominated by the two stimulation frequencies, and it was shown that the power in the frequency band designating the left- or right-eye driven assembly increases in epochs where the respective eye has contributed to perception[56,57]. Moreover, perception of a stimulus is associated with an increase in intra- and interhemispheric coherence of neuromagnetic signals at the stimulus frequency[57]. These data show that synchrony in neuronal assemblies can be modified as a function of perceptual state. In agreement with the study on binocular rivalry in cats discussed in the preceding section, this suggests that temporal binding mechanisms may contribute to selection of signals for access to awareness.

Finally, evidence from studies in humans suggests that working memory, as another important prerequisite for the emergence of consciousness, may also depend on temporal coordination of neuronal populations. The relationship between gamma-band synchrony and working memory has been investigated in a study by Tallon-Baudry *et al.*[58], who have shown that during a visual delayed-match-to-sample task changes occur specifically in the frequency band between 25–60 Hz, indicating an enhancement of precise synchronization over ventral occipital and prefrontal areas. A study by Sarnthein *et al.*[59] has also reported increased coherence between prefrontal and posterior electrodes during a visuospatial working memory task, which was observed in the gamma-band but interestingly also at lower (theta) frequencies. Taken together, these human data demonstrate that processes relevant to the buildup of awareness can be associated with specific changes in neural synchrony and, thus, corroborate the conclusions that have been drawn from the results obtained in animal studies.

Conclusions: synchrony and conscious states

The studies reviewed above strongly suggest that the temporal dynamics in neuronal activity may be critical for the production of conscious states. The experiments on binocular rivalry make it very likely that only strongly synchronized neuronal signals contribute to awareness. They suggest that activation of feature-detecting cells is *per se* not sufficient to grant access of the encoded information to consciousness (as indicated by the fact that cells representing a non-perceived stimulus are still well responding[43]). As we have proposed, the processes of arousal, segmentation, selection and working memory may together form (part of) the neural correlate of awareness. The core of our assumptions has been that all four processes relate to the operation of temporal binding mechanisms which, thus, may constitute a critical component of the NCC. Our proposal is summarized in the remainder of this section.

As mentioned above, arousal is characterized by an enhanced precision of neuronal synchrony and a shift to high oscillation frequencies, indicating that thalamocortical systems change from large-scale synchrony into states with more specific, regionalized temporal patterning. We propose that:

> *(NCC1) Central activating systems may act to modify, in a task- and context-dependent manner, the efficacy of temporal binding mechanisms. This may change both the spatial range and the specificity of neuronal interactions and, thus, contribute to more specific information processing.*

As an additional prerequisite, consciousness requires the completion of basic sensory processing steps, including feature detection and segmentation. The latter seems necessary because, on the one hand, phenomenal states always entail some degree of organization (phenomenal items always appear as embedded in some context) and, on the other hand, it is impossible to extract meaning out of sensory information without prior structuring. Although encoding of object features

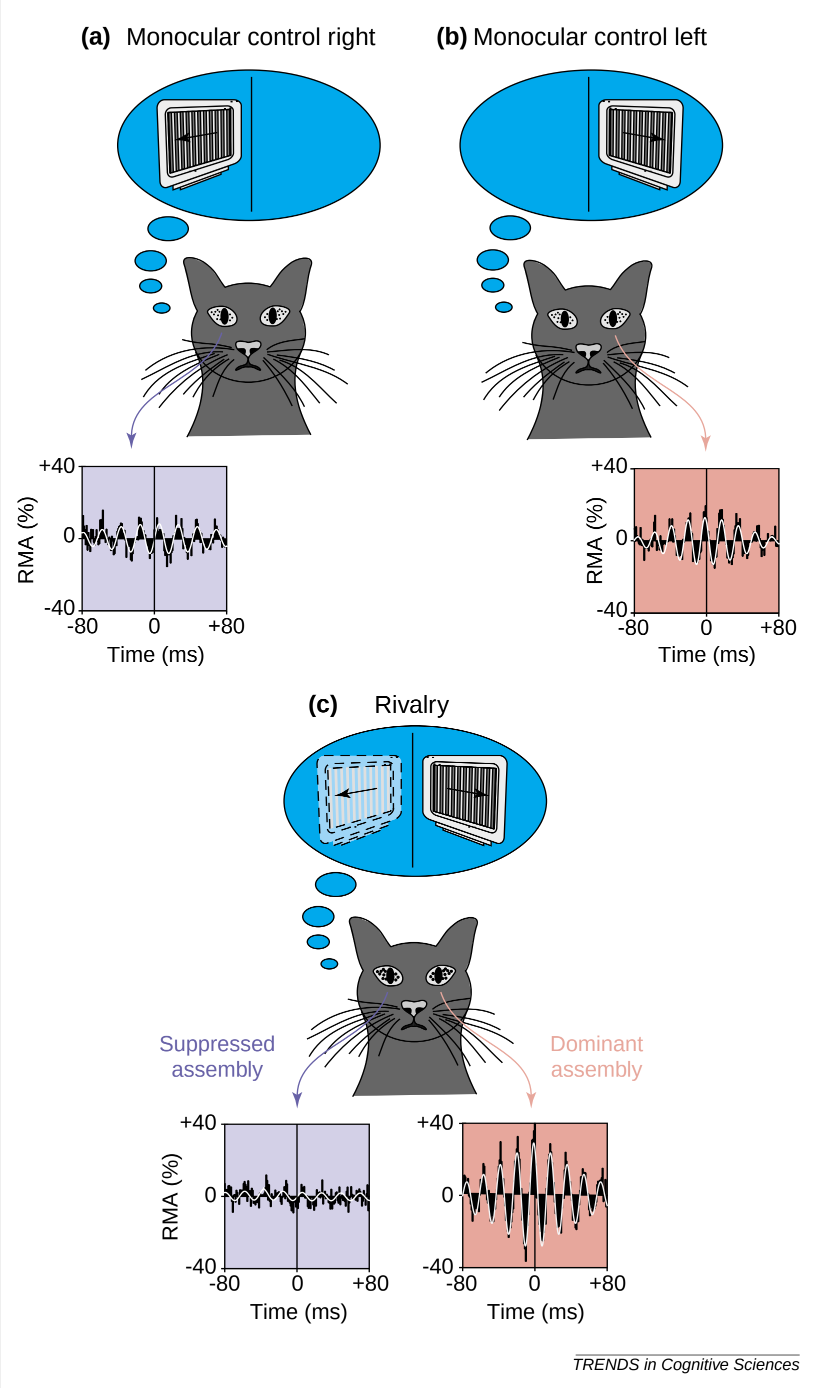

Fig. 2. Synchrony under conditions of binocular rivalry. Strabismic cats were used in these experiments because, in these animals, most cortical cells can be uniquely assigned to either the left or the right eye in terms of their ocular dominance. In front of the awake animal's head, two mirrors were mounted such that each eye viewed a separate computer monitor. Grating stimuli moving in different directions were presented on these monitors, resulting in perceptual rivalry between the two stimuli. (a,b) Cross-correlations are shown for two pairs of recordings driven by the right eye (blue plot) and left eye (red plot), respectively. Under a monocular control condition, both pairs of cells showed synchronized activity when their preferred eye was stimulated (as shown by clear peaks in the cross-correlograms). (c) Synchronization changed, compared with the monocular baseline,if both eyes were stimulated concurrently. Correlograms are shown for an epoch where the stimulus presented to the left eye was selected for perception. In this case, the cells driven through the left eye enhanced their correlation (dominant assembly, red plot), whereas the neurons that represent the suppressed stimulus (suppressed assembly, blue plot) decreased their temporal coupling. In epochs where the stimulus presented to the right eye dominates perception, the strength of the correlations reversed.The white continuous line superimposed on the correlograms represents a damped cosine function fitted to the data. RMA, relative modulation amplitude of the center peak in the correlogram, computed as the ratio of peak amplitude over offset of correlogram modulation. (Modified from Ref. 43.)

is presumably achieved by rate modulation in single neurons or across populations, segmentation requires dynamic binding. We suggest that:

(NCC2) Segmentation may be implemented in the temporal domain. Synchrony as a binding mechanism allows to establish specific relationships between neural discharges which are, in principle, independent of spatial proximity or direct neuronal connections. Synchrony is not only determined by the stimulus, but is modulated in a context- and task-dependent way by cooperative interactions within the cortical network. This leads to functional coherence among neurons that convey relevant information.

Current awareness theories assume that not all of the computational results of sensory processing contribute to consciousness. Rather, as an additional step, part of the information is subjected to a selection process that 'gates' access to awareness. We propose that:

(NCC3) Selection can be mediated by neural synchronization, as temporal coincidences are more easily 'detected' by other neural assemblies than temporally dispersed signals. Only activity patterns carrying a strong temporal signature may be functionally efficacious and globally available and, therefore, such a signature may be a fundamental prerequisite for making information available to other brain centers. The selection is controlled both by bottom-up (e.g. stimulus novelty) and top-down (e.g. expectancy, memory contents) influences, which can lead to competition among different assemblies and result in changes of synchrony.

It should be emphasized at this point that the notion of selection, as we employ it here, is broader than the notion of attention. Clearly, there are cases of response selection (e.g. procedural selection occurring during sensorimotor coordination) where very specific binding can occur without any awareness. The notion of attention, by contrast, always implies access to consciousness, and it may be viewed as the extreme case of very specific, 'very serial' selection of episodic contents. As such, we do not see attention as a 'force' that induces, or creates, synchrony[5,12] but as a process that itself may be *implemented by* dynamic changes in temporal relationships.

Finally, synchrony may be ideally suited to promote access of selected contents to working memory:

(NCC4) Synchronized assemblies may transiently stabilize in some reverberatory state, endowing them with competitive advantage over temporally disorganized activity. This may provide the basis for working memory necessary to achieve the 'holding' of situational context in the respective processing areas. The information carried by such assemblies during working memory states may become conscious.

As it stands, our proposal might contribute to explaining the coherence of conscious contents and the mechanisms of perceptual selection. Moreover, the model advocated here may account for the 'global availability'[6,21] of conscious information, because temporal signatures that reliably propagate across

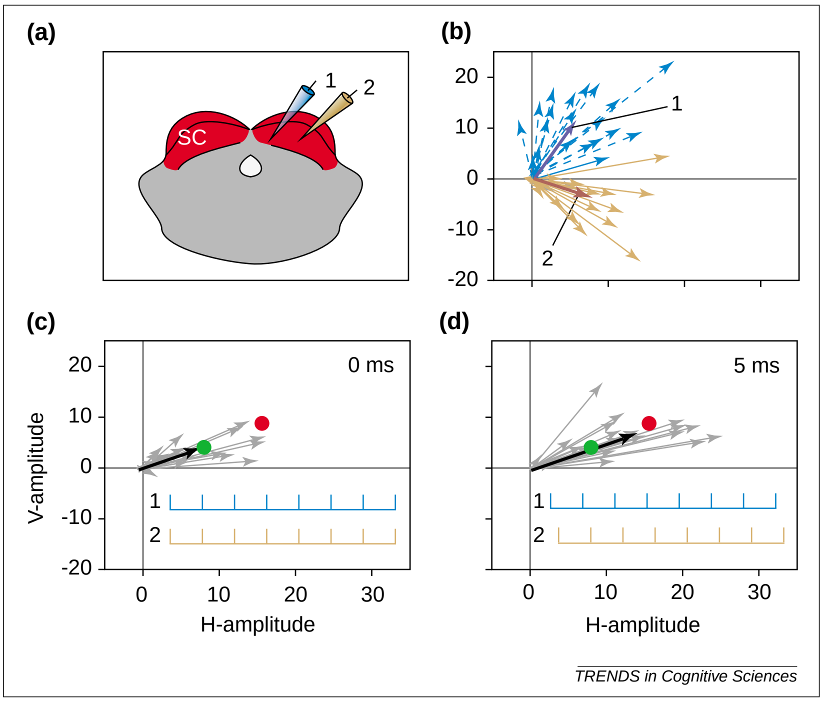

Fig. 3. Timing and saccade generation in the corticotectal system. In the awake cat, saccadic eye movements were evoked by electrical microstimulation in the superior colliculus. (a) Position of the stimulation electrodes. Both electrodes were located in the deep layers of the superior colliculus (SC). (b) Saccade vectors evoked by stimulating the two sites individually.Thin blue arrows refer to the individual saccades evoked by electrical microstimulation at site 1, whereas the thin brown arrows refer to effects of stimulating site 2.The thick blue and brown arrows indicate the respective mean vectors. (c,d) Saccade vectors obtained with different timing protocols for combined microstimulation at both sites. Vertical (V) and horizontal (H) saccade amplitudes are given in degrees of visual angle. Grey arrows show the vectors of individual saccades; the black arrow represents the mean vector.The pattern of microstimulation bursts is schematically indicated below each set of saccades. (c) Synchronous microstimulation of the two sites led to vector averaging, that is, to movements along a vector corresponding to the mean of the saccades evoked by stimulating the two sites individually (green dot indicates the predicted outcome of vector averaging). (d) A slight temporal offset of ≥5 ms between the microstimulation pulses delivered to the two sites resulted in a completely different movement pattern. In this case, the saccades corresponded to the sum, rather than average, of the individual vectors (red dot indicates the predicted outcome in case of vector summation); that is, they had the same direction as those evoked by synchronous pulse trains, but showed approximately double amplitude. (Modified from Ref. 47.)

systems may be suited to achieve coherence, or resonance, between assemblies in different neural systems (as required, for instance, during action planning[15] or language processing[16]).

Beyond sensory awareness, the temporal binding model could have implications for higher-order consciousness processes which, in addition, seem to require the activation of motivation and action planning systems, of episodic memory and, eventually, symbol processing capacities. In all likelihood, these faculties will require crossmodal and cross-system binding. We therefore complement hypotheses *NCC1–4* with two additional assumptions:

(NCC5) Temporal binding may establish patterns of large-scale coherence, thus enabling specific cross-system relationships that bind subsets of signals in different modalities.

An important point to be mentioned is that large-scale coherence is not equivalent to uniform synchrony. Indeed, global synchronization is associated with a low complexity of neural interactions which, as seen in deep sleep or epilepsy, is counterproductive to consciousness[7]. The requirement of an enhanced complexity[7] of the intrinsic structure of neural activation patterns leads us, finally, to the following postulate:

(NCC6) Consciousness may require the embedding of contents into progressively higher-order contexts, both in space and time. This recursive embedding might be mediated by hierarchical binding of assemblies into higher-order arrangements, which could be achieved, for instance, by multiplexing of interactions in different frequency bands. Such higher-order bindings could form the basis for 'meta-representations' necessary to incorporate low-level contents into global world- and self-models[19].

Admittedly, the hypotheses presented here are, at this point, largely speculative. In the current debate[48,60–62] about the significance of binding and its possible mechanisms, objections can, in principle, rely on two arguments: first, it could be denied that binding problems do exist altogether; and second, acknowledging the binding problem, one could still reject the idea that temporal binding may provide a theoretically viable or physiologically plausible solution[48]. With respect to the NCC, the first option seems a hard choice, because consciousness constitutes, without doubt, an integrative process *par excellence*. Choosing the second option presupposes the contemplation of alternative binding mechanisms. However, as discussed elsewhere in depth[3,4], it is not easy to find adequate candidates. In the case of consciousness, anatomical convergence onto 'higher-order' neurons or grouping of signals by place codes may be too inflexible, and attention[62] itself may be part of the problem, rather than part of the answer[4,8].

Outstanding questions

- Why does selection based on temporal binding lead to awareness in some cases but not in others? For instance, both the attentive search for a particular object as well as the visuomotor coordination in a frequently practised task such as driving require context-dependent selection. However, although in the former case the selection process usually leads to awareness, this does not necessarily hold for the latter. What makes the difference?
- Assuming that the processes discussed here constitute necessary conditions for awareness, what would be *sufficient* conditions for the instigation of awareness?
- What are possible mechanisms for the recursive embedding of assemblies and for the 'read-out' of such complex higher-order dynamics?
- What makes gamma-oscillations special? Why is this particular frequency band associated with arousal, attention and awareness more than other frequency ranges?
- What might be possible experimental strategies that allow selective perturbation of temporal binding mechanisms in order to directly test their involvement in consciousness?

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