THE ROYAL SOCIETY

The neuronal basis for consciousness

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Attempting to understand how the brain, as a whole, might be organized seems, for the first time, to be a serious topic of inquiry. One aspect of its neuronal organization that seems particularly central to global function is the rich thalamocortical interconnectivity, and most particularly the reciprocal nature of the thalamocortical neuronal loop function. Moreover, the interaction between the specific and non-specific thalamic loops suggests that rather than a gate into the brain, the thalamus represents a hub from which any site in the cortex can communicate with any other such site or sites. The goal of this paper is to explore the basic assumption that large-scale, temporal coincidence of specific and non-specific thalamic activity generates the functional states that characterize human cognition.

Keywords: consciousness; thalamocortical; gamma oscillations; facilitation; coincidence detection; voltage sensitive dye

1. INTRODUCTION

Perhaps one of the most insightful discussions relating to the nature of global brain function took place in England in the first decades of this century between Charles S. Sherrington (1906) and T. Graham Brown (1915). The former proposed, on the basis of animal physiological experimentation, that the spinal cord operated, fundamentally, as a set of complex reflexes. Indeed, this view followed the Jamesian postulate of reflex (James 1890), in which the nervous system is organized as a set of complex neuronal connectivity pathways triggered into action by the outside world. On this view, behaviour is fundamentally the resultant of sensory input. This general postulate contrasted with the point of view espoused by Graham Brown (1914, 1915) and more recently by Nicholas Bernstein (1967), who viewed spinal cord function as mostly organized as intrinsically generated neuronal activity. With this view sensory inputs are mostly modifiers of such intrinsic activity.

Brown worked, as did Sherrington, on the spinal cord but more specifically on locomotion. He was the first to demonstrate that locomotion was still supported by the spinal cord after bilateral dorsal root deafferentation, resulting in the total removal of sensory input (Brown 1914). On that basis, he proposed that the complex motor output required for locomotion is a property of the spontaneous activity of the neuronal circuits in the spinal cord and brainstem. Interestingly, such important observation and conclusion have been mostly ignored by present-day neuroscience, which continues to emphasize the primordial importance of sensory input in motor organization.

Likewise, in cognitive physiology the prevailing view today is that consciousness is mostly the resultant of sensory input brought into the brain by the different sensory afferents, the activity of which represent the functional basis for cognition.

2. COGNITION AS AN INTRINSIC FUNCTIONAL STATE OF THE BRAIN

We propose here, as we have done on past occasions (Llinás 1990), that consciousness, like locomotion, might be more a case of intrinsic activity than of sensory drive. Thus, it has been proposed that consciousness is an oneiric-like internal functional state modulated, rather than generated, by the senses (Llinás & Paré 1991). We may remember how in childhood the sound of a curtain fluttering in the dark could evoke rather worrying images that were immediately dispelled by turning on the lights. And so, the internal events that we know as thinking, imagining or remembering are, for the most part, related to intrinsic activity. This is of course very much in accordance with the fact that a very large percentage of the connectivity in the brain is recurrent and that much of its activity is related to such intrinsic connectivity not necessarily related to the immediacy of sensory input.

Perhaps the most spectacular difference concerning global brain states is that between wakefulness and dreamless sleep. We all recognize that no gross morphological changes occur in our brains during sleep, that could explain the enormous disparity between the two states. Indeed, the difference must be functional. We know full well that if we are tired we can fall asleep extraordinarily quickly and that if we are asleep and a strong stimulus is given to us (e.g. the havoc played by an alarm clock) we can awaken also extraordinarily fast. It is so fast, indeed, that the only substrate capable of supporting the speed of these two events must be electrical in nature given the large number of elements involved; electrical in the sense of the electrical activity of neurons and the synaptic input that initiate or terminate such activity.

The questions would then be: (i) what is the fundamental difference between being awake and being asleep? and (ii) what does it tell us about brain function? It seems to us that these are among the most important

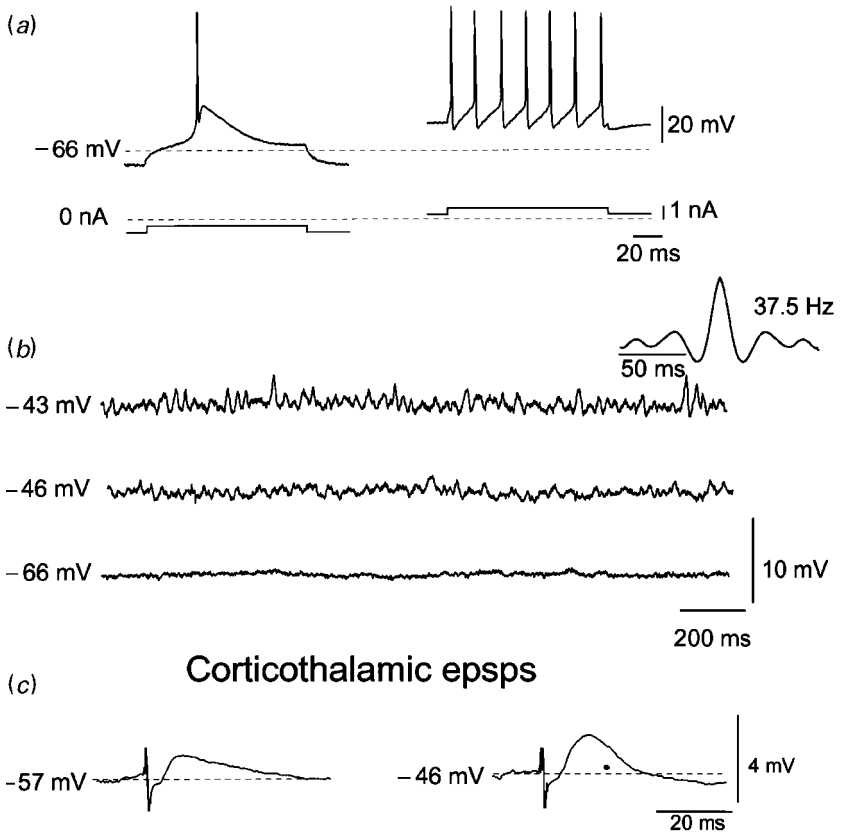

Figure 1. Oscillatory properties of thalamic neurons and corticothalamic excitatory postsynaptic potentials (EPSPs). (*a*) Direct activation of a thalamic cell evoked repetitive firing from V_m positive to −60 mV when depolarized up to −37 mV, whereas a burst of spikes was triggered by the activation of a low-threshold calcium spike when V_m was negative to −65 mV. (*b*) High-frequency subthreshold oscillations were evoked by depolarizing the membrane potential (−46 and −43 mV) by protracted outward d.c. injection. The autocorrelogram in the inset corresponds to the −43 mV trace. (*c*) In a different neuron, EPSPs were evoked by identical stimulation of the corticothalamic pathway at two different membrane potentials. Each trace is an average of ten single stimuli. Note the increase in EPSP amplitude when the membrane was −46 mV compared with the control at −57 mV. ((*a*) and (*b*) adapted from Pedroarena & Llinás (1997).)

clues about the nature of consciousness. The first conclusion to be drawn from such inference is that consciousness (i.e. being awake and able to feel, judge and remember) is but one functional state of our brain. Other states, such as being asleep, do not support consciousness or even the feeling of self-existence.

From classical neurology we know that damage to the cerebral cortex in mammals can cause a variety of well-defined dysfunctional conditions or syndromes. Visual cortex damage is accompanied by blindness that can be of different types depending on the precise location of the cortical insult. Similar findings are also encountered in other cortical structures. Thus, damage to the auditory, the somatosensory, the motor and pre-motor cortices are accompanied by well-defined conditions. In fact, the first such neurological lesion to be described in the terms used above was that which follows damage of Broca's area, generating dysarthria.

Given the above, we tend to equate consciousness with cortical function more or less exclusively, ignoring the fact that the nervous system is deeply cursive and that a strictly hierarchical organization, rather than a global order, is most unlikely. On the assumption that consciousness is a global functional state of the brain relating to more than cortical activity, we shall now attempt to define the functional parameters that support and generate consciousness.

3. THALAMOCORTICAL GAMMA-BAND RESONANT COLUMNS

The questions of coherent electrical activity in the cortex and its relation to cognitive binding have been addressed by several authors in recent years (Von der Malsburg 1981; Eckhorn *et al*. 1988; Gray *et al*. 1989; Gray & Singer 1989; Llinás 1990; Crick & Koch 1990; Llinás & Paré 1991; Llinás & Ribary 1992, 1993; Singer 1993).

Whereas it has been proposed that coherent events occur at the cortical level, and such cortical events are the primary binding substrate (Crick & Koch 1990; Singer 1993), others have proposed that the binding event must be not cortical but rather thalamocortical (Llinás 1990; Llinás & Paré 1991; Llinás & Ribary 1992, 1993). Some of the reasons for the latter view are sketched below.

How is it that damage to the thalamus is equivalent to cortical damage? Experimental results from studies using non-invasive techniques, such as magnetoencephalography (MEG) in humans (Ribary *et al*. 1991) and extracellular and intracellular recordings in cats *in vivo* (Steriade *et al*. 1996*a*,*b*), indicate that such activity is supported by resonance between thalamic and cortical structures at gamma-band frequencies, i.e. with frequencies between 20 and 50 Hz, often centred close to 40 Hz (Llinás 1990; Llinás & Paré 1991). Those results favoured the hypothesis that cognitive events depend on activity involving thalamocortical resonant columns. Indeed, the neuronal mechanisms responsible for high-frequency thalamic oscillations that support thalamocortical synchronization and coherence are presently beginning to be understood.

4. OSCILLATORY PROPERTIES OF THALAMIC CELLS

A decade ago it was suggested that the presence of neuronal elements with intrinsic oscillatory or resonant

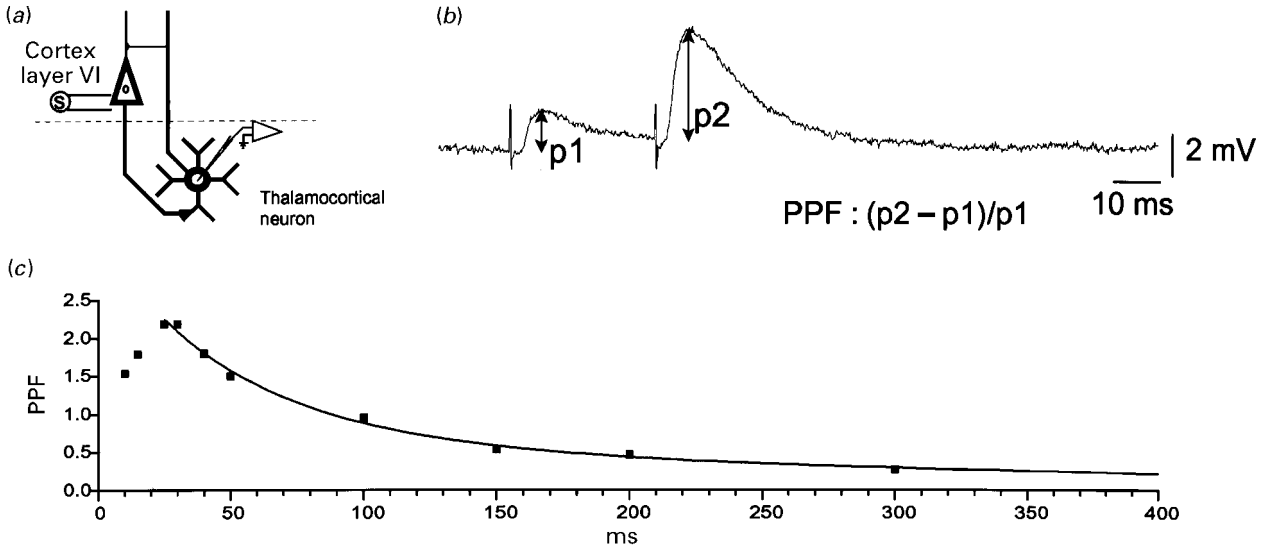

Figure 2. Thalamic relay cells responses to paired cortical extracellular stimuli with different interstimulus intervals (ISI). (*a*) Diagram representing experimental paradigm. (*b*) Responses of a TC cell to a pair of identical CT stimuli, showing facilitation. Paired pulse facilitation (PPF) was estimated as the fractional increase in the amplitude of the second EPSP. (*c*) Graph of the average of PPF for 22 neurons against ISI, showing that facilitation is maximal for intervals between 20 and 30 ms and then decays at longer intervals, being still detectable at 200 ms.

properties in a network facilitates the occurrence of coherence between interconnected elements (Llinás 1988). Indeed, we have characterized, in a series of studies *in vitro*, the intrinsic electrical properties of thalamic neurons that support high-frequency (20–50 Hz) subthreshold oscillations when thalamic neurons are depolarized beyond −45 mV (Pedroarena & Llinás 1997) (figure 1*b*). Previous studies *in vivo* had described similar oscillations in both relay and reticular thalamic neurons (Steriade *et al*. 1991, 1993*a*, 1996*b*; Pinault & Deschênes 1992); however, the electrophysiological properties supporting this activity were not understood.

High-frequency oscillations were described in the sparsely spiny inhibitory interneurons of cortical layer IV. The ionic mechanism for this activity is a persistent sodium conductance (Llinás *et al*. 1991). However, fast oscillations in thalamocortical cells depend on the activation of voltage-dependent calcium conductances. In these cells such conductances are preferentially located in dendrites (Pedroarena & Llinás 1997), demonstrating that the dendritic compartment of these neurons exhibits active membrane oscillations and suggesting that thalamic fast oscillations are supported in part by the intrinsic oscillatory properties of thalamic cells. These findings are in accordance with previous reports indicating that thalamic cells display highly rhythmic activity in the gamma range of frequencies (Adrian & Matthews 1928; Arnett 1975; Ghoose & Freeman 1992; Steriade *et al*. 1991, 1993*a*, 1996*a*,*b*; Pinault & Deschênes 1992).

Active dendritic oscillations are functionally significant because the return input from the cortex to thalamic neurons terminates in their distal dendritic segments (Wilson *et al*. 1984; Liu *et al*. 1995), providing a unique opportunity for resonance between intrinsic dendritic oscillation and rhythmic synaptic inputs. This issue is of further significance because waking and rapid-eye-movement (REM) sleep states are associated with thalamic neuron depolarization, whereas slow-wave sleep is associated with thalamic hyperpolarization (Hirsch *et al*. 1983), as are the intrinsic oscillatory properties of thalamic cells (Jahnsen & Llinás 1984*a*,*b*; Pedroarena & Llinás 1997). Given the above we can conclude that coherence of fast rhythms in thalamocortical loops might depend both on the pattern of synaptic inputs and on the responsive state of the neurons.

To determine whether synaptic input of cortical origin establishes a resonance interaction with the subthreshold electroresponsiveness of thalamic neurons, a set of experiments *in vitro* were implemented. In this study both single and repetitive stimulations of the corticothalamic pathway were employed to test possible synaptic gain changes as well as frequency-dependent dynamic resonance.

Intracellular recordings were obtained from thalamocortical ventrobasal (VB) neurons in slices of the thalamocortical system from the brain of young (3–6 weeks old) adult mice or guinea pigs (Agmon & Connors 1991). The corticothalamic pathway was stimulated with short current pulses (0.1 ms, 0.1–2 mA) repeated at low frequencies (0.2–0.3 Hz) by using bipolar microelectrodes placed in the internal capsule or in the layer VI of the cortex. These studies were designed to analyse the characteristics of evoked excitatory postsynaptic potentials (EPSPs) in VB neurons after corticothalamic activation. Averages of ten EPSPs obtained at two different membrane potentials (−57 and −46 mV) are shown in figure 1*c*. Note that the amplitude of the EPSPs at depolarized levels was larger than those at −57 mV. This amplification was also observed when the *N*-methyl-D-aspartate (NMDA) antagonist AP5 was added to the perfusing medium, indicating that it does not depend on the activation of the NMDA type of glutamate receptors. The voltage dependence of subthreshold fast oscillations and EPSP amplification are quite similar. This suggests that similar ionic mechanisms underlie both phenomena.

In a second set of experiments the frequency characteristics of the EPSPs evoked in the thalamus by cortical

stimulation were studied. Electrical pair pulse stimulation of the corticothalamic afferents with different interstimulus intervals demonstrated that corticothalamic EPSPs exhibit facilitation with interstimulus interval shorter than 200 ms. Maximum facilitation occurred at 25–30 ms intervals (30–40 Hz) (figure 2) with an increase in EPSP amplitude of four times that of the control, in agreement with previous experiments *in vivo* (Lindström & Wróbel 1990; Deschênes & Hu 1990). This facilitation might constitute an appropriate mechanism for selective amplification of those cortical inputs that originated in neurons firing with high frequencies, a pattern of activity associated with arousal and sensory-motor processing (Bouyer *et al*. 1981; Gray & Singer 1989; Murthy & Fetz 1992; Singer 1993).

Both sets of experiments illustrating signal amplification and facilitation indicate that the corticothalamic pathway can selectively enhance coherence and synchronicity of activity between selected groups of interconnected cortical and thalamic neurons during particular functional states. Modelling of the thalamocortical system (Lumer *et al*. 1997) suggests that a critical amount of activity is necessary to produce synchronous firing in thalamocortical loops. Although the coherence of corticothalamic activity during slow-wave sleep might depend on synchronously active large populations of thalamic and cortical cells with high degrees of synaptic convergence and divergence (Steriade *et al*. 1993*b*; Contreras & Steriade 1997), the evidence presented above suggests that during arousal a high degree of synaptic convergence into thalamic cells is not necessary to obtain coherence, but is instead an appropriate pattern of activity.

These results indicate that differences in responsiveness of thalamic neurons, associated with changes in the global brain-state, modify the effectiveness of cortical inputs. The state of responsiveness of thalamic neurons can be modulated by changes in the membrane potential induced by neuromodulatory inputs originating from the brainstem or the forebrain, but also by other central or peripheral synaptic inputs.

5. TEMPORAL BINDING AND THALAMOCORTICAL RESONANT COLUMNS

In an attempt at visualizing the functional consequences, if any, of different cortical activating frequencies a set of experiments with voltage-sensitive dyes was implemented *in vitro*. Optical data were collected from sagittal slices (400 μm) of guinea-pig visual cortex by our standard technique (Llinás & Sugimori 1981). Slices were exposed to the potentiometric probe RH-795 (Molecular Probes). Optical recordings were made with a video camera system (Fujix HRDeltaron 1700) with an image sensor of 128 pixels × 128 pixels and a temporal resolution of 0.6 ms per frame. Stimulation was performed by means of bipolar metal electrodes placed on the white matter. The average response to repetitive stimulation was obtained by initially averaging 16 trains of ten stimuli each, and subsequently averaging the ten stimuli into a single final averaged response. This averaging procedure lumped together the area activated by repetitive electrical stimulation at different frequencies, but eliminated the spatial dynamics during successive stimuli in the train.

(a) *The granularity of thalamocortical activation patches*

To understand the spatio-temporal properties of afferent inputs to the neocortex, stimuli were applied simultaneously by means of a single electrode or two electrodes placed 2–6 mm apart in the white matter.

Stimulation with a single shock to the white matter gave rise to an optical response that indicated depolarization and moved vertically to layer 1. Almost simultaneously the response spread horizontally, away from the site of stimulation, preferentially through layers 5–6 and 1 (figure 3). Stimulation with two electrodes gave rise to two waves of excitation moving horizontally and showing close to linear summation at the centre of the slice, where they fused (figure 3*b*). This pattern was observed for each of the individual stimuli within a train at 10 Hz. Thus, the average area of excitation after a train at 10 Hz spanned the cortical distance between the two stimulating electrodes (figure 4*a*). During stimulation at 40 Hz, subsequent stimuli in the train activated areas that were progressively smaller until only a restricted area, approximately a cortical column in width, overlying each of the two stimulating electrodes, was observed. In consequence, the average cortical area activated by a train at 40 Hz consisted of two distinct regions, separated by a gap of reduced activity between the two activated regions (figure 4*b*).

These results are in accordance with data showing that slow frequency rhythms (less than 15 Hz) in the brain, characteristic of slow-wave sleep such as sleep spindles or the slow oscillations, show long-range cortical coherence (Andersen & Anderssen 1968; Steriade *et al*. 1993*b*; Contreras & Steriade 1997*a*), sometimes spanning the entire neocortex. In contrast, during activated states, such as waking or REM sleep, high-frequency oscillations (20–50 Hz) show a pattern of coherence that is either restricted to its immediate vicinity (Steriade *et al*. 1996*a*) or occurs between distant discrete areas (Ribary *et al*. 1991).

More fundamentally, however, an examination by pharmacological means, of the mechanism by which the granularity of activation is engendered (results not shown) indicates that the areas of silence between patches of activity at 40 Hz are generated by active inhibition. Thus, in the presence of $GABA_A$ blockers, the spatial filtering of cortical activity described above disappears. These results are clearly in accordance with the findings that cortical inhibitory neurons are capable of high-frequency oscillation (Llinás *et al*. 1991) and with the view that, if such neurons are synaptically coupled and fire in synchrony, they might be formative in generating cortical gamma-band activity. However, our results indicate yet another function for coherent inhibition at cortical level; that of generating the 'thalamocortical resonant column'. From this point of view, the thalamocortical resonant column is the functional architecture of the active state that generates consciousness. Indeed, the thalamocortical connectivity can be viewed as a permissive network that displays spatial filter properties that are frequency dependent. Frequency in this view forges activity into a well-specified cortical activation geometry by increasing the encoding contrast, as the activity areas are both intensified and focused. By increasing the contrast

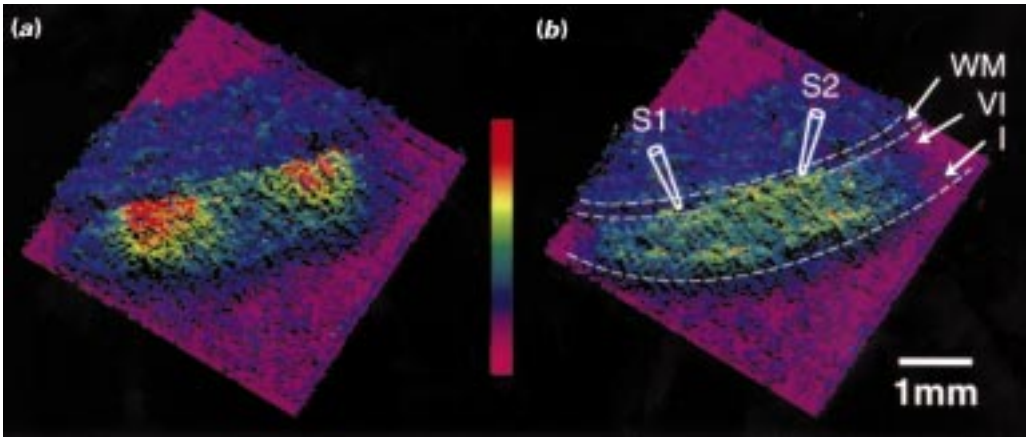

Figure 3. Voltage-sensitive dye response to a single stimulus applied to white matter. Two snapshots at 5 ms (*a*) and 10 ms (*b*). In (*b*) the positions of the two stimulating electrodes (S1 and S2) are indicated, as well as the position of the slice (dotted lines) in the field of the camera (WM, white matter; I and VI indicate layers I and VI). Intensity between 0 and 256 coded by the arbitrary colour scale.

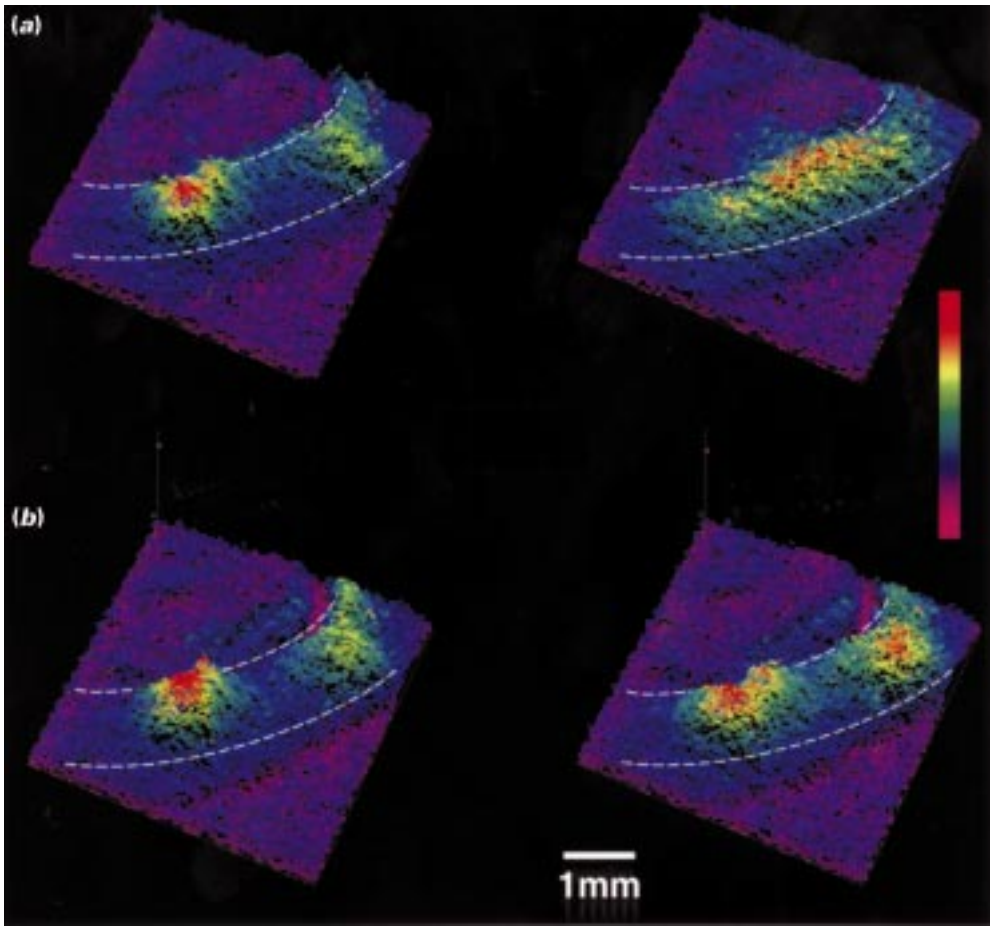

Figure 4. Voltage-sensitive dye response from visual cortical slices after stimulation of the underlying white matter. (*a*) Snapshots at 5 and 10 ms of the averaged response to repetitive stimulation at 10 Hz. (*b*) Snapshots at same times as in (*a*) of the response to stimulation at 40 Hz. Dotted lines indicate the position of the slice (see the scheme in figure 3).

between activation and inhibition this organization might underlie the columnar organization observed in preparations *in vivo* during physiological stimulation of the cortical mantle (Mountcastle 1997), with the added advantage of a thalamocortical resonance that might link these expanded columnar activation into the binding patterns required for consciousness.

6. THALAMOCORTICAL RESONANCE AS THE SUBSTRATE FOR CONSCIOUSNESS

To relate the type of activity encountered at the thalamocortical level in the experiments *in vitro* described above, on the one hand, to activity *in vivo* in human subjects, on the other, we have attempted to search for coherent thalamocortical activity in the human brain by using MEG.

Previous results with MEG from our laboratory have indicated that consciousness is accompanied by thalamocortical oscillatory activity as determined by the recording of evoked and spontaneous magnetic activity in humans (Ribary *et al*. 1991). On the basis of our research for the minimal temporal interval for sensory discrimination, we concluded that consciousness is a non-continuous event determined by synchronous activity in the thalamocortical system (Joliot *et al*. 1994).

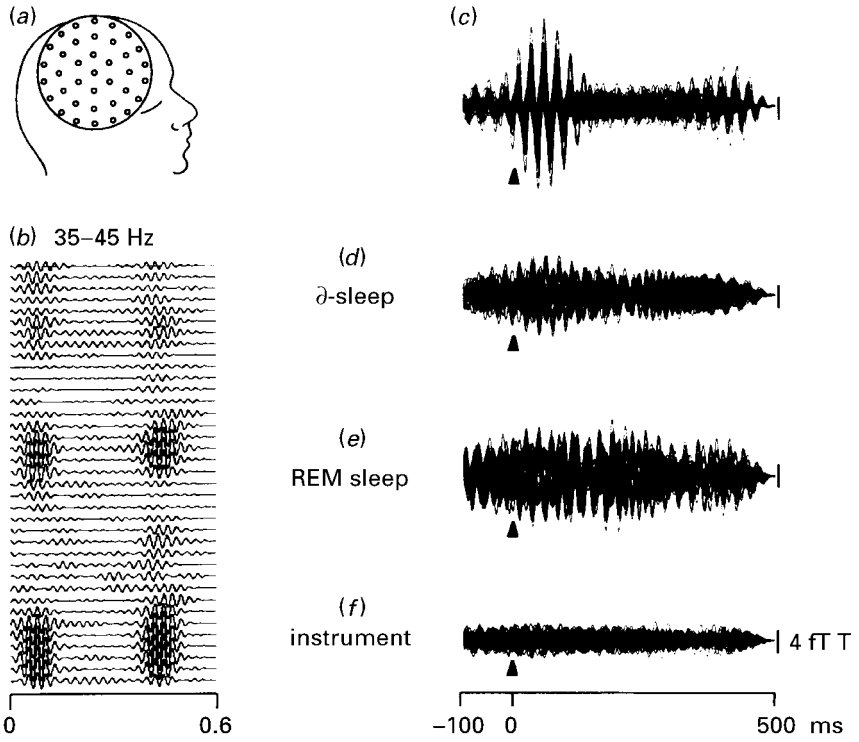

Figure 5. Oscillation at 40 Hz in wakefulness and a lack of 40 Hz reset in δ-sleep and REM sleep. Recording was with a 37-channel MEG. (*a*) Diagram of sensor distribution over the head; in (*b*) the spontaneous magnetic recordings from the 37 sensors during wakefulness are shown immediately below (filtered at 35–45 Hz). (*c–f*) Averaged oscillatory responses (300 epochs) after auditory stimulus: (*c*) subject awake and stimulus followed by a reset of 40 Hz activity; (*d*, *e*) stimulus produced no resetting of the rhythm; (*f*) noise of the system in femtoteslas (fT). (Modified from Llinás & Ribary (1993).)

Because this activity is present during REM sleep (Llinás & Ribary 1993) but is not seen during non-REM sleep, we postulated that the thalamocorticothalamic resonance is modulated by the brainstem and would be given content by sensory input in the awake state and by intrinsic activity during dreaming. These studies addressed issues concerning (i) the presence of gamma-band activity during sleep and (ii) the possible differences between gamma resetting in different sleep/wakefulness states.

Spontaneous magnetic activity was recorded continuously during wakefulness, slow-wave sleep and REM sleep by using a 37-channel sensor array positioned as shown in figure 5*a*. Because Fourier analysis of the spontaneous, broadly filtered rhythmicity (1–200 Hz) demonstrated a large peak of activity at 40 Hz over much of the cortex, we decided that it was permissible to filter the data at gamma-band frequency (35–45 Hz). Large coherent signals with a very high signal-to-noise ratio were typically recorded from all 37 sensors as shown in figure 5*b* for a single 0.6 s epoch of global spontaneous oscillations in an awake individual.

The second set of experiments examined the responsiveness of the oscillation to an auditory stimulus during wakefulness, slow-wave sleep and REM sleep. The stimulus comprised frequency-modulated 0.5 s tone bins, triggered 0.1 s after the onset of the 0.6 s recording epoch; recordings were made at random intervals over about 10 min. In agreement with previous findings (Llinás & Ribary 1993; Galambos *et al*. 1981; Pantev *et al*. 1991), auditory stimuli produced well-defined 40 Hz oscillation during wakefulness (figure 5*c*) but no resetting was observed during slow-wave sleep (figure 5*d*) or REM sleep (figure 5*e*) in this or the six other subjects examined.

The traces in figure 5*c–f* are a superposition of the 37 traces recorded during a single 600 ms epoch. Their alignment in figure 5*c* indicates the high level of coherence of the 40 Hz activity at all the recording points after the auditory stimulus. A high level of coherence is also typical of spontaneous 40 Hz bursts such as that in figure 5*b*.

These findings indicated that although the awake state and the REM sleep state are electrically similar with respect to the presence of 40 Hz oscillations, a central difference remains: that of the inability of sensory input to reset the 40 Hz activity during REM sleep. In contrast, during slow-wave sleep the amplitude of these oscillators differs from that of wakefulness and REM sleep but, as in REM sleep, there is no 40 Hz sensory response. Another significant finding is that gamma oscillations are not reset by sensory input during REM sleep, although clear evoked-potential responses indicate that the thalamoneocortical system is accessible to sensory input. We consider this to be the central difference between dreaming and wakefulness. These results suggest that we do not perceive the external world during REM sleep because the intrinsic activity of the nervous system does not place sensory input in the context of the functional state being generated by the brain (Llinás & Paré 1991). That is, the dreaming condition is a state of hyper-attentiveness to intrinsic activity in which sensory input cannot access the machinery that generates conscious experience.

An attractive possibility in considering the morphophysiological substrate is that the 'non-specific' thalamic system, particularly the intralaminar complex, has an important role in such coincidence generation. Indeed, neurons in this complex project in a spatially continuous manner to the most superficial layers of all cortical areas, including the primary sensory cortices. This possibility is particularly attractive given that (i) single neurons burst at 30–40 Hz (Steriade *et al*. 1993*a*), especially during REM sleep, a finding that is consistent with the macroscopic magnetic recordings observed in this study; and (ii) damage of the intralaminar system results in lethargy or coma (Façon *et al*. 1958; Castaigne *et al*. 1962).

(a) *Thalamo-cortical dysrhythmia and the edge effect*

From the above, we can see how high frequency thalamocortical oscillations may underlie consciousness, and how low frequency, having a lower dynamic granularity, might not. This is corroborated by the fact that low frequency thalamocortical oscillation is present not only in dreamless sleep, but also in the abnormal neurological states that occur during the waking state. Examples of such are Parkinson's disease (Volkmann *et al.* 1996) and petite mal epilepsy (Jeanmonod *et al.* 1996). In both these cases, abnormal low frequency thalamocortical activity due to low threshold calcium activation at the thalamic level is observable (Jeanmonod *et al.* 1996). We wonder what may happen when normal awake activity occurs side-by-side with abnormally slow oscillation. We would like to propose that at the interphase between these two, because of the asymmetry of inhibition due to interneuronal cortical activity, intrinsic high frequency thalamocortical oscillation will occur. This oscillation, out of context, may be responsible for the cognitive events that accompany this 'edge effect'. A clear example of what we mean by the edge effect is, for instance, the scintillating scotoma of migraine or in the epileptic or migraine auras (Russell & Olesen 1996), except that in a migraine, the moving boundary is probably related to the edge of spreading depression (Russell & Olesen 1996).

7. BINDING OF SPECIFIC AND NONSPECIFIC GAMMA-RANGE RESONANT ACTIVITY: THE ISSUE OF COINCIDENCE DETECTION

A schematic diagram of a neuronal circuit that might subserve temporal binding is presented in figure 6*a*. Gamma oscillations in neurons in specific thalamic nuclei establish cortical resonance through the direct activation of pyramidal cells and feedforward inhibition through the activation of 40 Hz inhibitory interneurons in layer IV (Llinás *et al.* 1991). These oscillations re-enter the thalamus via layer VI pyramidal cell axon collaterals, producing thalamic feedback inhibition via the reticular nucleus (Steriade *et al.* 1984). A second system is illustrated in figure 6*b*, where the intralaminar non-specific thalamic nuclei projection to cortical layers I and VI and to the reticular nucleus (Penfield & Rasmussen 1950) is illustrated. Layer V pyramidal cells return oscillations to the intralaminar nuclei. The cells in this complex have been shown to oscillate at gamma-band frequency (Steriade *et al.* 1993*a*) and to be capable of recursive activation.

We propose that neither of these two circuits alone can generate cognition. Indeed, as stated above, damage to the non-specific thalamus produces deep disturbances of consciousness, whereas damage to specific systems produces loss of the particular modality. Although at this early stage it must be quite simple in its form, the above suggests a hypothesis regarding the overall organization of brain function. This rests on two tenets. First, the 'specific' thalamocortical system is viewed as encoding specific sensory and motor activity by the resonant thalamocortical system specialized to receive such inputs (e.g. the lateral geniculate nucleus and visual cortex). The specific system is understood to comprise those nuclei,

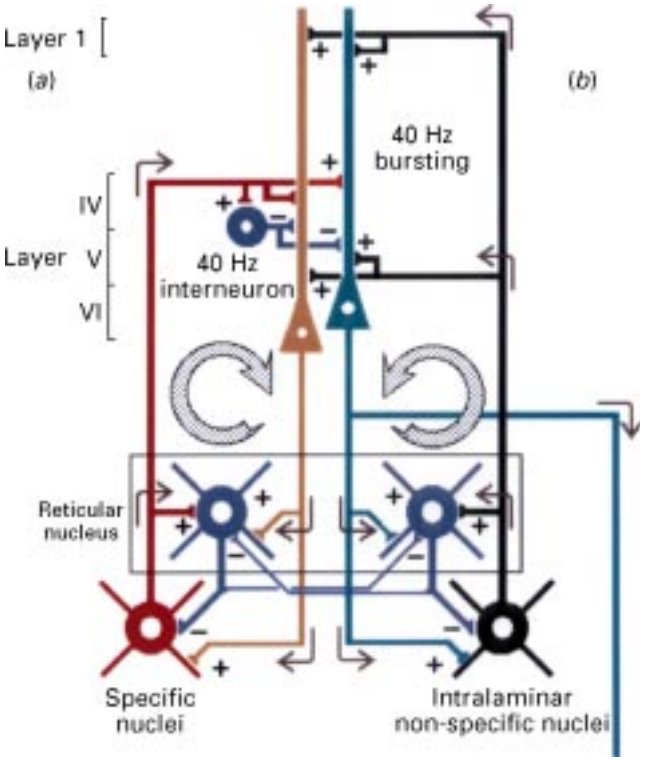

Figure 6. Thalamocortical circuits proposed to subserve temporal binding. Diagram of two thalamocortical systems. (*a*) Specific sensory or motor nuclei project to layer IV of the cortex, producing cortical oscillation by direct activation and feedforward inhibition via 40 Hz inhibitory interneurons. Collaterals of these projections produce thalamic feedback inhibition via the reticular nucleus. The return pathway (circular arrow on the right) re-enters this oscillation to specific- and reticularis-thalamic nuclei via pyramidal cells in layer VI. (*b*) Second loop shows non-specific intralaminary nuclei projecting to the most superficial layer of the cortex and giving collaterals to the reticular nucleus. Pyramidal cells in layer V return the oscillation to the reticular and the non-specific thalamic nuclei, establishing a second resonant loop. The conjunction of the specific and non-specific loops is proposed to generate temporal binding. (Modified from Llinás & Ribary (1993).)

whether sensorimotor or associative, that project mainly to layer IV in the cortex. Second, after optimal activation any such thalamocortical loop would tend to oscillate at gamma-band frequency, and activity in the 'specific' thalamocortical system could be easily 'recognized' over the cortex by this oscillatory characteristic.

In this scheme, areas of cortical sites 'peaking' at gamma-band frequency would represent the different components of the cognitive world that have reached optimal activity at that time. The problem now is the conjunction of such a fractured description into a single cognitive event. We propose that this could come about by the concurrent summation of specific and non-specific 40 Hz activity along the radial dendritic axis of given cortical elements; that is, by coincidence detection (Llinás & Ribary 1994). This view differs from the binding hypothesis in which cortical binding is attributed to the activation of cortical V4, pulvinar or claustrum (Crick & Koch 1990).

In conclusion, the system would function on the basis of temporal coherence. Such coherence would be embodied by the simultaneity of neuronal firing based on passive and active dendritic conduction along the apical dendritic core conductors. In this fashion the time-coherent activity of the specific and non-specific oscillatory inputs, by summing distal and proximal activity in given dendritic elements, would enhance *de facto* 40 Hz cortical coherence by their multimodal character and in this way would provide one mechanism for global binding. The 'specific' system would thus provide the content that relates to the external world, and the non-specific system would give rise to the temporal conjunction, or the context (on the basis of a more interoceptive context concerned with alertness), that would together generate a single cognitive experience.

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