Consciousness and Cognition **10,** 184–213 (2001)
doi:10.1006/ccog.2001.0508, available online at http://www.idealibrary.com on IDEAL®

A Field Theory of Consciousness

E. R. John

Department of Psychiatry, Brain Research Laboratories, New York University School of Medicine, 550 First Avenue, New York, New York 10016; and Nathan Kline Institute for Psychiatric Research, Orangeburg, New York 10962
E-mail: johnr01@popmail.med.nyu.edu

This article summarizes a variety of current as well as previous research in support of a new theory of consciousness. Evidence has been steadily accumulating that information about a stimulus complex is distributed to many neuronal populations dispersed throughout the brain and is represented by the departure from randomness of the temporal pattern of neural discharges within these large ensembles. Zero phase lag synchronization occurs between discharges of neurons in different brain regions and is enhanced by presentation of stimuli. This evidence further suggests that spatiotemporal patterns of coherence, which have been identified by spatial principal component analysis, may encode a multidimensional representation of a present or past event. How such distributed information is integrated into a holistic percept constitutes the binding problem. How a percept defined by a spatial distribution of nonrandomness can be subjectively experienced constitutes the problem of consciousness. Explanations based on a discrete connectionistic network cannot be reconciled with the relevant facts. Evidence is presented herein of invariant features of brain electrical activity found to change reversibly with loss and return of consciousness in a study of 176 patients anesthetized during surgical procedures. A review of relevant research areas, as well as the anesthesia data, leads to a postulation that consciousness is a property of quantumlike processes, within a brain field resonating within a core of structures, which may be the neural substrate of consciousness. This core includes regions of the prefrontal cortex, the frontal cortex, the pre- and paracentral cortex, thalamus, limbic system, and basal ganglia.

Key Words: consciousness; field theory; synchrony; coherence; anesthetic effects; QEEG; tomography.

INTRODUCTION

Information arriving into the brain via multiple sensory modalities is constantly fractionated into distinct features and processed by different brain regions relatively specialized for extracting these disparate components. A central problem of neuroscience is to explain how such distributed information is reassembled into an integrated multidimensional percept, which becomes experienced as the subjective content of consciousness: the perception of environmental events, a constantly updating complex of the location and movement of the body in space, the current state of emotional valence and motivation, on a background of relevant previous experience stored in memory. New theories of consciousness (Gazzaniga, 1994; Penrose, 1994; Bogen, 1995) and books, conferences, and symposia devoted to this topic have recently appeared (Jasper, 1998; Hameroff, 1998).

Evidence is reviewed herein from 4 decades of research in the endeavor to develop

This article is part of a special issue of this journal on A Consciousness Monitor.

1053-8100/01 $35.00

a theory as to how consciousness arises from processes in the brain. Due to the volume of relevant evidence only representative findings will be cited. The salient issues to be considered include (1) the synchronization of neural units within a brain region, (2) coherent activity between brain regions, (3) the role of coherence in brain encoding of information, (4) the role of coherent oscillations in binding, (5) the functional significance of distributed coherence, (6) the discontinuous nature of consciousness, (7) the role of a comparator in perception, (8) consciousness as a cooperative process, (9) quantum theoretical hypotheses, and (10) critical substances and structures versus global process. Although critically relevant to this topic, recent results from our comparative studies of invariant anesthetic effects are only summarized, as details can be found in a companion article in this volume. Evidence from these diverse areas provides building blocks for the theory of consciousness presented in this article.

FRACTIONATION, SELECTION, AND REASSEMBLY OF INFORMATION

Multimodal attributes of environmental stimuli are processed asynchronously by neurons in many distinct, functionally specialized brain areas (Zeki, 2000). Perception and subjective awareness are not thus fractionated. Integration of this dispersed information into global consciousness is not compatible with the capacities of any single cell. Dynamic interactions among continuously changing cell assemblies are being invoked as the processes by which consciousness arises (Tononi & Edelma, 2000).

Synchronization of neuronal activity within and coherence among spatially separated brain regions may bind distinct attributes into a holistic percept, a prerequisite for the emergence of subjective awareness (Engel, 2000). High-frequency oscillations have been proposed to play an essential role in such a binding process. Reports have appeared of phase locked oscillations with zero time delay between regions (Desmedt & Tomberg, 1994). Oscillations synchronized across brain regions have now been found in human intracranial recordings, enhanced during cognitive tasks and abolished by anesthesia (Tallon-Baudry, 2000; Varela, 2000).

Synchrony between distant brain regions with zero delay provides a crucial constraint on comprehensive theories of perception or consciousness and precludes explanations based on discrete synaptic transactions, which require appreciable time. Some propose that parallel influences from a remote common source may arrive simultaneously at all regions analyzing the attributes of a stimulus complex. However, this hypothetical generator must be credited with a priori knowledge of what features are to be bound, requiring multimodal sensitivity to those same attributes which are fractionated. This paradox rules out a common source as a plausible explanation and directs theoretical proposals toward concepts of electromagnetic field effects or resonance.

For these reasons, this article begins with an attempt to place observations of synchronization into perspective:

Evidence from Studies of Neural Units

Single- and multiple-unit recordings in brain slices *in vitro* and in anesthetized and unanesthetized animals reveal coherent discharges in distributed ensembles (Nowak et al., 1997; Nicolelis & Chapin, 1994; Contreras & Steriade, 1997; Brecht et al., 1998; Roelfsema et al., 1997). Oscillations increase such synchrony. Coherent neural activity is phase-locked to oscillatory waves in the 30 to 100 Hz range (Contreras & Steriade, 1997; Castelo-Branco & Neuenschwander, 1998). The reliable emergence of zero phase-locked synchrony across neural ensembles which have a critical degree of coupling has been shown in models of neural networks (Lumer et al., 1997).

Were neuronal activity in a brain region random, the unit discharges would be distributed approximately evenly across successive intervals of time. Spontaneous slow waves representing integrated excitatory and inhibitory postsynaptic potentials would be essentially isopotential and, after stimulation, poststimulus histograms (PSHs) of unit activity and averaged evoked potentials (EPs) would be flat. When PSHs or EPs depart significantly from the baseline, the neuronal activity is ‘‘nonrandom,’’ indicating regional involvement in processing stimulus-related information. Since many stimuli may elicit nonrandom neural activity, strategies are needed to identify responses which can be attributed to specific events, such as bursts of unit firing or evoked potential peaks at distinctive latencies. An alternative and powerful technique is to tag different peripheral stimuli at specific repetition rates and search for brain activity labeled at those distinctive frequencies (John & Killam, 1959).

Establishment of Common Temporal Response Patterns during Conditioning

Synchronized, nonrandom activity of sets of cells within local populations and across distributed brain regions may encode information in the brain rather than the discharges of isolated specialized cells sensitive to some particular attribute. Correlations have long been reported between unit firing probability and local slow wave fluctuations (Fox & O’Brien, 1965) as well as synchronization of slow waves and correlated multiunit poststimulus histograms among distant brain regions as information is processed (John, 1972; Ramos et al., 1976). More recently, it has been reported that synchrony is enhanced by stimulus input (Eggermont & Smith, 1996) and that information may be encoded by the Principal Components of spatially distributed synchronized activity (Nicolelis et al., 1995; Chapin & Nicolelis, 1996).

Such correlations and synchronization between macropotentials and multiple-unit poststimulus histograms in dispersed brain regions were examined by us in freely moving cats performing differentiated conditioned responses to auditory or visual stimuli. Studies over 3 decades led to the proposal that information was evaluated by the brain on the basis of nonrandom temporal firing patterns which were coherent across spatially distributed neuronal ensembles (essentially, ‘‘feature extracting cell assemblies’’). Some of this activity was ‘‘exogenous,’’ closely linked to the actual cues (sensation), while other ‘‘endogenous’’ activity reflected perception, as evidenced by the subsequent behavioral performance (John & Killam, 1959, 1960). It was hypothesized that coherent patterns of activity in dispersed analyzers were continuously evaluated in parallel by a global integration process, interpreting the environment in the context of previous experience (John, 1972).

EEG, EP, or unit data were collected from chronically implanted multiple fixed or moving electrodes in cats in a variety of behavioral tasks, all of which used a similar basic paradigm called ‘‘tracer technique.’’ Visual (V) or auditory (A) stimuli at two different nonharmonic tracer rates (1 or 2) were established in cats as differential cues for two discriminative conditioned responses (CR1 or CR2). V1 or A1 were the cues for CR1, while V2 or A2 were the cues for CR2.

The salient findings of that body of research relevant to our present concerns are summarized below.

EEG Studies

The initial studies used closely spaced (1 mm) bipolar macroelectrodes stereotaxically implanted into subcortical regions and epidural screws over cortical regions. EEGs were recorded continuously during every training session, as differentiated go (CR1)–no go (CR2) avoidance responses were established in a shuttle box. Full-field flickering lights delivered the discriminative stimuli, with one tracer rate providing the ‘‘go’’ cue (V1) while the same light source flickering at the second rate constituted the ‘‘no go’’ cue (V2).

Initial presentation of these cues elicited rhythmic EEG waves at the repetition rate of V1 (‘‘labeled rhythms’’) in the lateral geniculate body and the visual cortex. As CR1 was gradually acquired, rhythms at rate 1 also appeared in the hippocampus and the mesencephalic reticular formation (MRF). With fully established CR1, these latter regions showed diminution and even disappearance of labeled rhythms. When an error of omission occurred and aversive stimuli were administered, strong labeled rhythms at rate 1 reappeared in those regions. After negative reinforcement following such an error, as well as during early acquisition, strong rhythms at the tracer rate appeared during the intertrial intervals, when no cue was being presented. These ‘‘virtual labeled rhythms’’ would emerge in the visual cortex, hippocampus, and MRF. Quite often, the cat would perform a spontaneous hurdle jump, apparently induced by this spontaneous rhythmic activity (John & Killam, 1959). This phenomenon was reminiscent of rhythmic activity established by so-called cortical conditioning (Chow et al., 1957). Similar observations were reported by Russian neurophysiologists and were termed ‘‘assimilation of the rhythm’’ (Morrell, 1967). This phenomenon was the first indication that the brain might construct a spatially extensive representational system which was capable of endogenous replications or approximate reproductions of a previous meaningful event.

Discriminative go–no go conditioning was then initiated. Vigorous labeled rhythms now reappeared, spread to additional electrode locations, and did not thereafter diminish, even after the differential behaviors were overtrained. In long testing sessions, errors of commission as well as omission occasionally occurred. In many such instances, the rhythms in many brain regions corresponded accurately to the actually presented tracer stimulus. At the same time, however, nonsensory specific brain regions such as the hippocampus, amygdala, intralaminar nuclei, and MRF displayed the rhythm of the tracer which would have been the appropriate cue for the performed but erroneous behavior (John & Killam, 1960). Further, during generalization to neutral stimuli at some rate 3 which was intermediate to the tracer rates 1 and 2, labeled rhythms appeared at rate 3 upon initial stimulus onset but then shifted to rate 1 or 2 in these nonspecific regions as CR1 or CR2 were subsequently performed.

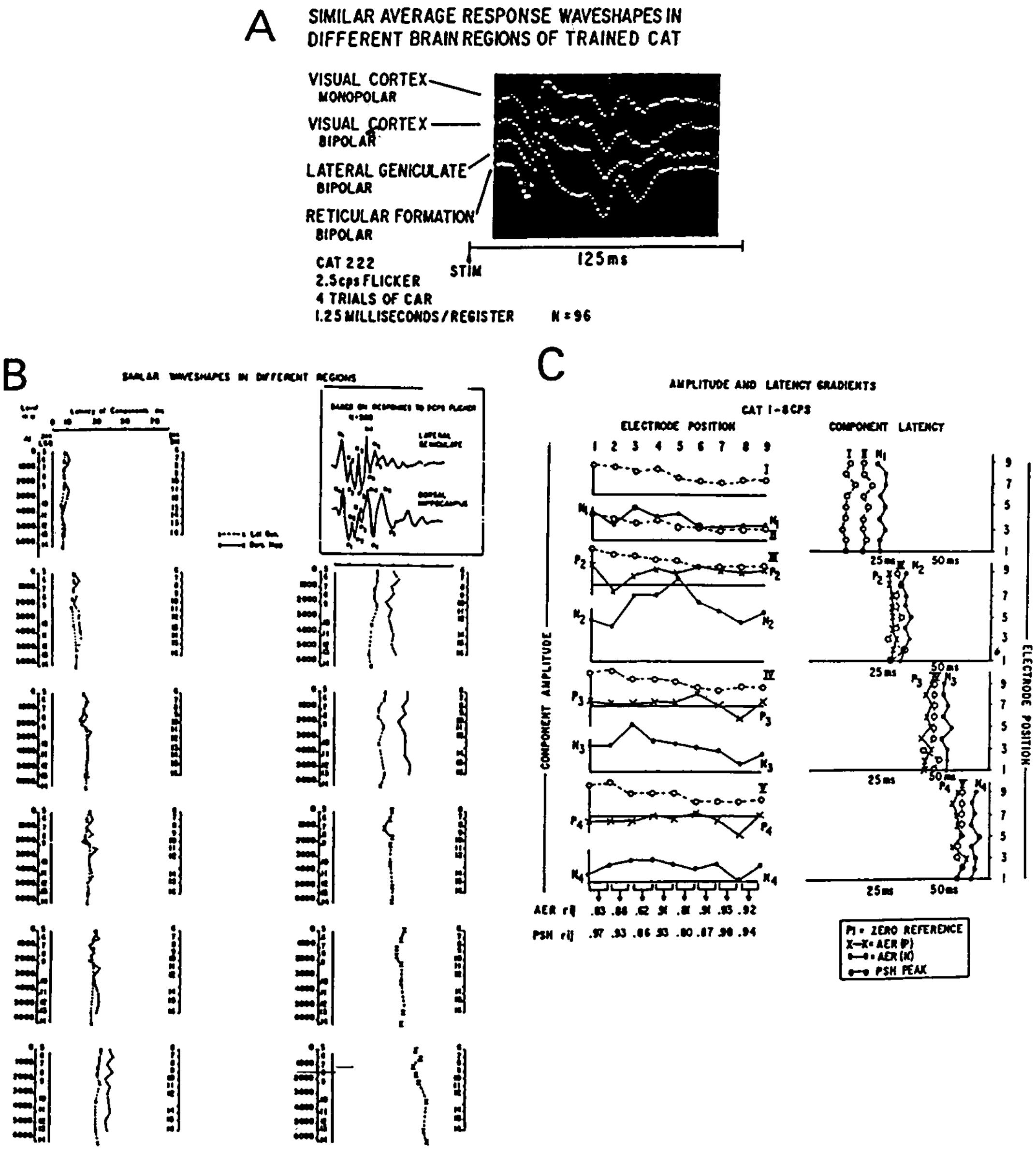

FIG. 1. (A) Average responses evoked by presentation of a train of full field flashes at a rate of 2.5/s, which was the cue for performance of a conditioned avoidance response by a cat differentially trained to an approach–avoidance discrimination between two rates of flicker. These averages were based upon 96 flashes collected over a set of four correct behavioral trials. The analysis epoch was 125 ms, with a resolution of 1.25 ms/bin. Within this resolution, the responses elicited from these closely spaced (1 mm) bipolar electrodes were simultaneous in regions of the brainstem, thalamus, and cortex. (B) In conditioned cats chronically implanted with multiple moving microelectrodes, with simultaneously recorded EPs and single or multiple unit activity separated by low-pass and high-pass filters, EP waveshapes from different brain structures were often observed with identical latencies for corresponding

Such observations provide evidence suggesting that two separate neuroanatomical processes contributed to the selection of a behavioral response, so that current sensory input from the environment was compared to a nonsensory specific representation of past relevant experience. Further, the prevalence of a particular endogenous activity could be strongly influenced by manipulating the emotional or motivational valence of cues which might be expected by the experimental subject, increasing shock intensity or the amount of food which was obtained.

Common Response Waveshapes in Different Brain Regions

When the first average response computers became available, the waveshapes of labeled responses (EPs) elicited by tracer conditioned stimuli could be examined in detail as a variety of instrumental behaviors were learned. It is ironic to realize that, had such ''advanced'' and convenient special purpose computers been available at the outset of our studies, these observations of assimilated rhythms and stimulus-incongruent but behaviorally appropriate brain electrical activity might well never have been made. Awareness that these endogenous neurophysiological correlates of cognition existed directed our attention to their further analysis and led to the collaboration which resulted in discovery of P300 (Sutton et al., 1965), now the most widely studied correlate of human cognitive processes.

At the onset of training, the tracer conditioned stimuli elicited EPs comprised of a single monophasic deflection in sensory-specific regions such as the primary sensory cortices, geniculates, or colliculi, positive-going in monopolar referential cortical recording. Little or no time-locked potentials appeared elsewhere. As undifferentiated conditioned responses were established, these simple waveshapes spread to a few other regions but then appeared to habituate.

With the onset of differential conditioning, vigorous EPs appeared in many brain regions from which they had previously been absent, and a second peak appeared such that the EPs became multiphasic, implying massive synchronous discharges at about the same latency in neuronal populations located in widespread anatomical regions. Evoked potential waveshapes in different brain regions became closely similar (John, 1968, 1972; John & Schwartz, 1978; Morrell, 1967). Differentially conditioned stimuli elicited evoked potentials with identical morphology in brain stem,

---

peaks. In this figure, each of the 11 graphs depicts the latencies of EPs recorded from the left lateral geniculate body and the right dorsal hippocampus as each bipolar electrode was traversed a distance of 6 mm. All data were obtained from trials resulting in correct behavioral outcome. (C) These data, collected from a different cat under the same conditions, show the correspondence between successive peaks of the simultaneously recorded EPs (AER) and PSHs as a microdrive carried the electrodes through 16 positions along a trajectory through the dorsal hippocampus. The graphs on the left (from top to bottom) depict the amplitude gradients of successive AER (x-x-x) and PSH peaks (o-o-o) on the vertical axis and the electrode positions on the horizontal axis. Consistently measurable PSH peaks were found between N1–P2 and N3–P4. The numbers along the baseline present the correlation coefficients between response profiles at successive positions. The graphs on the right depict the latencies of the corresponding peaks. The probability of coherent discharge in a neural ensemble appears to be related to the polarity transitions of nearby voltage fields.

thalamic, and cortical regions and with latencies of component peaks which were simultaneous to within a resolution of 1.25 ms. This is shown in Fig. 1A (John, 1968).

These identical synchronized waveshapes were recorded between bipolar electrodes in various brain structures. It is well known that bipolar derivations detect only local potentials. EPs with quite different waveshapes were recorded concurrently from electrodes at intermediate positions. Principal Component factor analysis of such data, collected simultaneously from many bipolar electrodes, revealed that the visual cortex, lateral geniculate body, nucleus reticularis, lateral posterior thalamic nucleus, dorsal hippocampus, and mesencephalic reticular formation showed high covariance only when visual cue stimuli were correctly discriminated, but not during incorrect performance.

Difference waveshapes were computed by subtracting the usually monophasic EP observed during the absence of behavioral performance from the multiphasic EP displayed during correct performance or upon generalization to a novel stimulus. A late component with essentially identical latency was found in certain cortical, limbic, thalamic, and brainstem regions (John, 1968). These results suggested that coherence of a late, stimulus-elicited but endogenously generated process, apparently released from long-term memory throughout an anatomically distributed network, plays an essential role in the information evaluation system of the brain.

Average Evoked Potential—Poststimulus Histogram (PSH) Correlations

Sound technical (closely spaced bipolar derivations) and logical (absence of this common mode activity from some electrodes at intermediate locations) considerations militated against the concern that volume conduction from some distant common source might explain this covariance and simultaneity among multiple separated brain regions. Nevertheless, it was important to establish that, under the same experimental conditions, synchronized temporal patterns of coherent discharges took place in distributed neuronal ensembles.

Accordingly, arrays of multiple moving microelectrodes were chronically implanted into conditioned cats. Using high-pass and low-pass filters to separate EPs and stimulus-locked multiple unit PSHs elicited by tracer stimuli, both kinds of data were recorded simultaneously as the movable electrodes were slowly traversed throughout different brain structures over periods of many months (John & Morgades, 1969). From the resulting trajectories of EPs and PSHs recorded concurrently from the same neuronal ensembles, it became evident that the latency of each EP peak not only corresponded closely to the time of maxima and minima in the stimulus phase-locked PSH, but that these latencies were identical to within 1 ms across lengthy trajectories (varying from 3750 to 6250 μ in different structures) traversed by the moving electrode tips. This is shown in Fig. 1B (John, 1972). Therefore, the observed covariance was due to local neuronal activity rather than to volume conduction from some common source in a distant region.

Synchronized Activity in Different Structures

This distributed synchrony establishes a ‘‘common mode’’ of neural activity coherent across an extensive system. After differential conditioning, comparison of data derived from recordings made simultaneously in different widely separated anatomical regions, such as the lateral geniculate body on one side and the hippocampus on the other side (a three-dimensional distance of 23 mm between the actual sites studied on the two sides or a minimum separation of 7 mm, assuming that such activity was probably bilaterally symmetrical), showed that different brain regions displayed similar PSHs as well as EPs. Further, the actual latencies of many of the salient peaks were identical across brain structures, with differences on the order of 1 ms. Different temporal patterns of EPs and PSHs were elicited by different behavioral cues. Temporal patterns of deviations from randomness in ensemble discharges in responses to a particular cue showed little change as electrode trajectories traversed distances so large that many different neuronal populations could be sampled, as shown in Fig. 1C (John & Morgades, 1969). However, this coherence between regions decomposed when behavioral errors were committed.

Ergodic Representation of Information

In unrestrained behaving animals, the firing pattern of single neurons in response to a specific stimulus is erratic. Responses to consecutive stimulus presentations display highly variable bursts of discharge. Many different stimuli can elicit firing from the same individual neuron and discharges also occur spontantaneously. In response to repeated presentations of a learned cue stimulus, the PSH of a single cell elicited by a very large number of stimuli converges slowly to the PSH from a large multiple-unit ensemble elicited by a relatively small number of repetitions (John, 1972).

If the time course of departure from random firing patterns is considered as reflecting information processing in a neural ensemble, this observation indicates that the brain may assemble weak unreliable influences on single cells to obtain powerful reliable effects when summed across a large neuronal ensemble. In this heretical view, the activity of any individual cell is informational only insofar as it contributes to the overall statistics of the population of which it is a member. In this sense, the representation of information by neuronal populations is ergodic, much like the generation of pressure by gas molecules in an enclosed volume. EP waveshapes might then better reflect information processing than the activity of single neurons.

Statistical analysis was performed on the multiunit PSH and EP responses to differentiated stimuli recorded from the numerous, spatially separated neuronal ensembles sampled by the moving electrode arrays. An ANOVA between the responses of each ensemble to the two tracer cues and among the different neuronal ensembles indicated that there were consistent, highly significant differences in every ensemble between the responses to the two discriminative stimuli. However, there were no significant differences among ensembles in their responses to any particular cue.

These results suggested that information about the differentiated stimuli was encoded as different temporal patterns of nonrandomness common to all of those neuronal populations rather than by selective discharges of cell(s) in any particular position (John & Morgades, 1969). This is shown in Fig. 2A.

THE BINDING PROBLEM

The above evidence poses the ‘‘binding problem,’’ the question of how might these spatially distributed statistical response patterns, sometimes synchronized in

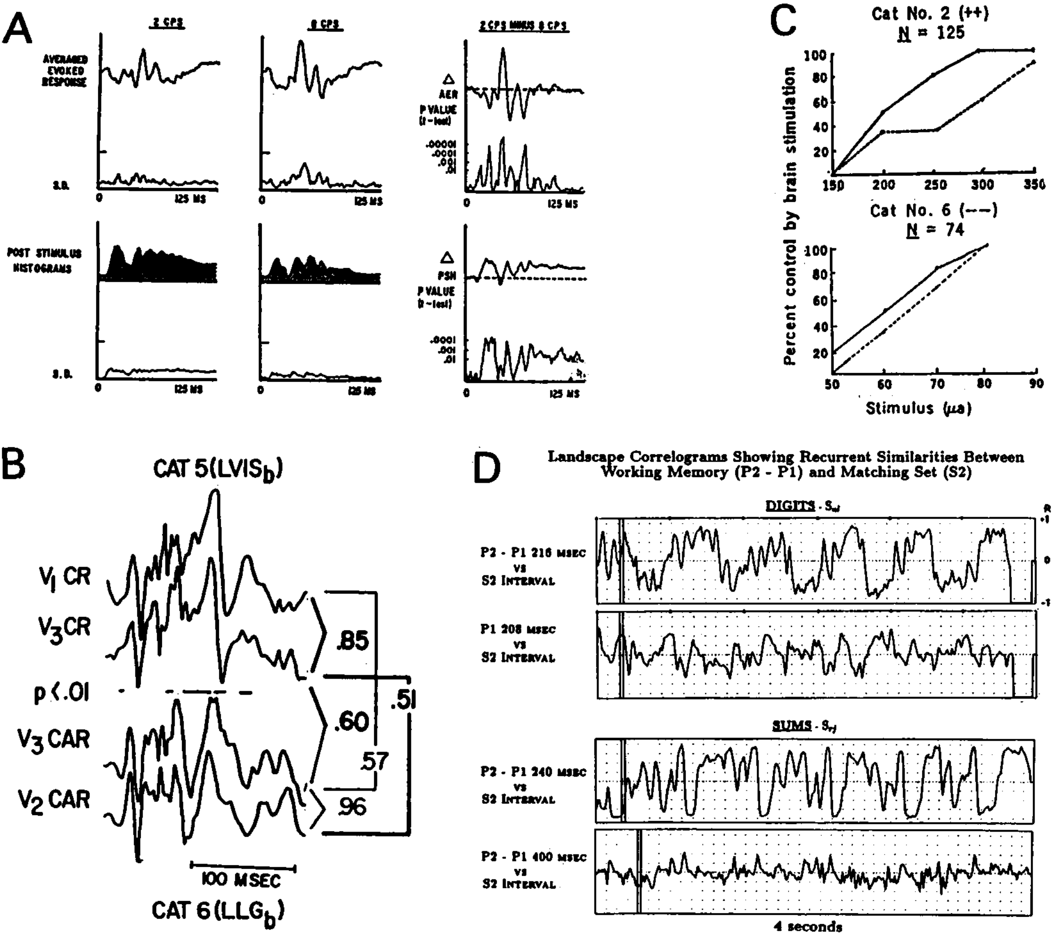

FIG. 2. (A) (Left column, top to bottom) Grand averages of EPs, standard deviation of EPs, grand averages of PSHs, and standard deviation of PSHs across nine electrode positions, collected during correct differential behavioral responses to a 2/s flicker cue; (Middle column, top to bottom) corresponding data, but collected in response to the discriminative 8/s flicker cue; (Right column, top to bottom) differences between grand average EPs, significance of EP differences (*t* test), differences between grand average PSHs, significance of PSH differences (*t* test). These results show that differential temporal patterns of departure from randomness characterized the responses of anatomically distributed ensembles to two discriminated signals, and were not unique to any individual neurons within those regions. The information appeared to be encoded by the temporal pattern of negative entropy. (B) EP waveshapes recorded from bipolar electrodes on the visual cortex of a cat trained to perform a Conditioned Response (pressing the left lever for food) in response to a flicker Approach Cue at rate 1 (V_1CR) but a Conditioned Avoidance Response (pressing the left lever to avoid shock) in response to the differentiated flicker Avoidance Cue at rate 2 (V_2CAR). A neutral flicker signal at rate 3 (V_3), midway between rates 1 and 2, was randomly interspersed in random sequences of the two differentiated cues and resulted in Differential Generalization. In response to the neutral signal, the cat sometimes performed the approach behavior (V_3CR) but at other times the avoidance behavior (V_3CAR). The figure shows that the EP waveshape evoked by V_3 depended on the meaning attributed to it, as inferred from the subsequent behavioral response. The numbers to the right of the waveshapes are the Pearson correlation coefficients between the pairs of waves indicated by the brackets. (C) Effectiveness of contradiction of differentiated visual

different regions but sometimes asynchronous across sensory modalities, be integrated into a unified whole that enters consciousness.

An Anatomical Substrate Possibly Critical for Synchronization and for Binding

Recent neuroanatomical studies have described a system which might play an important role in facilitating synchronization and binding of information in dispersed brain regions. This new information modifies previous views of the nonspecific diffuse projection system. In the thalamus, a ‘‘core system’’ has been identified by staining for the calcium-binding protein calbindin, consisting of cells in the principal sensory relay nuclei which receive afferent inputs from ascending sensory pathways and project topographically upon cells in middle layers of the corresponding primary sensory cortex. Cells stained for another calcium-binding protein, parvalbumin, form a background matrix within the whole thalamus, receive inputs from more diffusely organized pathways, and are not restricted by the borders of individual nuclei. Matrix cells project diffusely to multiple cortical areas and terminate in superficial layers of the cortex (Jones, 1998). Cortico-thalamic projections to the intralaminar and other thalamic nuclei as well as cortico-cortical projections can thus globally distribute information about current sensory input and interoceptive assessments of internal context and state throughout the cortex as well as to subcortical structures such as the basal ganglia. This widespread distribution of activity, enhanced by phase-locking oscillatory modulation, might be critical for establishment of the coherence and binding among neuronal ensembles throughout much of the cortex, thalamus, and subcortex, which might comprise the momentary instant of consciousness.

Functional Significance of Synchronized Distributed Ensembles

As with errors of omission or commission described above, when a dimensionally intermediate or ‘‘neutral’’ stimulus was inserted into random sequences of two dis-

---

(V1 or V2) or auditory (A1 or A2) conditioned cues for an approach–approach (++) or avoidance–avoidance (−−) discrimination by electrical pulse trains delivered to the reticular formation at either of two repetition rates, R1 or R2. The graphs display the percentage of behavioral control by the electrical pulses versus the amount of current per pulse. The solid lines indicate that the peripheral stimulus was at the higher rate (V1R2 or A1R2) and the dotted curve shows results when the higher repetition rate was delivered electrically (R1V2 or R1A2). N refers to the total number of conflict trials carried out (three sessions in each cat). (D) The voltage fields across the scalp elicited by a meaningless Noncontingent Probe before (P1) and after (P2) presentation of visual Priming Stimuli (S1) were subtracted. The computed Difference Field (P2 − P1) was then cross-correlated against the voltage fields (‘‘landscapes’’) subsequently elicited by presentation of Matching Stimuli (S2), which the subject had to evaluate. The figure presents four landscape correlograms: (Row 1) the similarity between the Difference Field at a 216-ms latency versus the sequence of fields elicited by presentation of a series of numbers (S2). This latency was chosen because it yielded the highest values of correlation; (Row 2) the similarity between the first probe P1 and S2; (Row 3) the similarity between the Difference Image at 240 ms versus fields elicited by a series of numbers which had to be summed (in a second subject); (Row 4) as Row 3, but for the Difference Field at a 400-ms latency. These data suggest that a virtual image of an event being held in working memory engages an anatomically distributed population of neurons during the time interval corresponding to the late secondary components of the response evoked by a visual stimulus.

criminative tracer stimuli, the EP waveforms and multiple-unit PSHs during differential generalization corresponded to those usually elicited by the appropriate cue for the subsequently performed discriminative conditioned response (see Fig. 2B). The broad anatomical distribution of these ‘‘readout processes’’ was further evidence for spatial binding and endogenous release of distributed cell assemblies mediating memory (John, 1972).

Whether the appearance of similar temporal patterns of nonrandomness in widely separated brain regions reflected mere correlations or were a critical component of information processing was a basic issue. Electrical stimuli, delivered directly to the chronically implanted electrodes from which such observations had been recorded, were used to simulate naturally occurring coherence within local neuronal populations. Trains of electrical pulses were delivered into various brain regions at rates which contradicted simultaneously presented tracer visual or auditory cues. Using a crossover design, the central electrical stimulus was presented simultaneously with the peripheral conditioned stimulus. As current increases in brain electrical stimuli, the deviation from randomness increases in the stimulated neural ensembles. As shown in Fig. 2C, the percentage of conditioned response behavior appropriate to the rate of the electrical input was found to increase proportional to the amount of current in the pulse and could reach 100% (John & Kleinman, 1975). This differential behavioral control by the rate of electrical pulses could be achieved by brain stimulation in the mesencephalic reticular formation, intralaminar or midline thalamic nuclei, lateral or medial geniculate, and the visual cortex.

Cross-modal integration was demonstrated between interleaved central and peripheral stimuli, using a design in which rate $2 = 2 \times$ rate 1. When V1 or A1 were delivered plus central electrical pulses at rate 1, with no offset in time, CR1 was performed. However, when the central pulses were delivered at rate 1, but offset 50% so that the global input to the brain was at rate 2, CR2 was performed. Further, when electrical pulses at rate 1 were delivered simultaneously to two different brain regions, with no offset in time, CR1 was performed. However, when the same two sites were stimulated at rate 1, but offset so that the global input to the brain was at rate 2, CR2 was performed. When such behaviorally evidenced integration of the two pulse trains at rate 1 took place, recordings made during such behavioral trials displayed activity at rate 2 in the intralaminar nuclei (John & Kleinman, 1975). This informational integration of artificially imposed nonrandomness was not restricted to only certain neuroanatomical structures, but was shown for many different pairs of brain regions. These findings provide strong support for the assertion that nonrandom neuronal activity, relatively independent of any dedicated set of neurons in some particular brain region, is how the brain trades information.

In a recent study which examined working memory in a delayed match from sample paradigm, we computed the voltage differences between EPs elicited by noncontingent probe stimuli presented before and after presentation of a priming stimulus, which had to be compared to a subsequent matching stimulus. The differences between the pre- and postpriming probe EPs, maximal at about 200 ms of latency, were postulated to reflect sustained engagement of a distributed population of neurons occupied by mediation of working memory and therefore inhibited from activation during the delay period. The voltage field across the scalp representing this virtual image of the working memory of the priming stimuli demonstrated extremely high cross-correlations with the voltage field elicited by subsequent presentation of the matching stimuli. It is noteworthy that the maximal correlations between the virtual image field and the stimulus-evoked field occurred at about 200 ms after presentation of the matching stimulus (Fig. 2D). Taken together with analysis of the spatial principal components of the scalp voltage fields, these data were interpreted as evidence that binding of information might be accomplished by zero phase coherence between nonrandom activity among anatomically distributed neuronal ensembles (John et al., 1997).

Binding through Synchrony

Cortical and thalamic regions display fast subthreshold oscillations, occasionally leading to single spikes, upon direct depolarization (Llinas et al., 1991; Steriade et al., 1991). Corticothalamic projections, from layers V and VI, may reflect inputs to the thalamus, producing fast rhythmic bursts upon depolarization (Steriade et al., 1996, 1998; Contreras & Steriade, 1997; Llinas et al., 1994). Fast spontaneous oscillations in intrathalamic and thalamo-cortical networks may play a decisive role in binding. Synchronization of fast rhythms may be subserved by intralaminar neurons which fire rhythmic (gamma frequency range) spike bursts and have diffuse cortical projections (Jones, 1998; Llinas et al., 1994; Steriade et al., 1993).

Proposals have been made that such synchronized discharges of neurons in different brain regions may serve to bind spatially dispersed representations of a multimodal stimulus into an integrated percept (Kreiter & Singer, 1996; Gray et al., 1989). Many electrophysiological proposals for possible binding mechanisms have been concerned with high-frequency components of sensory evoked potentials. Oscillatory modulation and neuronal synchronization in the gamma frequency range (30–80 Hz) has been suggested as a necessary condition for awareness of stimuli to occur (Engel et al., 1997; König et al., 1995). Phase-locking of 40 Hz oscillations with zero delay between the prefrontal and parietal human cortex has been reported during focused attention and conscious perception of recognized auditory or visual events (Desmedt & Tomberg, 1994; Tallon-Baudry et al., 1997). These findings have been confirmed by the observation of such phase-locked synchrony between brain regions in human intracranial recordings, lending support to proposals that perception involves activation of many distinct, functionally specialized areas (Tallon-Baudry, 2000) and that the self may be a transient dynamic signature of a distributed array of many brain regions integrated by such synchrony (Varela, 2000).

As pointed out above, the logical implications of phase-locking with zero delay among regions that need to be integrated focus attention on and increase the plausibility of field theoretical explanations. Phase-locked cortico-thalamic volleys converging from different brain regions on the intralaminar nuclei may establish a cortico-thalamic-cortical resonance essential for binding and perception to be accomplished.

CONSCIOUSNESS IS DISCONTINUOUS

Behavioral studies by Efron (1970) suggest that consciousness is temporally discontinuous, parsed into sensory sampling intervals or ‘‘perceptual frames’’ estimated to be about 70 to 100 ms in average duration. It was earlier speculated that sensory systems integrate discrete temporal samples of incoming information in a sequential, stepwise process, called the ‘‘traveling moment of perception’’ (Allport, 1968). It may be relevant that the durations of long lasting EPSP–IPSP sequences, omnipresent in mammalian forebrain neurons, commonly range from 80 to 200 ms (Purpura, 1972). Temporal extension of neural activity has been considered critical for binding (Flohr, 1995). Data from magnetoencephalography has led to similar proposals that consciousness is discontinuous and is parsed into sequential episodes by synchronous thalamo-cortical activity (Llinas & Ribary, 1998).

A mechanism has been proposed elsewhere to reconcile the evidence that perceptual framing takes place with the apparent continuity of perceptual experience. Essentially, that proposal envisaged a multiplexed, temporally offset, and asynchronous cascade of momentary perceptual frames converging on primary cortical areas to establish a steady-state perturbation from baseline activity, with a spatiotemporal signature of sustained nonrandomness independent of the contributions of individual neurons (John, 1990).

Recently, another kind of evidence has been interpreted to suggest that the apparently continuous stream of consciousness consists of discrete, discernible units. In the continuous sequence of momentary maps of the distribution of brain electrical fields on the scalp, there are brief moments of stability of topographic landscapes (Lehmann et al., 1987; Lehmann, 1971). These landscapes are discontinuous, concatenated by sudden transitions into the next landscape, and can be parsed into intervals of quasistability, or ‘‘microstates’’ (Strik & Lehmann, 1993; Pascual-Marqui et al., 1995). Different map landscapes have been associated with different modes of spontaneous thoughts (Koenig & Lehmann, 1996) and with spontaneous visual imagery or abstract thoughts (Lehmann et al., 1998).

EVIDENCE OF A COMPARATOR

Neurons may fire spontaneously or may be dynamically inhibited or in a postdischarge refractory state. The brain is also continuously bombarded by afferent input from innumerable sources. Only an unknown fraction of the neuronal activity at any moment may possess informational utility for the control of adaptive behavior, which is how the brain contributes to survival. Some process beyond mere synchrony or nonrandomness must be invoked if the brain is to identify the relevant, informationally meaningful activity which is to be combined into an integrated percept. Further, what mechanism parses time into discontinuous intervals, ‘‘closes’’ the microstate, and assesses the meaning of the different neuronal events which occur within the duration of the ‘‘perceptual frame’’?

The global population of coherent neurons must be evaluated, irrelevant activity (‘‘noise’’) excluded, and informationally significant activity (‘‘signal’’) bound into a percept or ‘‘qualia,’’ a subjective instant of awareness. Otherwise, consciousness would be overwhelmed by a continuous, noisy sensory barrage. Theorists have long postulated that perceptual closure must involve a comparator between exogenous sensory specific information about the environment and endogenous nonsensory specific reports of context, emotion, valence, and relevant recent memories contained in the ‘‘internal state’’ (John, 1968). The exogenous information assessment must be accomplished by genetically determined, reliable feature analysis in the brain, which are relatively automatic mechanisms developed during evolution of the human species. Conversely, the endogenous internal state must represent the hedonic motivational relevance and episodic memories established by the unique life experiences of every individual.

Evidence that such a comparator is involved in subjective awareness and perception comes from various sources. For example, ‘‘backward masking’’ or metacontrast is well known, consisting of the ability of a later sensory input to block perception of an event earlier in time (Alpern, 1952). Yet, the momentary subjective continuity of the present with the past is also a large part of consciousness, i.e., a degree of constancy must persist across a sequence of perceptual frames, analogous to a ‘‘sliding comparator.’’

In our earlier studies mentioned above, EPs from trained animals displayed widespread emergence of late positive components as sensory stimuli acquired cue value, with appetitive/aversive meaning or utility. These components were present in EPs from trials in which appropriate conditioned responses were elicited, but were absent when performance failed. The early positive component was proposed to reflect projections from specific pathways activated by the sensory cues, while the late positive component was released from a nonsensory specific representational system (John, 1968). This system, established by previous learning, reflected contributions of memory, motivation, and affect related to the stimuli. Concordance of these specific and nonspecific processes was assessed by a comparator system, presumably but not necessarily at the cortical level. Acceptable correspondence (matching) achieved perception of the stimulus and identified its informational significance (John, 1972). Similar evidence and interpretations were provided by other workers (Galambos & Sheatz, 1962).

In such conditioned animals, direct electrical stimulation that was phase-locked with a brief delay after the presentation of a peripheral conditioned stimulus, in order to block the primary positivity reflecting sensory specific input to cortical sensory receiving areas, had little effect on performance of conditioned responses. This absence of effect might indicate that electrically induced activation at this early latency actually mimicked the effects of afferent input, a plausible interpretation in view of the surrogate capability of direct brain stimulation described above. However, identical electrical disturbances that were similarly phase-locked but further delayed, in order to block the later nonsensory specific component, greatly decreased performance (John, 1968). This indicates that electrical stimulation at this later interval, coincident with the arrival of nonsensory influences arriving at the cortex from thalamic nuclei of the diffuse projection system, disrupted some ongoing process essential for perception and subjective awareness.

In human subjects, electrical stimuli phase-locked to peripheral stimuli but delayed to coincide with the later component and delivered to the somatosensory cortex (Libet, 1973) or centre median nucleus of the thalamus (Hassler, 1979) blocked perception of median nerve stimulation in conscious neurosurgical patients. In patients nonresponsive after head trauma, presence of early but not late components of multisensory evoked potentials has been used to scale the degree of brain injury

(Greenberg et al., 1981). Return of late evoked potential components is predictive of recovery from coma (Alter et al., 1990). Such data support the proposal that a comparator between neuronal activity in sensory specific and nonspecific systems is critical for perception.

CONSCIOUSNESS AS A COOPERATIVE PROCESS

Multidimensional binding provides the fine texture of consciousness, the global content of a momentary cognitive instant of experience. The actual binding process has been envisaged by some as a global resonance state (Llinas & Ribary, 1998), resulting from the coincidence detection of concurrent specific and nonspecific neuronal processes. This formulation is reminiscent of the concept of scanning by a subcortically timed modulation, proposed a half-century ago (Pitts & McCulloch, 1951).

The current proposition for a binding mechanism denies that any individual neuron or discrete set of neurons might mediate the required integration of globally distributed coherent activity. No cell in an ensemble can assess the nonrandom behavior of that ensemble. The content of consciousness must depend on the integration of dispersed, coherent neural activity and emerge from a statistical process. It is not dependent on the discharge of any particular neuron or neurons but derived from the synchronous significant departure from randomness across spatially distributed neuronal masses (John, 1972). It can be conceptualized as global negative entropy, the totality of improbable brain activity.

Binding as a Field Property

A voltage field must be generated by the inhomogeneity of ionic charge distribution within the space of the brain. The measurements provided by magnetoencephalography establish that, in the brain, substantial currents flow between regions of different charge density. Libet (1998) proposed that subjective experience may arise from a field emerging from appropriate nerve cell activities (i.e., synchrony and coherence), reflecting relational properties not reducible to the description of any of its parts. Consciousness is postulated to arise as an emergent property of such a field. Squires (1998) suggested that consciousness may be a primitive ingredient of the world, i.e., not reducible to other properties in physics, and includes the qualia of experience. It has been suggested that bundles of pyramidal cells bound together by cooperative processes produce spatio-temporal patterns coupled by long-range coherence in microtubular connections which may establish consciousness, or ‘‘awareness’’ (Eccles, 1994).

In a recent review of psychophysical and anesthesiological studies of components of auditory evoked potentials, ranging from the very short latency brainstem auditory evoked response to the late P300, it was concluded that the midlatency responses from 10 to about 100 ms poststimulus are essential for sensation and probably arise from the secondary as well as primary auditory cortex. No specific suggestion was proposed for the processes critical for perception. However, it was hypothesized that consciousness was identical with the spatiotemporal pattern of an electromagnetic field surrounding neuronal activity rather than the firing of particular neurons (Pockett, 1999).

Neuron–Wave Duality

Many observations cited earlier came from spatially localized discharges of neurons at specific times and represent discrete events. When one attempts to relate these discrete events to statistically significant deviations from randomness as shown by population behavior, uncertainty arises as to the contribution of any particular discharge to those statistics. This is much like the uncertain contribution of any molecule of a gas to its partial pressure in a closed volume and might be conceptualized as ‘‘neural thermodynamics.’’ In parallel with the behavior of these elements that can be analogized to particles, waves of voltage fluctuations can be observed within the volume of the brain. The voltage waves and coherences are defined by the nonlocal relationships among elements and their organization, while neuronal discharge is defined by influences impinging upon a single element. These two aspects of brain activity, neuronal discharges and potential waves, appear to be intrinsic to the principles by which the brain operates and demand to be reconciled in any explanation of its functional capabilities.

It is difficult to resist comparing these uncertain particlelike and wave-like phenomena to the paradoxes which forced physicists early in the last century to resort to a quantum mechanical resolution. Is this conceptual similarity merely the basis to draw an attractive analogy or might there be some physical correspondence between the two classes of phenomena, physical and neurophysiological?

Quantum Theoretical Proposals

Faced with this paradox, some neuroscientists have suggested that there might be a literal correspondence between the two classes of observations. It has been proposed that discrete moments of experience may be comparable to quantum state reductions (Shimory, 1993) and that the noncomputable performance of a conscious brain may be understood only by invoking a quantum-mechanical state collapse or a state-selection mechanism (Penrose, 1994). State selection is only possible if well-defined quantum states are present and collapse into one of the components.

Some theories propose that brain substrates might sustain a variety of quantum fields. Interactions between states defined by sensory quantum fields and cognition/memory quantum fields might occur in a bioplasma of ions or charged particles interacting with the electromagnetic field. Matching between these superposed quantum fields might collapse their wave functions, resulting in consciousness of that state (Stapp, 1993). Chalmers (1996) has postulated the existence of two clouds of ions or ‘‘ionic plasmas’’ within the brain (specific and nonspecific). Each is the source of a distributed voltage field, which generates a quantum wave function. When these two wave functions achieve a sufficient degree of coherence to exceed some threshold, the quantum fields collapse. Consciousness is postulated to emerge from the collapse of these two wave functions, generating a perceptual frame. Hameroff and Penrose (1998) have pointed out that the microtubal structure within neurons constitutes channels where mitochondria pump ions. The conformational states of microtubule subunits (tubulins) are coupled to internal quantum events and interact cooperatively with other tubulins. Microscopic coherent superposition of quantum-coupled tubulin conformational states is assumed to occur throughout significant brain volumes, providing the global binding essential to consciousness, which results from the collapse of superpositioned states.

It is understandable that the quandary raised by the apparent wave-particle paradox has persuaded some to propose such literal correspondence to quantum mechanical description of physical systems. While such explanations may eventually be shown to be legitimate, there are major obstacles to their acceptance at the present time. There is no evidence that quantum mechanical processes can apply to the slow processes which transpire in the brain in times on the order of milliseconds and involve many cubic centimeters of cells at body temperature. For these reasons, quantum mechanical proposals seem implausible and unlikely.

THE SEARCH FOR A CRITICAL STRUCTURE

Does the whole brain contribute to the postulated global processes or are certain neuroanatomical structures or certain local properties of neurons endowed with a unique contribution to consciousness? Historically, in the absence of scientific evidence, philosophers have conjectured that consciousness might reside in some specific loci in the brain, such as the pineal gland or the cerebral ventricles. With the development of modern neuroscience, this search has resumed. Various strategies have been resorted to by neuroscientists in the attempt to identify anatomical structures or brain processes critical for consciousness, including lesioning, imaging, and pharmacological techniques.

Recent suggestions of specific critical brain structures have included a reticulo-thalamo-cortical distributed network, or ‘‘Global Workspace’’ (Baars, 1996); the intralaminar nuclei of the thalamus (Bogen, 1995); nucleus reticularis (Taylor & Alavi, 1993); anterior cingulate (Cotterill, 1994); or hippocampus (Gray, 1995). It has been suggested that prolonged activity in some sparsely distributed, specialized set of ‘‘awareness cells’’ with unique properties constitutes the neural correlate of consciousness (NCC), distributed over neocortex, limbic system, thalamus, and claustrum (Koch, 1998). Based on imaging studies of brain activation in two types of blindsight, it has been proposed that what is critical for awareness may be the pattern of activity among regions rather than in a particular brain region (Weiskrantz, 1998). A ‘‘Dynamic Core Hypothesis’’ has been proposed, constituting a set of thalamo-cortical elements spatially distributed and metastable, sustaining an ensemble of interactions which maintain unity even if its composition is constantly changing (Tononi & Edelman, 1998).

INSIGHT FROM ANESTHETIC EFFECTS

Previous Studies

One approach to whether such a dynamic core might exist is to determine whether a particular set of brain regions changes its state with the loss of consciousness due to the action of anesthetics. Alkire et al. (1998) studied ^{18}FDG PET during propofol anesthesia. Mean cerebral metabolic rate (CMRGlu) was globally reduced by 38% at loss of consciousness (LOC), rather uniformly throughout the brain, but relatively more in cortex than subcortex. In sedation, very similar but lesser global reduction was found. Similar global quantitative results were found with isoflurane. It was concluded that LOC was not caused by changes within a specific circuit, but rather by a uniform reduction below a critical level in a distributed neural system. In a study using $H_2{}^{15}O$ PET to measure dose-related changes in rCBF during sedation with midazolam, a similarly global reduction of about 12% was found (Veselis et al., 1997). In addition, however, a discrete set of brain regions displayed a significantly more extreme reduction in cerebral blood flow. These regions included multiple areas in the prefrontal cortex, the superior frontal gyrus, the anterior cingulate gyrus, parietal association areas, the insular, and the thalamus.

More recently, patients were studied using ^{18}FDG PET to study CMRGlu and $H_2{}^{15}O$ PET to study rCBF before and after recovery from vegetative state, where arousal may be preserved but awareness is abolished. While in the vegetative state, overall metabolism was reduced by 60%. Sensory stimulation still activated primary but not secondary cortical regions. In patients who regained consciousness, reversal of this reduction was seen in bilateral prefrontal cortices, Broca’s area, left superior frontal gyrus, the inferior parietal lobule, and the precuneus. Previously disconnected thalamic and cortical areas resumed functional relationship (Laureys et al., 2000).

Franks and Lieb (1998) proposed that most clinical effects of general anesthetics arise from direct interactions with proteins, hyperpolarizing membranes, and blocking receptor channels, perhaps perturbing microtubule polymerization. LOC might result from widespread interference with signal processing, blocking perception. Anesthetics are believed by many to act primarily through GABA receptors, while some have also suggested that major effects may occur at cholinergic receptors. Flohr (1998) proposed that normal functioning of the NMDA synapse is necessary and sufficient for consciousness. Blockade of the NMDA receptor complex or Ca^{2+}-dependent processes by anesthetics, perhaps hyperpolarizing the postsynaptic membrane, might disrupt possible function of the NMDA synapse as a coincidence detector of pre- and postsynaptic inputs within a relatively long time window. Hameroff (1998) suggested that anesthetics may prevent quantum-coherent superposition of membrane or tubulin proteins, acting at certain hydrophobic sites throughout the brain which were essential for consciousness.

In many EEG studies of anesthesia, quantitative features have been extracted from EEG power spectra (QEEG), such as the median frequency or the spectral edge; those frequencies below which one finds 50 or 95% of the EEG power, respectively; as well as bispectral measures. Such variables have been repeatedly related to clinical signs or to anesthetic end points (e.g., Rampil & Matteo, 1987). A recently developed anesthesia monitor, which has undergone extensive investigation, combines a variety of EEG features from one or two electrodes into a single number, the bispectral or ‘‘BIS’’ index (Sebel et al., 1997). While such descriptive features may correlate well with drug concentrations and clinical states, they provide little or no insight into the underlying neurophysiological mechanisms of consciousness.

However, the apparent clinical utility of such indices supports the belief that a thorough study of EEG changes during anesthesia might provide better understanding of the physiology underlying the loss and return of consciousness caused by anesthetic agents. Detection of a set of reversible changes in electrophysiological state and interactions among brain regions, invariantly associated with loss and return of consciousness and independent of the causative agents, might identify brain processes and systems critical for consciousness. There has been relatively little comparative study of quantitative physiological effects common to a variety of anesthetics and their action upon consciousness.

CURRENT QEEG STUDIES OF INVARIANT EFFECTS OF ANESTHESIA

In a study of 176 surgical procedures, in which a wide variety of anesthetic agents were administered using standard clinical practices, we continuously monitored the EEG to quantify changes in brain electrical activity. Our goal was to identify those variables which showed the earliest and statistically most significant changes from the onset of induction to the loss of consciousness (LOC), as well as the earliest and most significant reversal of such changes during the transition from surgical maintenance to return of consciousness (ROC), independent of the agents used for induction or maintenance. Changes associated with LOC and which reverse with ROC were considered to identify those features which reflect the level of consciousness. Features reflecting ancillary effects of anesthetic agents may reverse partially or not at all.

This research not only identified a set of reversible QEEG changes invariant with LOC and ROC, but also led to the development of a clinical instrument (PSA 4000) which provides quantitative assessment of the depth of anesthesia induced by any agents.[1] A detailed description of the subjects, inclusion and exclusion criteria, anesthetic protocols, surgical procedures, EEG data collection, editing and quantitative analysis methods, and the findings of these studies can be found in a companion article in this issue (John et al., 2001).

In this research, four types of invariant changes were found to occur with LOC, independent of the specific agents used for induction, and to reverse upon ROC no matter what anesthetics had been used during surgical maintenance: (1) At LOC, a global increase in absolute power occurred across the entire frequency range from 1.5 to 25 Hz, somewhat diminished but not completely reversed at ROC. In contrast, in the gamma range (25–50 Hz), a global decrease of power appeared at LOC which was sharply reversed at ROC (especially in gamma 2, 35–50 Hz). (2) At LOC, marked anteriorization of increased power took place in all bands which was decreased but not reversed at ROC. This anterior shift of power during anesthesia was first described in monkeys (Tinker et al., 1977) and has since been repeatedly reported in human EEG studies. In contrast, no comparable shift in power was observed in the gamma band. (3a) At LOC, hypercoupling between the prefrontal and frontal regions within each hemisphere took place in the delta and theta bands. At the same time, there was uncoupling of anterior from posterior regions of each hemisphere as well as of homologous frontal and more posterior regions between hemispheres.

---

[1] The Patient State Analyzer, or PSA 4000, has Food and Drug Administration approval and is manufactured by Physiometrix, Inc., North Billerica, MA.

These changes in cortical interactions at LOC, although lessened during emergence, were not completely reversed at ROC. (3b) In the gamma 1 band (25–35 Hz), the prefrontal and frontal regions remained relatively hypercoupled throughout the surgical procedures. Interhemispheric and intrahemispheric transactions were disrupted at LOC, severely uncoupled during maintenance, gradually recoupled during emergence, and finally returned to a high level at ROC. This pattern was also seen in gamma 2 (35–50 Hz) where the shifts were even more striking. No evidence was found of a traveling wave rhythmically sweeping across the cortex, as proposed by some workers. Rather, a high proportion of rhythmic covariance was zero phase-locked. (4) The anteriorized hypersynchrony was most strongly localized in a common system of neuroanatomical structures throughout the duration of anesthesia, independent of the fact that different agents were utilized for induction and surgical maintenance. All of these findings are illustrated in the companion article (John et al., 2001).

EEG absolute power increases as discharges in neuronal populations in subjacent cortex become more synchronous, i.e., less differentiated, with decreased processing of specific information. Slow oscillations in the low delta range (approximately 0.5–1.0 Hz), generated in the neocortex, have been associated with a prolonged deep hyperpolarization of cortical cells (Contreras & Steriade, 1997). The huge slow hypersynchrony here reported to occur at LOC probably results in a generalized disfacilitation or inhibition of cortical and subcortical regions, which might account for the diffuse diminution of rCBF during slow wave sleep (Hofle et al., 1997), of rCBF during sedation (Veselis et al., 1997), and of rCMR during anesthesia (Alkire et al., 1998) or in vegetative state (Laureys et al., 2000). This diffuse decrease, caused by the slow hypersynchrony at LOC, must cause dedifferentiation and depression of neural activity with disruption of informational transactions, probably a major reason why anterior brain regions are functionally disconnected from posterior regions and the left is disconnected from the right hemisphere.

The present findings implicate anterior structures which display a profound change in state reversibly with LOC and ROC, independent of the anesthetic agent, and plausibly correspond to the ‘‘critical system’’ sought by many others. Three-dimensional QEEG source localization techniques were applied to find the probable neuroanatomical generator of the most salient power changes (3.5 Hz) which occurred upon LOC. A full description of this method, called Variable Resolution Electromagnetic Tomography, or VARETA, can be found elsewhere (Bosch-Bayard et al., 2001). (Figure 3 presents VARETA results which are representative for all agents, illustrated here for only two.) This system includes the mesial orbital and rectus gyri of the prefrontal cortex; the superior frontal gyrus; the pre- and paracentral gyri; the anterior cingulate gyrus; the amygdala; the basal ganglia; and, by implication, the thalamus. Recent evidence indicates that VARETA may localize thalamic changes quite accurately (Prichep et al., 2001). It is noteworthy that this set of brain regions corresponds very closely to those where rCBF decreases most markedly during deep sedation (Veselis et al., 1997), rCMR decreases in vegetative state (Laureys et al., 2000) and where rCMR changes most upon LOC (Alkire et al., 2000), reversing upon recovery. The enormous anteriorization of power manifested at LOC, especially at the low end of the EEG spectrum, must suppress cooperative processes within the constituent

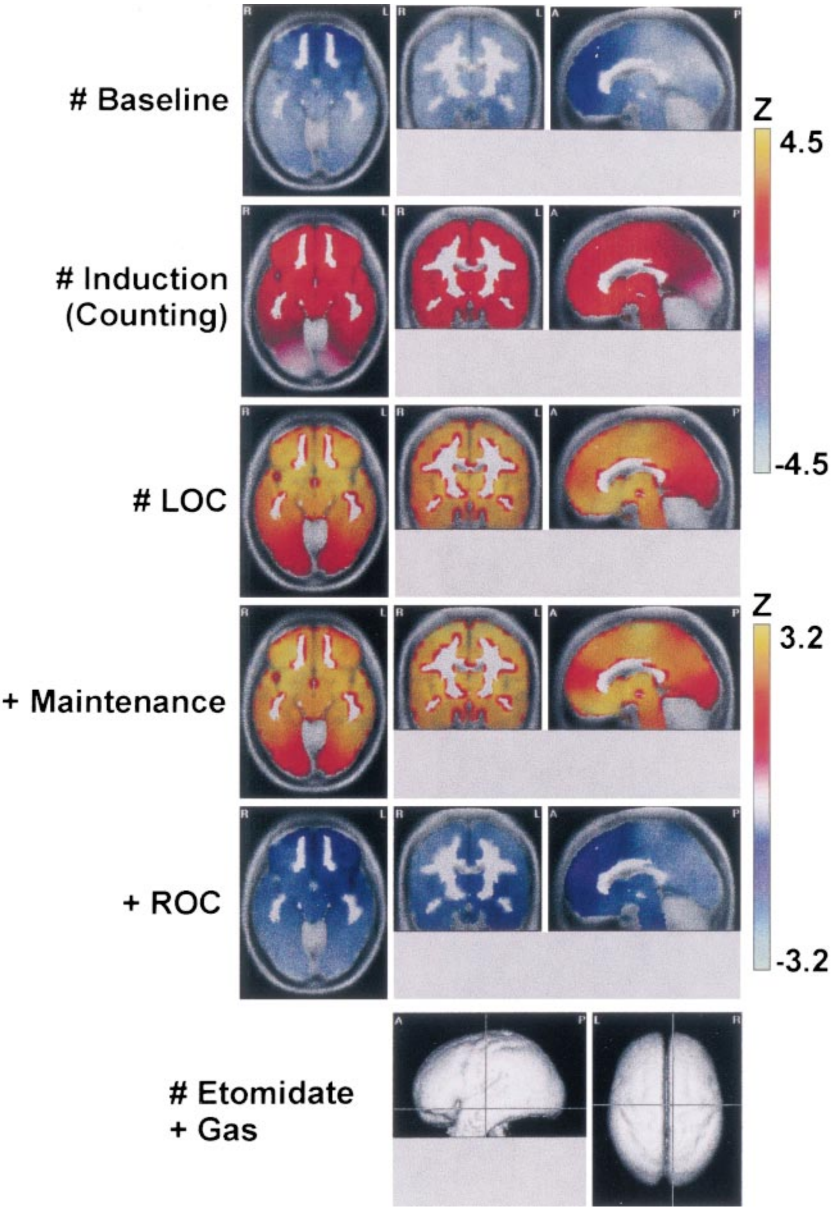

FIG. 3. Representative mean VARETA (Bosch-Bayard et al., 2001) images, averaged across 15 patients, of serial slices from a statistical MRI atlas (Evans, 1993). Each voxel is color-coded to correspond to the *z* score of the deviation from the normal resting voxel distributions of absolute power in a 0.39-Hz spectral window centered at 3.5 Hz. (Top) At baseline before sedation; (second panel from top) during induction with etomidate, while counting; (third panel from top) upon cessation of counting, just after loss of consciousness (LOC); (fourth panel from top) during maintenance at surgical plane by sevoflurane, just before emergence; (bottom) just after opening eyes in response to loud calling of patient's name (ROC). (For more details, see John et al., 2001.)

neuronal populations of these regions. Together with the intra- and interhemisphere decrease in coherence, this functional system becomes disorganized. The uncoupling of anterior from posterior hemispheric regions, together with this anteriorized increased power, indicates that a blockade of perception must accompany the electrophysiological changes at induction and strongly implies that such perception depends upon this critical system in anterior brain regions. As the global slow waves are replaced upon ROC, these inhibitory influences reverse. Normal patterns of coherence are restored and redifferentiation occurs. High common mode resonance must reappear across the cerebral cortex.

A FIELD THEORY OF CONSCIOUSNESS

A complex neuroanatomical system, described elsewhere (Hughes & John, 1999), has been proposed to be responsible for homeostatic regulation of the frequency composition of the EEG, found to be stable in all healthy individuals, independent of ethnic background, but disturbed in developmental, neurological, and psychiatric disorders. Disruption of this system must underlie the observed invariant electrophysiological effects of anesthesia agents. Across all anesthetics, the mean frequency within every frequency band in the EEG decreased very significantly at LOC. Considering these findings together with those discussed above, the overall data indicate that a salient contribution to these changes may be attributed most immediately to hyperpolarization of thalamic neurons by GABAergic influences from nucleus reticularis.

However, this inhibitory action might reflect a cascade of consequences initiated by inhibition of the mesencephalic reticular formation (MRF). Blockade of ascending reticular cholinergic influences will disinhibit nucleus reticularis, allowing it to hyperpolarize thalamic neurons. Pacemaker cells will slow their oscillations, causing a global decrease in the mean frequency of the EEG down into the theta range. Transmission of activating influences via the diffuse thalamic projection system to the cortex will be blocked. Not only will this disinhibit the cortical cells which generate the delta rhythm, but the late components of the sensory evoked potential normally transmitted to the cortex from these nonspecific nuclei will disappear. While sensory relay nuclei may continue to transmit afferent volleys to the cortex as primary EP components, the comparator critical for sensory perception will be unable to function. Further compounded by diminution of the gamma oscillations, postulated below normally to enhance signal-to-noise ratio, the diffuse dissemination of information through the cortex by the parvalbumin matrix will be interrupted.

What might be the role of ubiquitous gamma oscillations? Consider that a weak rhythmic modulation of membrane potentials, insufficient in itself to produce spike discharges and perhaps synchronized by the intralaminar neurons, is superimposed on the neurons throughout the brain. The neuronal population at any moment displays a range of excitability, depending on the recency and number of synaptic inputs affecting their membrane potentials. As the modulating gamma influences impinge on these populations, those neurons should discharge whose state of membrane depolarization plus the oscillatory modulatory depolarization exceeds the local threshold. At the other end of the excitability distribution, neurons already in a refractory state or below that critical threshold should be further inhibited by the subsequent hyperpolarizing phase of the fast oscillation. The temporal patterns of negative as well as positive deviations from randomness across the cerebral cortex, due to afferent and interoceptive signals, must thereby be amplified.

The evidence from moving electrode arrays, illustrated in Fig. 2A above, supports the contention that the temporal pattern of deviation from randomness identifies that part of the neuronal activity which is of informational utility in the brain, independent of the particular subset of cells active within an extensive neural ensemble. The evidence from studies of differential generalization, illustrated in Fig. 2B, indicates that it is not only the appearance of nonrandomness but the temporal pattern of deviation from randomness which denotes the specific content of that information. The evidence from studies of direct electrical stimulation of the brain, illustrated in Fig. 2C, demonstrates that the same behavioral significance may be attributed by an animal to a particular temporal pattern of nonrandomness, no matter where in the brain it arises.

Some years ago we computed the mean zero phase coherence across all 19 electrodes of the International 10/20 System and the whole EEG power spectrum (John et al., 1990). This computation was based on 2 min of artifact-free resting, eyes-closed EEGs obtained from 109 normal healthy adults. The resulting mean values ranged from 40 to 65% at different electrode positions. These values represent the participation of every brain region in ‘‘common mode resonance’’ subsuming all EEG frequencies, possibly mediated by the parvalbumin matrix described above (Jones, 1998). It is interesting that these values are approximately the percentage of variance accounted for by the first spatial principal component of the EEG across all 19 electrodes (John et al., 1990). Local temporal patterns of nonrandomness reflecting current processing of afferent information, together with ‘‘housekeeping’’ activities must account for the remaining variance within each region (i.e., 100% minus common mode). The observed decreases in global coherence which occur at LOC across all frequency bands must totally disrupt the common mode resonance, while the dedifferentiation imposed by the inhibitory consequences of the slow waves must interrupt local processing.

The normally observed persistence of microstates, sustained during intervals very much longer than the effects of an input upon the polarization potentials of neuronal membranes, may reflect asynchronous reciprocal cortical-cortical and cortical-subcortical interactions among anatomically distributed ensembles. These reverberations may be conceptualized as a concatenated series of afferent volleys which will each elicit a coherent evoked response in those neurons with an acceptable level of excitability within each region. The result of these nested interactions will be a voltage pattern which may be sustained in time and space. This spatio-temporal pattern (microstate) will possess invariant statistical features due to this resonance, independent of the momentary contributions of any individual neurons, much like the ‘‘Dynamic Core Hypothesis’’ (Tononi & Edelman, 1998). Sustained thalamo-cortical reverberations mediated by different neurons in successive volleys have previously been reported (Verzeano & Negishi, 1960). A detailed model for how such a stable field might be preserved across a significant time interval spanning multiple perceptual frames has been presented elsewhere (John, 1990).

Such resonance might arise from two independent sources. One source might be multidimensional and sensory-specific influences, impinging primarily on the axosomatic synapses of pyramidal cells in the cortex. These inputs would reflect the momentary state of the external and internal environments, including the tone of the musculature. Another related but independent source of resonant processes might be the nonsensory specific influences, which might arise from many neuronal sources. These factors might arise from many sources, including prefrontal and frontal cortical areas and the limbic system, and might impinge primarily on axodendritic synapses of cortical cells.

The two resulting anatomically extensive coherence patterns might establish two clouds of ions in the brain. Temporal patterns of local nonrandomness would reflect afferent information which would dynamically produce and redistribute heterogeneous charge density in clouds of ions. These clouds of charge result from cooperative processes engaging large numbers of neurons and are not defined by the firing of any individual neuron in an ensemble. It is current flow between such clouds which is detected by magnetoencephalography. Each cloud would consist of anisotropic spatial distributions of electrical charges. These heterogeneous charge densities would exist in some anatomical compartment, perhaps the microtubules as suggested by some (Hameroff & Penrose, 1998) but more plausibly extraneuronal, perhaps in the glia. The local charge density in different regions within this space would be proportional to the percentage of the local population which was activated, analogous to an ionic signal-to-noise ratio.

Only a comprehensive description of these two global charge distributions, such as their wave functions, would be sufficient to encompass hypothetically the binding of the spatially distributed nonrandomness necessary to define the fluctuating content of the perceptual moment. A detailed proposal for how such wave functions can be defined is in preparation. Essentially, a ground state can be defined for the brain from existing precise knowledge of homeostatic set points (Hughes & John, 1999). Momentary local deviations from those set points define excited states, for which local probabilities can be computed and combined into a spatial wave function describing global negative entropy (John, unpublished MS).

The electromagnetic fields dispersed throughout the brain as a result of these processes appear similar to the quantum fields or ‘‘bioplasmas’’ suggested by some (Chalmers, 1996; Stapp, 1993). It may be that subjective experience arises from an instant of consciousness, generated by the quantumlike collapse of these two wave functions when adequately superimposed, although no evidence has been found for such processes in the brain. Each interval in which reverberation was sustained might correspond to a microstate or a ‘‘perceptual frame.’’ The salient dimensions, or ‘‘qualia,’’ of momentary subjective experience would reflect the relative charge density of temporal patterns of nonrandomness within regions of brain space resulting from local synchrony. Such patterns of synchrony or coherence can be considered to reflect the time rate of change of local negative entropy.

The functional neuroanatomical system, which this study has shown to change state reversibly with the LOC and ROC, includes regions of the thalamus and the prefrontal cortex, which receive updating projections from all sensory systems. The system also includes limbic structures which interpret the momentary sensory experience in terms of a past personal context. All of these elements are contained in the instantaneous stream of subjective experience. These various dimensions of each instant are defined by the temporally synchronized, zero lag covariation of temporal patterns of nonrandomness within multiple spatially separated neuronal populations and by the global spatio-temporal fluctuations of negative entropy of the whole brain. It might be necessary that both the amount and the rate of change of negative entropy exceed some critical threshold within some restricted volume of space (analogous to a critical packing fraction) for a change in the environment to enter consciousness. The perceptual ''figure'' might be identified by such a change, while the perceptual ''ground'' would be the sustained constancies in the field. An additional process must also exist such that the global state retains access to the local fluctuations of entropy, perhaps by global–local resonance, to achieve the ability to relate regional coherence patterns to representation of specific information.

No conceivable network of synaptic connections could evaluate this continuous fluctuation of negative entropy in space, which can only be described as a field. No neuron can encode the multidimensional complexity of these cooperative processes. Therefore, we postulate that consciousness arises as a property of a field resonating within a coherent dynamic core, composed of the anatomical structures herein found to change state reversibly with loss and return of consciousness.

Essentially, this postulate envisages the brain as a hybrid device, with local, ''bottom-up'' digital informational processes, comprised of particular temporal patterns of coherence within cell assemblies, being converted to a global, analog subjective experience produced by a field comprised of an ionic plasma. In order for an organism which experiences its environment and internal state in this manner to survive and adapt, the converse ''top-down'' process must follow as a corollary. The global state defined by the field must be able to activate discrete processes. Efferent neuronal influences facilitated by differential ionic densities in certain regions of the anterior system must impinge on posterior structures of the sensory cortex and thalamus to focus attention and sharpen perception; on the limbic system to select, label, and weight experiences for storage; and on the motor system to alter muscle tone and to activate the musculature to perform appropriate movements. Feedforward and feedback must coexist. Each region making an efferent contribution to the ionic field of the anterior system must receive a reciprocal afferent modulation of its propensity for coherent discharge. Perhaps this happens as the perceptual frame or microstate ends. With such reciprocal interactions, the brain may be viewed as a dual hybrid discrete to global and global to discrete device.

ACKNOWLEDGMENTS

The author acknowledges the constructive criticisms and comments made by numerous friends and colleagues, especially Leslie S. Prichep, which helped greatly in the attempt to formulate and clarify these ideas. I also acknowledge Laverne D. Gugino, Wolfgang Kox, Pedro Valdes-Sosa, Simone Wolter, MeeLee Tom, Henry Merkin, and Bryant Howard for collection and analysis of the anesthesia study. Collection and analysis of the anesthesia data was supported by Physiometrix Inc., North Billerica, MA.

REFERENCES

Alkire, M. T., Haier, R. J., & Fallon, J. H. (1998). Toward the neurobiology of consciousness: Using brain imaging and anesthesia to investigate the anatomy of consciousness. In S. R. Hameroff, A.

Kaszriak, & A. Scott (Eds.), *Toward a science of consciousness II—The second Tucson discussions and debates,* pp. 255–268. Cambridge, MA: MIT Press.

Alkire, M. T., Haier, R. J., & Fallon, J. H. (2000). Toward a unified theory of narcosis: Brain imaging evidence for a thalamocortical switch as the neurophysiologic basis of anesthetic-induced unconsciousness. *Consciousness and Cognition,* **9**(3), 370–386, doi:10.1006/ccog.1999.0423.

Allport, D. A. (1968). Phenomenal simultaneity and perceptual moment hypotheses. *British Journal of Psychology,* **59,** 395–406.

Alpern, M. (1952). Metacontrast. *American Journal of Optometry,* **29,** 631–646.

Alter, I., John, E. R., & Ransohoff, J. (1990). Computer analysis of cortical evoked potentials following head injury. *Brain Injury,* **4**(1), 19–26.

Baars, B. J. (1996). The workspace of the mind. In *The theater of consciousness.* New York: Oxford Univ. Press.

Bogen, J. E. (1995). On the neurophysiology of consciousness, Part I—An overview. *Consciousness and Cognition,* **4,** 52–62.

Bosch-Bayard, J., Valdés-Sosa, P., Virues-Alba, T., Aubert-Vázquez, E., John, E. R., Riera-Díaz, J., & Trujillo-Barret, N. (2001). Statistical parametric mapping of EEG source spectrum by means of variable resolution electromagnetic tomography (VARETA). *Clinical EEG,* **32**(2), 47–61.

Brecht, M., Singer, W., & Engel, A. K. (1998). Correlation analysis of corticotectal interactions in the cat visual system. *Journal of Neurophysiology,* **79**(5), 2394–2407.

Castelo-Branco, M., & Neuenschwander, S. (1998). Synchronization of visual responses between the cortex, lateral geniculate nucleus, and retina in the anesthetized cat. *Journal of Neuroscience,* **18**(16), 6395–6410.

Chalmers, D. J. (1996). *The conscious mind: In search of a fundamental theory.* Oxford, UK: Oxford Univ. Press.

Chapin, J. K., & Nicolelis, L. M. A. (1996). Neural network mechanisms of oscillatory brain states: Characterization using simultaneous multi-single neuron recordings. *Electroencephalography and Clinical Neurophysiology,* **45,** 113–122.

Chow, K. L., Dement, W. C., & John, E. R. (1957). Conditioned electrocorticographic potentials and behavioral avoidance response in cats. *Journal of Neurophysiology,* **20,** 482–493.

Contreras, D., & Steriade, M. (1997). Synchronization of low-frequency rhythms in corticothalamic networks. *Neuroscience* **76**(1), 11–24.

Cotterill, R. (1994). On the unity of conscious experience. *Journal of Consciousness Studies* **2,** 290–311.

Desmedt, J. D., & Tomberg, C. (1994). Transient phase-locking of 40 Hz electrical oscillations in prefrontal and parietal human cortex reflects the process of conscious somatic perception. *Neuroscience Letters,* **168,** 126–129.

Eccles, J. C. (1994). *How the self controls its brain.* New York: Springer-Verlag.

Efron, E. (1970). The minimum duration of a perception. *Neuropsychologia,* **8,** 57–63.

Eggermont, J. J., & Smith, G. M. (1996). Neural connectivity only accounts for a small part of neural correlation in auditory cortex. *Experimental Brain Research,* **110**(3), 379–391.

Engel, A. K. (2000). PL-03. Temporal binding and the neural correlates of consciousness. *Consciousness and Cognition,* **9**(2, pt. 2), S26.

Engel, A. K., Roelfsema, P. R., Fries, P., Brecht, M., & Singer, W. (1997). Role of the temporal domain for response selection and perceptual binding. *Cerebral Cortex,* **7,** 571–582.

Flohr, H. (1995). Sensations and brain processes. *Behavioral and Brain Research,* **71,** 157–161.

Flohr, H. (1998). On the mechanism of action of anesthetic agents. In S. R. Hameroff, A. Kaszriak, & A. C. Scott (Eds.), *Toward a science of consciousness II—The second Tucson discussions and debates,* pp. 459–467. Cambridge, MA: MIT Press.

Fox, S. S., & O'Brien, J. H. (1965). Duplication of evoked potential waveform by curve of probability of firing of a single cell. *Science,* **147,** 888–890.

Franks, N. P., & Lieb, W. R. (1998). The molecular basis of general anesthesia: Current ideas. In *Toward a science of consciousness II—The second Tucson discussions and debates,* pp. 443–457. Cambridge, MA: MIT Press.

Galambos, R., & Sheatz, G. C. (1962). An electroencephalograph study of classical conditioning. *American Journal of Physiology,* **203,** 173–184.

Gazzaniga, M. (1994). *Cognitive neuroscience.* Cambridge, MA: MIT Press.

Gray, C. M., Konig, P., Engel, A. K., & Singer, W. (1989). Oscillatory responses in cat visual cortex exhibit inter-columnar synchronization which reflects global stimulus properties. *Nature,* **338,** 334–337.

Gray, J. A. (1995). The contents of consciousness: A neuropsychological conjecture. *Behavioral and Brain Sciences,* **18,** 659–722.

Greenberg, R. P., Newlon, P. G., & Hyatt, M. S. (1981). Prognostic implications of early multimodality evoked potentials in severely head-injured patients: A prospective study. *Journal of Neurosurgery,* **55,** 227–236.

Hameroff, S., Kaszniak, A. W., & Scott, A. C. (Eds.). (1998). *Toward a science of consciousness II—The second Tucson discussions and debates.* Cambridge, MA: MIT Press.

Hameroff, S., & Penrose, R. (1998). Quantum computation in brain microtubules: The ''Orch OR'' model for consciousness. *Philosophical Transactions Royal Society of London* (A), **356,** 1869–1896.

Hameroff, S. R. (1998). More neural than thou. In S. R. Hameroff, A. Kaszriak, & A. C. Scott (Eds.), *Toward a science of consciousness II—The second Tucson discussions and debates,* pp. 197–213. Cambridge, MA: MIT Press.

Hassler, R. (1979). Striatal regulation of adverting and attention directing induced by pallidal stimulation. *Applied Neurophysiology,* **42,** 98–102.

Hofle, N., Paus, T., Reutens, D., Fiset, P., Gotman, J., Evans, A. C., & Jones, B. E. (1997). Regional cerebral blood flow changes as a function of delta and spindle activity during slow wave sleep in humans. *Journal of Neuroscience,* **17**(12), 4800–4808.

Hughes, J. R., & John, E. R. (1999). Conventional and quantitative electroencephalography in psychiatry. *Journal of Neuropsychiatry and Clinical Neuroscience,* **11**(2), 190–208.

Jasper, H. H. (1998). *Advances in neurology: Consciousness of the frontiers of neuroscience.* Philadelphia: Lippincott–Raven.

John, E. R. (1990). *Machinery of the mind.* Boston, MA: Birkhauser.

John, E. R., & Morgades, P. P. (1969). Patterns and anatomical distribution of evoked potentials and multiple unit activity by conditioned stimuli in trained cats. *Communications in Behavioral Biology,* **3,** 181–207.

John, E. R. (1968). *Mechanisms of memory.* New York: Academic Press.

John, E. R. (1968). Observation learning in cats. *Science,* **159,** 1489–1491.

John, E. R. (1972). Switchboard versus statistical theories of learning and memory. *Science,* **177,** 850–864.

John, E. R., Easton, P., & Isenhart, R. (1997). Consciousness and cognition may be mediated by multiple independent coherent ensembles. *Consciousness and Cognition,* **6**(1), 3–39.

John, E. R., & Killam, K. F. (1959). Electrophysiological correlates of avoidance conditioning in the cat. *Journal of Pharmacology and Experimental Therapeutics* **125,** 252–274.

John, E. R., & Killam, K. F. (1960). Electrophysiological correlates of differential approach–avoidance conditioning in cats. *Journal of Nervous and Mental Disease,* **131,** 183–193.

John, E. R., & Kleinman, D. (1975). Stimulus generalization between differentiated visual, auditory and central stimuli. *Journal of Neurophysiology,* **38,** 1015–1034.

John, E. R., Prichep, L. S., Chabot, R., & Easton, P. (1990). Cross-spectral coherence during mental activity. *Electroencephalography & Neurophysiology,* **75**(1), 568–569.

John, E. R., Prichep, L. S., Kox, W., Valdés-Sosa, P., Bosch-Bayard, J., Aubert, E., Tom, M., diMichele, F., & Gugino, L. D. (2001). Invariant reversible QEEG effects of anesthetics. *Consciousness and Cognition,* **10**(2), 165–183, doi:1006/ccog.2001.0507.

John, E. R., & Schwartz, E. (1978). The neurophysiology of information processing and cognition. *Annual Review in Psychology* **29,** 1–29.

Jones, E. G. (1998). A new view of specific and non-specific thalamocortical connections. In H. H. Jasper, L. Descarries, V. F. Castelucci, & S. Rossignol (Eds.), *Consciousness: At the frontiers of neuroscience (Advances in Neurology),* Vol. 77, pp. 49–71. Philadelphia: Lippincott–Raven.

Koch, C. (1998). The neuroanatomy of visual consciousness. In H. H. Jasper, L. Descarries, V. F. Castelucci, & S. Rossignol (Eds.), *Consciousness: At the frontiers of neuroscience (Advances in Neurology),* Vol. 77, pp. 229–241. Philadelphia: Lippincott–Raven.

Koenig, T., & Lehmann, D. (1996). Microstates in language-related brain potentials show noun–verb differences. *Brain & Language* **53,** 169–182.

König, P., Engel, A. K., & Singer, W. (1995). The relation between oscillatory activity and long-range synchronization in cat visual cortex. *Proceedings of the National Academy of Sciences of the USA,* **92,** 290–294.

Kreiter, A. K., & Singer, W. (1996). Stimulus-dependent synchronization of neuronal responses in the visual cortex of the awake macaque monkey. *Journal of Neurosciences,* **16**(7) 2381–2396.

Laureys, S., Faymonville, M.-E., Janssens, N., Degueldre, C., Peigneux, P., Del Fiore, G., Damas, P., Lambermont, B., Luxen, A., Lamy, M., Moonen, G., & Maquet, P. (2000). CS4-3.3. Brain function during vegetative state and after recovery: A lesional approach to the study of human consciousness. *Consciousness and Cognition,* **9**(2, pt. 2), S60.

Lehmann, D. (1971). Multichannel topography of human alpha EEG fields. *Electroencephalography and Clinical Neurophysiology,* **31,** 439–449.

Lehmann, D., Ozaki, H., & Pal, I. (1987). EEG alpha map series: Brain micro-states by space oriented adaptive segmentation. *EEG Clinical Neurophysiology,* **67,** 271–288.

Lehmann, D., Strik, W. K., Henggeler, B., Koenig, T., & Koukkou, M. (1998). Brain electrical micro-states and momentary conscious mind states as building blocks of spontaneous thinking. I. Visual imagery and abstract thoughts. *International Journal of Psychophysiology,* **29,** 1–11.

Libet, B. (1973). Electrical stimulation of cortex in human subjects and conscious sensory aspects. In A. Iggo (Ed.), *Handbook of sensory physiology,* Vol. II, pp. 743–790. New York: Springer-Verlag.

Libet, B. (1998). Do the models offer testable proposals of brain functions for conscious experience. In H. H. Jasper, L. Descarries, V. C. Costelucci, & S. Rossignol (Eds.), *Advances in neurology: Consciousness: At the frontiers of neuroscience (Advances in Neurology),* Vol. 77, pp. 213–217. Philadelphia: Lippincott–Raven.

Llinas, R., & Ribary, U. (1998). Temporal conjunction. In *Thalamocortical transactions: Consciousness: At the frontiers of neuroscience,* Vol. 77, pp. 95–103. Philadelphia: Lippincott–Raven.

Llinas, R., Ribary, U., Joliot, M., & Wang, X. J. (1994). Content and context in temporal thalamocortical binding. In G. Buzsaki, R. Llinas, & W. Singer (Eds.), *Temporal coding in the brain,* pp. 251–272. Berlin: Springer-Verlag.

Llinas, R., Grace, A. A., & Yarom, Y. (1991). In vitro neurons in mammalian cortical layer 4 exhibit intrinsic oscillatory activity in the 10 to 50 Hz frequency range. *Proceedings of the National Academy of Sciences of the USA,* **88,** 897–901.

Lumer, E. D., Edelman, G. M., & Tononi, G. (1997). Neural dynamics in a model of the thalamocortical system. 1. Layers, loops and the emergence of fast synchronous rhythms. *Cerebral Cortex,* **7,** 207–227.

Morrell, F. (1967). Electrical signs of sensory coding. In G. C. Quarton, T. Melnechuk, & F. O. Schmitt (Eds.), *The neurosciences: A study program,* pp. 452–469. New York: Rockefeller Univ. Press.

Nicolelis, M. A., Baccala, L. A., Lin, S. R. C., & Chapin, J. K. (1995). Sensorimotor encoding by synchronous neural ensemble activity multiple levels of the somatosensory system. *Science,* **268,** 1353–1358.

Nicolelis, M. A., & Chapin, J. K. (1994). Spatiotemporal structure of somatosensory responses of many-neuron ensembles in the rat ventral posterior medial nucleus of the thalamus. *Journal of Neuroscience,* **14**(6), 3511–3532.

Nowak, L. G., Sanchez Vives, M. V., & McCormick, D. A. (1997). Influence of low and high frequency inputs on spike timing in visual cortical neurons. *Cerebral Cortex,* **7**(6), 487–501.

Pascual-Marqui, R., Michel, C., & Lehmann, D. (1995). Segmentation of brain electrical activity into microstates. *IEEE Transaction on Biomedical Engineering,* **42**(7), 658–665.

Penrose, R. (1994). *Shadow of the mind.* Oxford, UK: Oxford Univ. Press.

Pitts, W., & McCulloch, W. S. (1951). Why the mind is in the head. In L. A. Jeffress (Ed.), *Cerebral mechanisms of behavior (The Hixon Symposium),* pp. 42–111. New York: Wiley.

Pockett, S. (1999). Anesthesia and the electrophysiology of auditory consciousness. *Consciousness and Cognition,* **8,** 45–61.

Prichep, L. S., John, E. R., & Tom, M. L. (2001). Localization of deep white matter lymphoma using VARETA: A case study. *Clinical EEG,* **32**(2), 62–66.

Purpura, D. P. (1972). Functional studies of thalamic internuclear interactions. *Brain and Behavior,* **6,** 203–234.

Ramos, A., Schwartz, E. L., & John, E. R. (1976). Evoked potential unit relationships in behaving cats. *Brain Research Bulletin,* **1,** 69–75.

Roelfsema, P. R., Engel, A. K., Konig, P., & Singer, W. (1997). Visuomotor integrations associated with zero time-lag synchronization among cortical areas. *Nature* **385**(6612), 157–161.

Sebel, P. S., Lang, E., Rampil, I. J., White, P. F., Cork, R., Jopling, M., Smith, N. T., Glass, P. S., & Manberg, P. (1997). A multicenter study of bispectral electroencephalogram analysis monitoring anesthetic effect. *Anesthesia and Analgesia,* **84,** 891–899.

Shimory, A. (1993). *Search for a nationalistic world view.* Cambridge, MA: Cambridge Univ. Press.

Squires, E. J. (1998). Why are quantum theorists interested in consciousness? In S. R. Hameroff, A. Kaszriak, & A. C. Scott (Eds.), *Toward a science of consciousness II—The second Tucson discussions and debates,* pp. 609–618. Cambridge, MA: MIT Press.

Stapp, H. P. (1993). *Mind, matter and quantum mechanics.* New York: Springer-Verlag.

Steriade, M., Amzica, F., & Contreras, D. (1996). Synchronization of fast (30–40 Hz) spontaneous cortical rhythms during brain activation. *Journal of Neuroscience,* **16,** 392–417.

Steriade, M., Curró Dossi, R., & Paré, D. (1993). Electrophysiological properties of intralaminar thalamocortical cells discharging rhythmic (∼40 Hz) spike-bursts at ∼1000 Hz during waking and rapid-eye-movement sleep. *Neuroscience,* **56,** 1–19.

Steriade, M., Curró Dossi, R., Paré, D., & Oakson, G. (1991). Fast oscillations (20–40 Hz) in thalamocortical systems and their potentiation by mesopontine cholinergic nuclei in the cat. *Proceedings of the National Academy of Sciences of the USA,* **88,** 4396–4400.

Steriade, M., Timofeev, I., Durmuller, N., & Grenier, F. (1998). Dynamic properties of corticothalamic neurons and local cortical interneurons generating fast oscillations. *Journal of Neurophysiology,* **79,** 483–490.

Strik, W. K., & Lehmann, D. (1993). Data-determined window size and space-oriented segmentation of spontaneous EEG map series. *Electroencephalography and Clinical Neurophysiology,* **87,** 169–174.

Sutton, S., Braren, M., John, E. R., & Zubin, J. (1965). Evoked potential correlates of stimulus uncertainty. *Science,* **150,** 1187–1188.

Tallon-Baudry, C. (2000). PL-0Z. Oscillatory synchrony as a signature for the unity of visual experience in humans. *Consciousness and Cognition,* **9**(2, pt 2), S25–S26.

Tallon-Baudry, C., Bertrand, O., Delpuech, C., & Pernier, J. (1997). Oscillatory g-band (30–70 Hz) activity induced by a visual search task in humans. *Journal of Neuroscience,* **17,** 722–734.

Taylor, J. G., & Alavi, F. N. (1993). Mathematical analysis of a competitive network for attention. In J. G. Taylor (Ed.), *Mathematical approach to neural networks.* New York: Elsevier.

Tinker, J. H., Sharbrough, F. W., & Michenfelder, J. D. (1977). Anterior shift of the dominant EEG rhythm during anesthesia in the JAVA monkey. *Anesthesiology,* **46**(4), 252–259.

Tononi, G., & Edelman, G. M. (2000). *A universe of consciousness.* New York: Basic Books.

Tononi, G., & Edelman, G. M. (1998). Consciousness and the integration of information. In H. H. Jasper, L. Descarries, V. C. Costelucci, & S. Rossignol (Eds.), *Advances in neurology,* Vol. 77, pp. 245–280. Philadelphia: Lippincott–Raven.

Varela, F. J. (2000). Neural synchrony and consciousness: Are we going somewhere? *Consciousness and Cognition,* **9**(2, pt 2), S26–S27.

Verzeano, M., & Negishi, K. (1960). Neuronal activity in thalamus and cortical networks. *Journal of General Physiology* **43**(Suppl.), 177.

Veselis, R. A., Reinsel, R. A., Beattie, B. J., Mawlawi, O. R., Feschenko, V. A., Di Resta, G. R., Larson, S. M., & Blasberg, R. G. (1997). Midazolam changes cerebral blood flow in discrete brain regions. *Anesthesiology,* **87**(5), 1106–1117.

Weiskrantz, L. (1998). Consciousness and commentaries. In S. R. Hameroff, A. Kaszriak, & A. C. Scott (Eds.), *Toward a science of consciousness II—The second Tucson discussions and debates,* pp. 371–377. Cambridge, MA: MIT Press.

Zeki, S. (2000). The disunity of consciousness. *Consciousness and Cognition,* **9**(2, pt 2), S30.

Received February 18, 2000