Coherent 40-Hz oscillation characterizes dream state in humans

(cognition/sleep-wakefulness/consciousness/magnetoencephalography)

RODOLFO LLINÁS* AND URS RIBARY

Center for Neuromagnetism, Department of Physiology and Biophysics, New York University Medical Center, New York, NY 10016

Contributed by Rodolfo Llinás, December 8, 1992

ABSTRACT Magnetic recording from five normal human adults demonstrates large 40-Hz coherent magnetic activity in the awake and in rapid-eve-movement (REM) sleep states that is very reduced during delta sleep (deep sleep characterized by delta waves in the electroencephalogram). This 40-Hz magnetic oscillation has been shown to be reset by sensory stimuli in the awake state. Such resetting is not observed during REM or delta sleep. The 40 Hz in REM sleep is characterized, as is that in the awake state, by a fronto-occiptal phase shift over the head. This phase shift has a maximum duration of $\approx 12-13$ msec. Because 40-Hz oscillation is seen in wakefulness and in dreaming, we propose it to be a correlate of cognition, probably resultant from coherent 40-Hz resonance between thalamocortical-specific and nonspecific loops. Moreover, we proposed that the specific loops give the content of cognition, and a nonspecific loop gives the temporal binding required for the unity of cognitive experience.

Present research in neuroscience indicates that 40-Hz oscillatory activity is prevalent in the activated mammalian central nervous system (1-3). Such activity is present at the single-cell level (4-6) and also has been observed at the multicellular- and extracellular-field-potential levels (7-12). This oscillatory activity has been viewed as a possible mechanism for the conjunction of spatially distributed visual sensory activity (13).

More recently it was proposed that, in addition to visual sensory binding, 40 Hz could serve a broader binding function, where the circuits containing single-cell oscillators and the conduction time of the intervening pathways resonate to generate large functional states that bring about cognition (14. 15). On that account, conjunction is viewed as a form of global temporal mapping where sensory inputs that relate to each other are bound by their temporal coincidence. In addition, it was proposed that in the human brain the macroscopic 40-Hz waves are organized in a coherent rostrocaudal wave having a phase shift that appears to scan large portions of the brain and that this mechanism may be the basis for global binding (16). Such coherent scanning is viewed as an intrinsic property of the brain that may be reset by the presence of sensory stimuli (12, 14-16). In more general terms it is proposed that consciousness is an intrinsic event modulated by the activity of the senses (16, 17). If this were to be the case, it should be possible to observe such 40-Hz activity during dreaming. We report here that 40-Hz activity occurs in an organized fashion and shows a rostrocaudal phase shift during the dreaming state.

Magnetoencephalography—a technique to localize (18-21)and monitor dynamic normal and pathological human brain function, having a high temporal resolution, better than 1 msec (12, 22), was utilized in this study. In particular, three sets of studies were designed to address issues concerning (*i*) the presence of 40-Hz activity during sleep, (*ii*) the possible differences between 40-Hz resetting in different sleep/ wakefulness states, and (*iii*) the question of 40-Hz scan during rapid-eye-movement (REM) sleep.

METHODS AND RESULTS

A 37-channel magnetoencephalography system (Biomagnetic Technology, San Diego) was used and consisted of a magnetically shielded room, one cryogenic Dewar flask with 37 magnetic sensors, and a sensor-position indicator to determine position and orientation of the sensors with respect to the head (20).

Magnetic recordings were obtained from the right cerebral hemisphere of five healthy adult subjects. The subjects were asked to lie on a bed with their eyes closed and to stay awake and attentive. The magnetic-sensor array was positioned such that the phase shift of the 40-Hz activity could be recorded over a large area of the hemisphere simultaneously (16).

First sessions were recorded in the afternoon in the fully awake state. The second sessions were obtained during sleep on the same day, beginning at midnight and lasting for 4-5 hr. The different sleep stages were monitored by using bipolar electroencephalography recordings between Fz-Cz and Cz-Pz and by recording bilateral electro-oculograms. The ground was placed on the earlobes. The subjects were also monitored by video equipment during the entire procedure. The stages of REM sleep and delta sleep (deep sleep characterized by delta waves in the electroencephalogram) were carefully determined (23), and subjects were monitored during both sleep stages as described for the awake state.

Spontaneous magnetic activity at 40-Hz was recorded during wakefulness, delta sleep, and REM sleep. Spontaneous brain activity was recorded over several epochs, each lasting 0.6 sec or 3 sec, at a sample rate of 1041 Hz. The 37-channel sensor array was positioned on the right side of the head to cover most of the right hemisphere (Fig. 1, diagram on left). Continuous recordings were made and filtered off-line, with filtering set at 35-45 Hz. Large coherent signals with a high signal-to-noise ratio were recorded from all 37 sensors, corresponding to activity in different regions of the cortex (Fig. 1, traces under diagram). This single 0.6-sec epoch illustrates the global spontaneous oscillation in an awake individual.

The level of coherence present at all recording points is clearly seen by superimposing the 37 traces recorded during a single 3-sec epoch (Fig. 1, subject JV). A small segment of recording A is expanded immediately underneath (dashed lines) to show the 37 overlaid traces in more detail. It is clear from such recordings that while there is coherence among the different recording sites, there is also a phase shift of the oscillation along the different sites. Recordings obtained from

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Abbreviation: REM, rapid eye movement.

^{*}To whom reprint requests should be addressed at: Department of Physiology and Biophysics, New York University Medical Center, 550 First Avenue, New York, NY 10016.



the same sites are illustrated during delta sleep (recording B) and during REM sleep (recording C). The baseline noise level of the instrument recorded during a single epoch with the same settings as for recordings A–C is shown in recording D. Similar recordings made from another subject are shown at 5 times the sweep speed in recordings E–H. The results demonstrate the presence of a well-defined 40-Hz oscillation during wakefulness and dreaming and a marked reduction during delta sleep. Similar results were obtained in three other subjects and demonstrate a parallel in overall brain function during wakefulness and dreaming as opposed to that during delta sleep.

A second set of experiments examined the responsiveness of the 40-Hz oscillation to stimuli during these three different functional states. As shown previously, 40-Hz oscillation may be reset by sensory stimuli (8, 12, 16). This is clearly observed after auditory stimulation.

In these experiments, the auditory stimulus consisted of frequency-modulated 500-msec tone bins, triggered 100 msec after the onset of the 600-msec recording epoch, randomly sampled over a time period of ≈ 10 min. Each tone bin contained auditory stimuli having a randomly modulated frequency between 150 and 650 Hz, which swept upwards or



FIG. 2. Lack of 40-Hz reset in delta and REM sleep. (Left) Averaged oscillatory responses following auditory stimulus. In recording A, 300 stimuli were averaged. Note that the stimulus produces well-defined reset of the 40-Hz event. Similar sets of stimuli in recordings B and C show no resetting of the spontaneous rhythms during delta and REM sleep, respectively. (Right) Single-epoch recordings. In recording E, the subject is awake, and the stimulus is followed by two spontaneous oscillations. In recordings F and G, the stimulus produced no resetting of the rhythm. Note the difference in amplitude for records in Left and Right. The calibration bars are 4 (Left) and 100 (Right) femtotesla (fT), respectively.

FIG. 1. Forty-hertz oscillation in wakefulness, delta sleep, and REM sleep. A diagram of sensor distribution over the head is shown on the far left, and the spontaneous magnetic recordings from the 37 sensors are shown immediately below (filtered at 35-45 Hz). These 37 traces were superimposed in recording A of subject JV and demonstrate a high level of coherence throughout the hemisphere. A portion of this overlay (dotted lines) is shown below the trace at a faster time base. Recording B and its corresponding enlargement represent delta sleep, while C represents REM sleep and D shows the noise of the system. Recordings A-D show 3-sec recordings for subject JV. On the right, recordings for subject ER are similar to those for subject JV but with an expanding time base (600 msec). Recordings (E-G) show typical oscillatory events for the same three states shown in recordings A-C, and the lowest trace (H) is again the background noise. fT, Femtotesla.

downwards within this range and time interval (16). Magnetoencephalography data were filtered between 35 and 45 Hz off-line; single epochs and averages of 300 epochs were analyzed.

By using the paradigm described above, stimuli were delivered to the subject during conditions of wakefulness, delta sleep, and REM sleep. As shown in Fig. 2 *Left* and in agreement with previous findings (8, 12, 16), auditory stimuli (arrowhead) produced a well-defined 40-Hz oscillation, which was particularly clear when several responses were averaged, as in Fig. 2, recording A. When a similar set of stimuli was delivered during delta sleep, no resetting was observed (Fig. 2, recording B). This finding was confirmed in



FIG. 3. Rostrocaudal phase shift of 40-Hz activity during REM sleep. The upper trace (A) shows synchronous activation in all 37 channels during a 3-sec recording period. The oscillation in the left part of trace A (shown as trace B) has been expanded in trace C to show five different recording sites over the head. The five recording sites of trace C are displayed in diagram D for a single epoch to demonstrate the phase shift for the different 40-Hz waves during REM sleep. The direction of the phase shift is illustrated by an arrow above diagram D. The actual traces and their site of recordings for a single epoch are illustrated in diagram E for all 37 channels. fT, Femtotesla.

the other four subjects. Similarly, resetting was not elicited during REM sleep (Fig. 2, recording C). The background noise control is shown in recording D. This same pattern of response is also seen in single 0.6-sec epochs shown for another subject (Fig. 2, recordings E–H). Note that a clear reset was observed in the awake state (recordings A and E), while very little or no signal is seen during delta sleep (recordings B and F) and REM sleep (recordings C and G). Random 40-Hz bursts that were generated in a manner totally unrelated to sensory stimulation are marked by "S," indicating their spontaneous nature.

These findings indicated that, while the awake and REM sleep states are similar electrically with respect to the presence of 40-Hz oscillations, the central difference between these states is the lack of sensory reset of the REM 40-Hz activity. By contrast, during delta 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.

Therefore, these findings indicate that during wakefulness and REM sleep the very specific 40-Hz thalamocortical resonance (12, 15, 16) is active and has very similar global properties. Moreover, while both states can generate cognitive experiences, the recordings indicate, as is commonly known, that the external environment is for the most part excluded from the imaging oneiric states. This further substantiates a recent proposal (17) that the dream state is characterized by an increased attentiveness to an intrinsic state in the sense that external stimuli do not perturb the intrinsic activity.

This third set of experiments addressed the issue of the front-to-back phase shift of the 40-Hz activity over the head during REM sleep. Recordings A and B in Fig. 3 show spontaneous 40-Hz activity during single 3- and 0.6-sec epochs in REM sleep. The first burst in recording A is expanded in recording B to show traces from the 37 different sensors. A portion of this burst recording, expanded in C, shows the well-organized 12-msec phase shift for the 40-Hz oscillation observed from recording sites 1 to 5, as seen in the schematic diagram D. All of the recording sites are illustrated in diagram E for the epoch shown in recording A. A similar 12-msec phase shift was also observed in the same individual in the awake state with the exception that, during REM sleep, the rostrocaudal sweep is better organized and more repeatable, probably since the sweep is not continually reset by incoming sensory stimuli.

DISCUSSION

It has long been known that the global electrical activity of the brain is characterized by distinct oscillatory components at different frequencies and that they correlate well with such large functional states as wakefulness and sleep (24). The significant previously unreported finding in this paper is the fact that during the period corresponding to REM sleep (in which a subject, if awakened, reports having been dreaming), 40-Hz oscillation similar in distribution phase and amplitude to that observed during wakefulness is observed. In the five individuals in whom these recordings were made, the overall speed of the rostrocaudal scan, which averaged ≈ 12.5 msec,



FIG. 4. Thalamocortical circuits proposed to serve temporal binding. (A) Diagram of two thalamocortical systems. (Left) Specific sensory or motor nuclei project to layer IV of the cortex, producing cortical oscillation by direct activation and feed-forward inhibition via 40-Hz inhibitory interneurons. Collaterals of these projections produce thalamic feedback inhibition via the nucleus reticularis. The return pathway (circular arrow on the right) reenters this oscillation to specific and reticularis thalamic nuclei via layer VI pyramidal cells. (Right) Second loop shows nonspecific intralaminary nuclei projecting to the most superficial layer of the cortex and giving collaterals to the reticular nucleus. Layer V pyramidal cells return oscillation to the reticular and the nonspecific thalamic nuclei, establishing a second resonant loop. The conjunction of the specific and nonspecific loops is proposed to generate temporal binding. (B) Diagram of the intralaminary nuclear complex, seen as a circular neuronal mass (stippled shading). Other nuclei in the thalamus are shown as hatched shading. The intralaminary nuclear complex projects throughout neocortical layer I.

corresponded quite closely to half of a 40-Hz period. This number is the same as that calculated by Kristofferson (25) for a quantum of consciousness in his psychophysical studies in the auditory system.

In addition to the finding that the electric activity during the waking and oneiric states is quite similar, a second significant finding was that during the dreaming state, 40-Hz oscillations are not reset by sensory input, although evoked potential responses indicate that the thalamoneocortical system is similarly accessible to sensory input in both states (17, 26). This we consider the central difference between dreaming and wakefulness. It indicates 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 at that time (17). We may consider the dreaming condition a state of hyperattentiveness in which sensory input cannot address the machinery that generates conscious experience.

Beyond this we theorize that a similar mechanism may also be found in conditions where hallucinations are evoked and while "daydreaming," where the immediate happenings of the external world may be ignored (17). Relating to the morphophysiological basis for this scanning property, a very attractive hypothesis could be that the "nonspecific" thalamic system-in particular, the intralaminar complex-may be an important part of this process. Indeed, the intralaminar complex represents a cellular mass that projects to the most superficial layers of all cortical areas to include primary sensory cortices (27) in a spatially continuous manner. The cells in this group may also have the necessary interconnectivity to sustain a propagation wave within the nucleus, which could result in the 40-Hz phase shift observed at the cortical level. This possibility is particularly attractive given that damage of the intralaminar system results in lethargy coma (28, 29) and that the electrophysiological properties of single neurons, especially during REM sleep, burst in firing with a 30- to 40-Hz periodicity (5, 30) as in keeping with the macroscopic magnetic recordings observed in this study.

The results reported above and other recent findings indicate that 40-Hz oscillation is present at many levels in the central nervous system. Indeed, such property is found in sites as peripheral as the retina (3) and olfactory bulb (7); in the thalamus, both specific (5) and nonspecific (30); in the thalamic reticular nucleus (6); and in the neocortex (4). Moreover, it has been shown that some of the 40-Hz oscillation recorded in the visual cortex are correlated with retinal 40-Hz oscillation (3). Thus, 40-Hz oscillation involves not only the cortical but also the thalamocortical interactions. Such possibility is indicated in the diagrams in Fig. 4. A 40-Hz oscillation of specific thalamocortical neurons (5) can establish (Fig. 4A Left) thalamocortical resonance via inputs from layer IV, which resonates with inhibitory interneurons at that level (4). Such oscillation can reenter the thalamus via the layer VI pyramidal cells (31) and can resonate with both the nucleus reticularis and in the specific thalamic nuclei (4).

On the other hand, a second system (Fig. 4A Right and B) is represented by the intralaminary cortical input to layer I of the cortex and its return-pathway projection via fifth and sixth layer pyramidal systems to the intralaminary nucleus, directly and indirectly, via collaterals to the nucleus reticularis (32). The cells in this system have been shown to oscillate in 40-Hz bursts (30) and to be organized in a circular nucleus (33), which could result in recurrent activity ultimately responsible for the rostrocaudal cortical activation found in the present magnetoencephalography recordings.

Finally, it is also evident from the literature that neither of these two circuits alone can generate cognition. Indeed, as stated above, damage of the nonspecific thalamus produces deep disturbances of consciousness, while damage of specific systems produces loss of the particular modality. As such, consciousness may arise by the resonant 40-Hz coactivation of at least these two systems, which would temporarily conjoin cerebral cortical sites specifically activated at or around 40-Hz frequency. In this manner the specific system would provide the content, and the nonspecific system would provide the temporal binding, of such content into a single cognitive experience evoked either by external stimuli or, intrinsically, during dreaming.

The authors acknowledge the continued support of Biomagnetic Technologies; the assistance of A. Mogilner, F. Lado, R. Jagow, J. Volkmann, and M. Joliot from the Center for Neuromagnetism; and Dr. M. Steriade for comments on the paper.

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