Episodic multiregional cortical coherence at multiple frequencies during visual task performance

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THE way in which the brain integrates fragmentary neural events at multiple locations to produce unified perceptual experience and behaviour is called the binding problem[1,2]. Binding has been proposed to involve correlated activity at different cortical sites during perceptuomotor behaviour[3–5], particularly by synchronization of narrow-band oscillations in the γ-frequency range (30–80 Hz)[6,7]. In the rabbit olfactory system, inhalation induces increased γ-correlation between sites in olfactory bulb and cortex[8]. In the cat visual system, coherent visual stimuli increase γ-correlation between sites in both the same and different visual cortical areas[9–12]. In monkeys, some groups have found that γ-oscillations transiently synchronize within striate cortex[13], superior temporal sulcus[14] and somatosensorimotor cortex[15,16]. Others have reported that visual stimuli produce increased broad-band power, but not γ-oscillations, in several visual cortical areas[17,18]. But the absence of narrow-band oscillations in itself does not disprove interregional synchronization, which may be a broad-band phenomenon. We now describe episodes of increased broad-band coherence among local field potentials from sensory, motor and higher-order cortical sites of macaque monkeys performing a visual discrimination task. Widely distributed sites become coherent without involving other intervening sites. Spatially selective multiregional cortical binding, in the form of broad-band synchronization, may thus play a role in primate perceptuomotor behaviour.

We recorded local field potentials (LFPs) from up to 15 cortical sites in one hemisphere of adult rhesus macaque monkeys (Fig. 1) performing a visual pattern discrimination task and found task-related multiregional synchronization over the entire frequency range examined. Our results are compatible with the hypothesis that perceptuomotor integration involves the broad-band binding of widespread cortical sites.

A total of 5,827 correctly performed trials from three monkeys (G.E., T.I. and L.U.) were studied, including 2,974 trials with a response (GO) to one visual pattern type and 2,853 trials with the response withheld (NO-GO) to another type. The transcortical field potential at each site was localized by differential recording with a surface-to-depth bipolar electrode. The amplifier reduced common contributions to the two electrode tips by more than 10,000 times, eliminating propagated fields from sources more than a few millimetres away. The precision of localization was demonstrated in LFP averages which, following the visual stimulus, showed visual receptive field specificity in striate and prestriate regions but not in others. All LFP averages had a high degree of day-to-day reliability over multiple recording sessions covering weeks to months.

Coherence and phase spectra, the frequency domain equivalent of temporal cross-correlation, were used to test for intersite synchronization over a range of frequencies[19]. Multiple episodes of elevated coherence, lasting 50–200 ms and involving multiple frequencies, were observed after the stimulus (Fig. 2). Changes in coherence over time generally followed the same pattern at multiple frequencies. The range of peak times for these

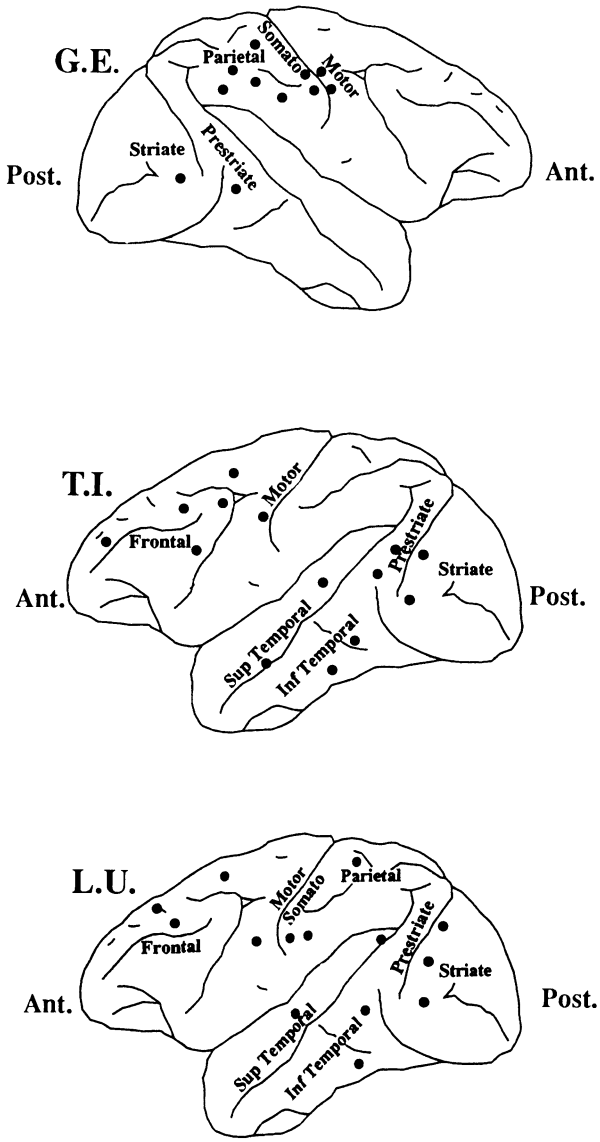

FIG. 1 Locations of recording sites in monkeys G.E., T.I. and L.U. At each site, the signal from a transcortical bipolar electrode (51-μm-diameter Teflon-coated platinum wires: 2.5 mm tip separation, 0.5 mm exposed surface per tip, less-advanced tip at the pial surface) was differentially amplified by a Grass model P511J amplifier (−6 dB at 1 and 100 Hz, 6 dB per octave falloff), digitized at 200 samples s^{-1}, and stored in 12-bit digital form.

METHODS. Experiments were done at the Laboratory of Neuropsychology at NIMH. Animal care was in accordance with institutional guidelines. Surgical procedures were as described in ref. 26. Monkeys were trained to accept chair restraint readily, to respond (GO condition) to one visual pattern type (line or diamond), and to withhold responding (NO-GO condition) to the other. Equiprobable GO and NO-GO trials were randomly presented in 1,000-trial sessions lasting about 45 min (intertrial interval randomly varied between 0.5 and 1.25 s). The monkey initiated each trial by depressing a lever with the preferred hand. The head was held 57 cm from the display screen, with 1 deg cm^{-1} visual angle. The computer-generated visual stimulus was presented for 100 ms through a silenced piezoelectric shutter, beginning about 115 ms after data collection began. On GO trials, a water reward was provided 500 ms after stimulus onset if the hand was lifted within 500 ms. On NO-GO trials, the lever was depressed for 500 ms. The stimulus set consisted of four diagonal patterns with two dots (9 mm per side) at opposite corners of an outer square, 6 cm per side, and two dots at opposite corners of a concentric inner square, 2 cm per side. The outer and inner dots were slanted in the same direction in two patterns (lines), and in opposite directions in the other two (diamonds). Thus, no single dot could be used to discriminate between lines and diamonds.

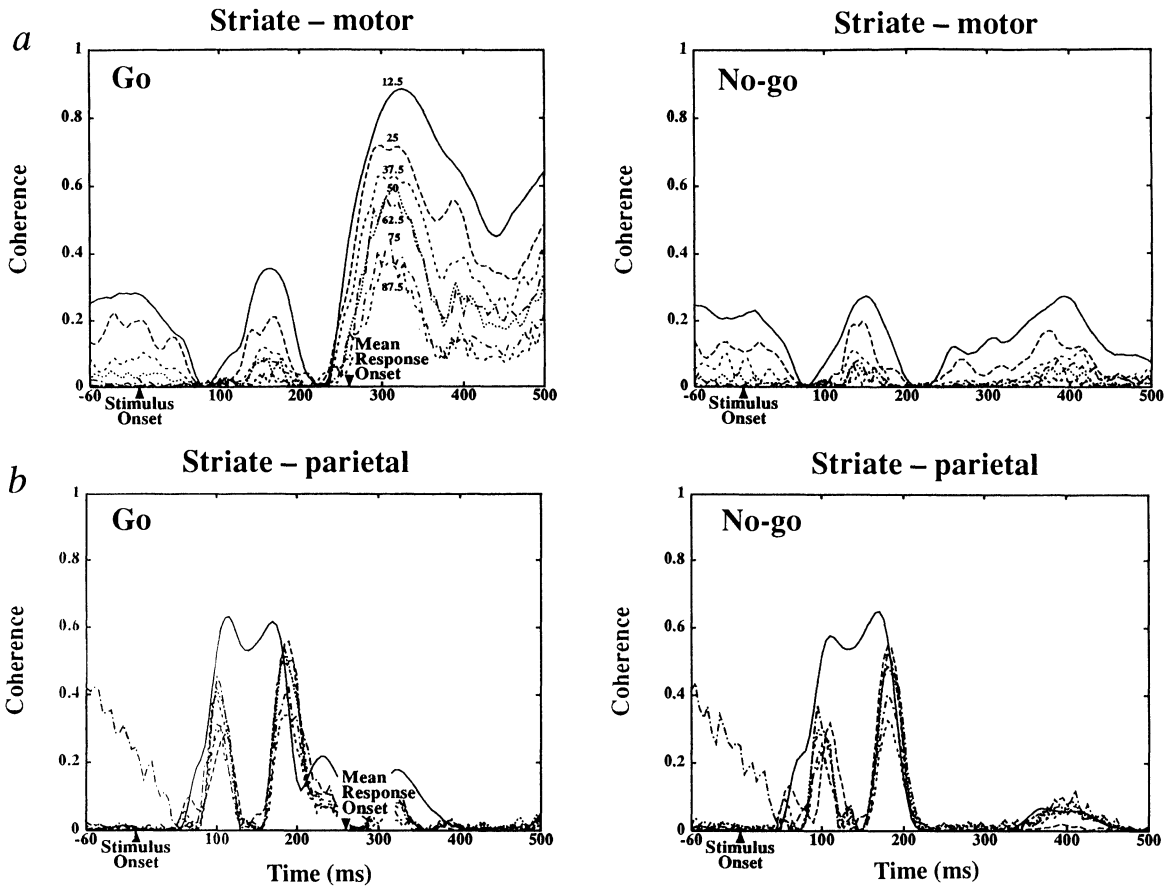

FIG. 2 Coherence time-series for two different site pairs in monkey G.E. Time-series for 7 frequency bins (12.5, 25, 37.5, 50, 62.5, 75 and 87.5 Hz) are displayed in each plot. Left, GO condition (488 trials). Right, NO-GO condition (482 trials). *a*, There is a large increase in broad-band coherence between striate and motor sites at the time of the response in the GO condition. *b*, The same striate site shows elevated broad-band coherence with a parietal site between 100 and 200 ms post-stimulus. (The striate site does not show significant coherence with other intervening sites.)

METHODS. Spanning the period from 115 ms before until 500 ms after stimulus onset, coherence and phase spectra were computed at each of a series of 80-ms time windows. The spectra had frequency bins at 12.5 Hz (1 cycle per 0.08 s) intervals. Coherence time-series, formed for each frequency bin as the time window was stepped, point by point, across the analysis period, were computed for all pairwise combinations of sites for both GO and NO-GO conditions in each session. All GO or NO-GO trials from a session were used to estimate each site pair's coherence. For statistical evaluation, the Fisher *z*-transform was first applied to the bounded coherence distribution to yield a roughly normal one. Six sessions were examined: two from each of the three monkeys. Coherence values were considered significant when exceeding the 95% confidence limit for the mean coherence over all site pairs from both conditions in the analysis period of a session. Two-way analysis of variance was done for each site pair (response condition and time as major effects, frequency bins as cases). Significance of between-condition difference was determined at the 95% level after correction for multiple comparisons by the Bonferroni method. Scheffé comparisons were later made to determine the time points showing significant between-condition differences.

episodes extended from 90 ms after stimulus onset to beyond response onset.

Coherence was significantly above baseline in at least one frequency bin during the analysis period for about 66% of the site pairs in G.E., 93% in T.I. and 90% in L.U. Data became significant in all bins by about 37% of the site pairs in G.E., 56% in T.I. and 20% in L.U. The sites involved were in striate, prestriate, inferotemporal, superotemporal, posterior parietal, somatosensory, motor and frontal cortices. In no case were two sites coherent with zero phase variance over trials, indicating that synchronization was not simply an externally imposed artefact.

Of the site pairs having significant coherence in all bins, 50% had a significant difference between coherence in the GO and NO-GO conditions. The mean time of significant between-condition difference (285 ± 24 ms) occurred shortly after the mean response onset time (279 ± 15 ms). Thus, between-condition differences in coherence (Fig. 2*a*) appeared to be largely related to response processing. Signal power (Fig. 3) also significantly differed between conditions at 60% of the sites (mean time of significant difference $= 319 \pm 20$ ms). Power was significantly different for at least one site in 96% of those site pairs having significant between-condition coherence differences, and for both sites in 54% of the pairs. Like coherence, changes in power were generally similar across frequencies, with no evidence of a concomitant low-frequency decrease and γ-frequency increase as has been previously suggested[6,20,21].

Single trials were identified in which the LFP waveforms from two sites were synchronized during the time when their coherence was elevated (Fig. 4). Like coherence overall, cross-correlation on these trials was also elevated because of waveform synchronization (Fig. 4*a*). Synchronization of γ-frequency components was not apparent because of their relatively small amplitude. But when γ-frequency waveforms were isolated by digital filtering, their synchronization was also evident (Fig. 4*b*).

Elevated coherence, rather than simply appearing because of common activation of multiple cortical areas by an imposed stimulus, manifested spatially and temporally complex patterns in the period after stimulus presentation, when the monkeys had to discriminate successfully between two visual forms and then perform correctly. These task-related patterns of multiregional synchronization are consistent with those previously observed below 10 Hz in human scalp-recorded averaged event-related potentials[22–24]. But the finding of broad-band elevated coherence during the motor response differs from those of studies in monkey[15,16] and cat[25] reporting narrow-band γ-synchronization in relation to motor activity.

The rapid rise in coherence over a broad frequency range during specific stages of task processing may reflect instantaneous inter-regional cortical coupling on multiple timescales, providing a flexibility to cortical information processing not available through operation on a single characteristic timescale. The present results suggest that synchronization can potentially

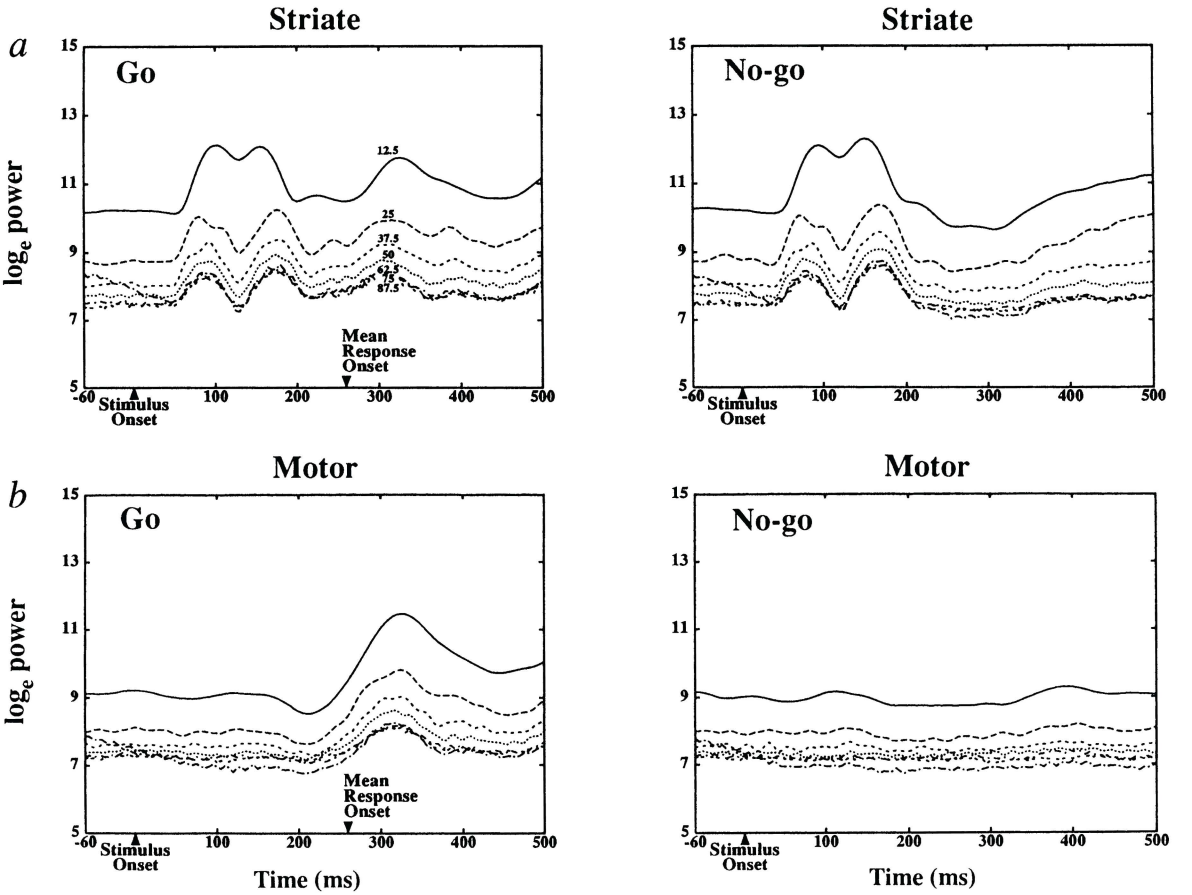

FIG. 3 Average power time-series for the striate and motor sites of Fig. 2*a*. Time-series for 7 frequency bins (12.5, 25, 37.5, 50, 62.5, 75 and 87.5 Hz) are displayed in each plot. Power was down nearly to the size of a single amplitude step at 100 Hz. The striate site (*a*), but not the motor site (*b*), shows elevated power after stimulus onset. Both the striate and motor sites show elevated power after response onset in the GO condition (left), but not at this time in the NO-GO condition (right). Averages were over 488 GO and 482 NO-GO trials.
METHODS. Spanning the period from 115 ms before until 500 ms after stimulus onset, power spectra were computed by the Fast Fourier Transform for the same series of 80-ms time windows used in computing coherence. The power spectra also had frequency bins at 12.5 Hz intervals. Power time-series were computed for all sites for both GO and NO-GO conditions and averaged over the trials of each session. Similar statistical procedures were used in determining significance as for coherence.

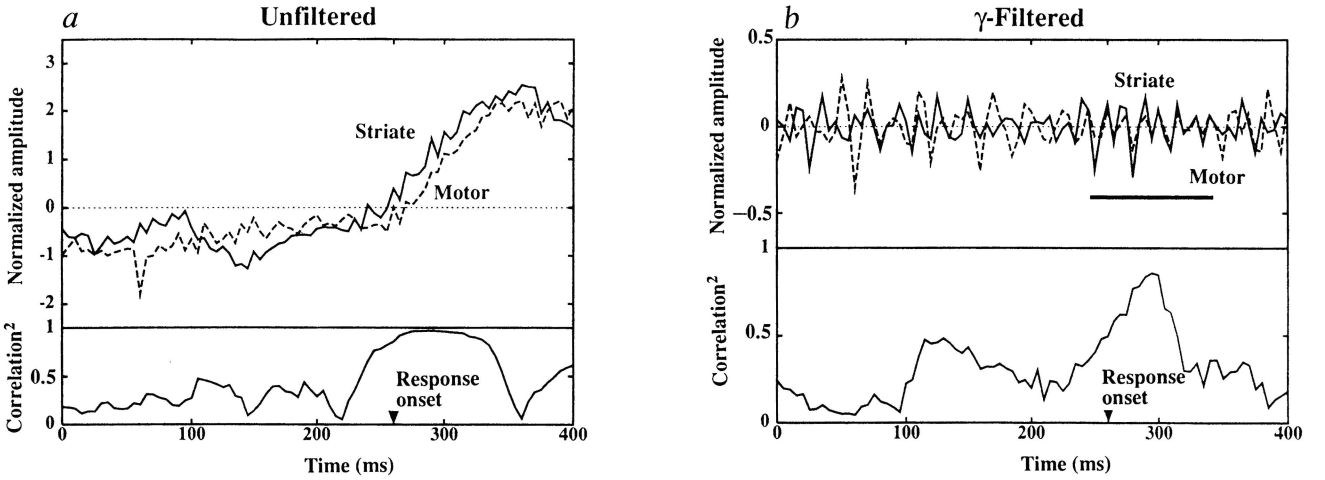

FIG. 4 *a*, Unfiltered waveforms from the striate and motor sites of Fig. 2*a* for a single GO trial, with their squared cross-correlation plotted below as a function of time. The period of elevated cross-correlation in this trial corresponds to the broad-band peak in coherence (over all GO trials) in Fig. 2*a*. *b*, The waveforms in *a* after digital filtering to show activity in the γ-frequency range. The period of synchronization (marked by the bar), corresponding to the cross-correlation peak below, demonstrates that the similarity in single-trial temporal structure extends to the γ-range. The maximum squared cross-correlation value (0.86 at 295 ms) exceeded the upper 95% confidence limit (0.50) for the mean value of the time-series.
METHODS. Cross-correlation functions were computed on single-trial records for the same 80-ms time windows used to compute coherence. Cross-correlation time-series were then constructed using the maximum of the squared cross-correlation function in each window. The γ-frequency signals were obtained by time-domain convolution with a bandpass (−6 dB at 30 and 80 Hz, 864 dB per octave falloff) digital filter.

occur between any cortical areas, and provide direct evidence in support of theories[1,2] proposing that multiregional binding underlies whole-brain functions such as perception and action. □

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