

Oscillatory Activity in Sensorimotor Cortex of Awake Monkeys: Synchronization of Local Field Potentials and Relation to Behavior

VENKATESH N. MURTHY AND EBERHARD E. FETZ

Department of Physiology and Biophysics and Regional Primate Research Center, University of Washington, Seattle, Washington 98195

SUMMARY AND CONCLUSIONS

1. Oscillations of 20–40 Hz were observed in local field potentials (LFPs) and unit activity in sensorimotor cortices of three awake monkeys while the monkeys performed trained wrist movements and untrained exploratory arm movements. The mean frequency of LFP oscillations was 25.9 ± 1.4 (SD) Hz and the number of cycles of oscillations per episode was variable, with a mean of 4.2 ± 0.5 (mean \pm SE).

2. Oscillatory episodes occurred most often when the monkeys retrieved raisins from a Klüver board (0.59 ± 0.23 episodes per s, mean \pm SD) or from unseen locations with the use of somatosensory feedback (0.62 ± 0.12 episodes per s); they occurred less often when the monkeys performed repetitive wrist flexion and extension movements (0.22 ± 0.04 episodes per s) or sat quietly at rest (0.23 ± 0.17 episodes per s).

3. The amplitude of LFP oscillations increased with depth in cortex, reaching a maximum between 1 and 2 mm. LFP oscillations at the surface of the cortex were 180° out of phase with oscillations in the deep cortical layers. The phase shift (with respect to the deep layers) decreased with depth in the cortex and disappeared at depths of >1 mm.

4. LFPs were recorded simultaneously at multiple sites in the sensorimotor cortex when monkeys retrieved raisins from a Klüver board or from unseen locations. Cross-correlation of LFPs recorded at different sites indicated that oscillations in the 20- to 40-Hz range could become synchronized at sites separated by up to ≥ 14 mm in the precentral cortex.

5. The probability of occurrence of significant correlations between LFP oscillations at paired sites and the average correlation amplitude decreased with increasing horizontal separation of sites in precentral cortex. The phase shift between LFP oscillations recorded at paired sites did not change significantly with increasing horizontal separation.

6. For paired sites in precentral cortex, the average strength of correlations and the proportion of oscillations that were significantly correlated were greater during exploratory behaviors such as retrieving raisins from slots of the Klüver board than during periods of rest or overtrained wrist movements.

7. Oscillations could become synchronized with small phase shifts (0.5 ± 1.6 ms) between pre- and postcentral cortical sites. Average strength and probability of occurrence of significant correlations between pre- and postcentral LFPs increased during exploratory behaviors.

8. Oscillations occurred simultaneously in the left and right motor cortex and could become synchronized with negligible phase shifts when the monkey performed bimanual manipulations. However, synchronization occurred as often and as strongly for unimanual as for bimanual manipulations.

9. These results indicate that episodes of 20- to 40-Hz oscillations occur often and become synchronized over a large cortical area during exploratory forelimb movements. However, they have no reliable relation to particular components of the movement and therefore seem unlikely to be involved directly in movement execu-

tion; instead, they may represent a neural correlate of attention during demanding sensorimotor behaviors.

INTRODUCTION

The oscillatory neural activity in the frequency range of 20–70 Hz observed in various sensory cortical areas in awake and anesthetized mammals (Adrian 1942; Buzsáki et al. 1994; Eckhorn et al. 1988; Engel et al. 1991a,b; Freeman 1978; Galambos et al. 1981; Gray 1994; Gray and Singer 1989; Kreiter and Singer 1992; Murthy and Fetz 1992; Pantev et al. 1994; Singer 1993) raises questions about its functional role. Specific spatiotemporal patterns of oscillations in the olfactory bulb and cortex can be induced by odorants and have been suggested to play a role in odor recognition (Freeman 1978). Stimulus-evoked oscillations in the visual cortex are hypothesized to play a binding role in associating stimulus features and in segmentation of objects in the visual scene (Eckhorn et al. 1988; Engel et al. 1991b; Gray et al. 1989). Synchronous 20- to 40-Hz oscillations of local field potentials (LFPs) have also been observed in the sensorimotor cortices of cats (Bouyer et al. 1987; Rougeul-Buser 1994), behaving monkeys (MacKay and Mendonca 1995; Murthy and Fetz 1992; Sanes and Donoghue 1993), and humans (Llinás and Ribary 1993; Murthy et al. 1995; Pfurtscheller and Neuper 1992; Ribary et al. 1991). Awake, behaving monkeys exhibit LFP oscillations during performance of trained motor tasks (Sanes and Donoghue 1993) and during unconstrained exploratory movements of the arm and hand (Murthy and Fetz 1992). LFPs recorded in visual and motor areas show synchronization across a broad range of frequencies in behaving monkeys (Bressler et al. 1993).

In sensorimotor cortex, we observed LFP oscillations more frequently during exploratory hand and arm movements that involved ongoing sensorimotor coordination than during periods of repetitive constrained wrist movements (Murthy and Fetz 1992). Oscillations occurred synchronously over wide areas, suggesting that, in analogy to the binding hypothesis, the oscillations in sensorimotor cortex might facilitate associations between cells involved in the same task. This association hypothesis would predict that synchronization of LFP oscillations should occur preferentially between task-related sites and during particular movements. Moreover, oscillations in pre- and postcentral sites could become synchronized during tasks that involve integration of somatosensory signals with movements. To test these predictions, we quantified the coherence of LFPs between paired sites in pre- and postcentral cortex during different behaviors. Recordings were also made bilaterally in the

hand area of the motor cortex when the monkey performed manipulatory tasks with either hand alone and with both hands together. This paper extends our preliminary findings (Murthy and Fetz 1992; Murthy et al. 1995) to three monkeys and describes the cortical extent of synchronous oscillations and the relation between synchronization and behavior.

METHODS

Experimental animals

Cortical activity was recorded in two *Macaca mulatta* (monkeys 1 and 2) and one *Macaca nemestrina* (monkey 3) while they were seated in primate chairs with their heads fixed. Observations were made under four behavioral conditions. In the "F-Ex" task the monkeys generated isometric torques about their wrists, alternating between flexion and extension zones while tracking visual targets on a video monitor. With the hand and arm free, the monkeys also retrieved food pieces from the experimenter's hand at unseen locations to the sides of their heads (called the "Side" task) and from the slots of a Klüver board located in front of them (called the "Klüver" task). These two tasks did not involve any operantly cued movement; instead, the monkeys reached for the food as it was offered. The onset and time course of movements were defined by recording electromyographic (EMG) activity of selected muscles in the forearm. Spontaneous cortical activity was also documented during periods of quiet sitting (called "Spont"). The relative timing of behavioral events and cortical oscillations was documented by recording the monkeys' behavior on video tape simultaneously with LFPs and audio clicks generated from each cycle of the oscillatory episodes.

The experiments were approved by the Institutional Animal Care and Use Committee at the University of Washington. The animals were cared for as directed in the National Institutes of Health "Guide for the Care and Use of Laboratory Animals."

Surgical procedures

In an aseptic surgery under halothane anesthesia, the animals had cortical recording chambers (22 mm diam) implanted in the skull over the motor cortex contralateral to the trained hand. The chamber held an annular ring with a clear Silastic center, which protected the dura while allowing insertion of electrodes for recording. *Monkey 1* had a second chamber (10 mm ID) implanted over the right motor cortex. This small chamber was capped with a threaded nylon screw, which was removed during recording sessions. The right hemisphere of one monkey was prepared for chronic implantation of multiple subdural microelectrodes (described below). The scalp over the right hemisphere from premotor area to the occipital ridge was removed and six vitalium screws were threaded into the skull. The exposed area of the skull was covered with a thin layer of ethyl-methacrylate (Kooliner, Coe Laboratories). After the monkey recovered from surgery, recording electrodes were implanted subdurally for chronic recording of field potentials (described below). All the monkeys were monitored postoperatively and analgesics were administered as necessary.

EMG recording

Forearm EMGs were recorded in some sessions to identify movement periods in the non-cued reaching tasks and to correlate EMG with oscillations. Teflon-insulated multistranded stainless steel wires (Cooner Wire) were implanted in the muscles transcutaneously with a 20-gauge needle while the monkey was anesthetized. An array of 12 wires connected to gold-plated terminals held in a strip connector (Amphenol) was inserted in each synergistic group of muscles. Muscles were identified on the basis of surface anatomy and movement evoked by unipolar intramuscular stimula-

tion (1–5 mA, 100 Hz, 0.1-ms biphasic, 50-ms train). A pair of wires was inserted into each muscle for differential intramuscular recording. Custom-designed vests prevented the monkeys from removing the wires. Recordings were made from five flexor muscles (flexor digitorum sublimis, flexor digitorum profundus, flexor carpi radialis, flexor carpi ulnaris, palmaris longus) and seven extensor muscles (extensor digitorum communis, extensor digiti 4 and 5, extensor digiti 2 and 3, extensor carpi radialis longus, extensor carpi ulnaris, abductor pollicis longus, extensor pollicis longus), plus pronator teres and supinator.

Recording procedures

ELECTRODES. Two kinds of metal microelectrodes were used to record LFPs and unit activity. Movable electrodes consisted of glass-coated tungsten electrodes, manufactured by etching a 0.2-mm-diam tungsten rod to a sharp tip and coating it with glass to leave a 4- to 10- μ m tip exposed. Fixed electrodes, called pin electrodes, were also made of tungsten. Miniature strip connector sockets were shortened and crimped to 10-mm lengths of 0.2-mm diameter tungsten rod. The exposed part of the tungsten rod was etched to a sharp tip, then the tungsten rod and the socket were coated with insulating varnish (EpoxyLite No. 6001, EpoxyLite) and baked overnight at $\sim 100^{\circ}\text{C}$. The tips were ground on emery paper to the desired impedance, usually $\sim 1\text{ M}\Omega$. These electrodes were cemented in the skull with their tips in the deep layers of the cortex. The signal from each electrode was filtered at two band-pass settings to record LFPs (10–100 Hz) and unit activity (0.3–3.0 kHz).

DUAL RECORDINGS. For each of the three monkeys, dual recordings were obtained simultaneously from two independently driven microelectrodes. A dual-electrode drive holder facilitated stable recordings from two sites in the same recording chamber. Each electrode was advanced by a manually controlled hydraulic microdrive (Narishige model 95A). Electrode tips could be separated by up to 15 mm, thus allowing a systematic study of the synchrony of the oscillations at sites separated by varying distances. At the end of each recording session, depth readings of the microdrive were noted and the electrodes were slowly withdrawn to the surface of the cortex (as estimated by loss of neural activity and drastic reduction in the amplitude of LFP signals). The relative locations of the electrode tips were reconstructed under a dissecting microscope; the tip separation was taken to be the best estimate of the physical separation between the neurons recorded by each electrode.

MULTIPLE RECORDINGS. In some experiments in *monkey 1*, 4–12 glass-coated tungsten electrodes were inserted into the cortex ipsilaterally via an array of guide tubes embedded in acrylic. Adjacent electrodes in the array were located 2 or 4 mm apart. Each electrode was inserted separately into the cortex and left in place during the recording session. Single-unit isolation was not attempted in these experiments. Instead, multiunit activity was monitored to determine the task modulation of the neurons and their synchronization with LFP oscillations. The electrodes were removed at the end of the recording session.

PIN ELECTRODE RECORDINGS. To obtain chronic recordings from multiple sites, we implanted pin electrodes in 14 sites in the sensorimotor cortex of each hemisphere of *monkey 1*. The monkey was sedated with a mixture of ketamine hydrochloride, xylazine, and atropine and placed in the recording chair. A small hole was drilled through the acrylic and the skull, a small incision was made in the dura, and a pin electrode was slowly lowered through the hole. The monkey's contralateral arm and face were stimulated to identify the response properties of the multiunit activity. Then the electrode was advanced for 2 mm beyond the depth at which neural activity was first encountered, the hole was filled with dental acrylic, and the pin electrode was left in place. In subsequent recording sessions, a mating minipin was connected to each pin

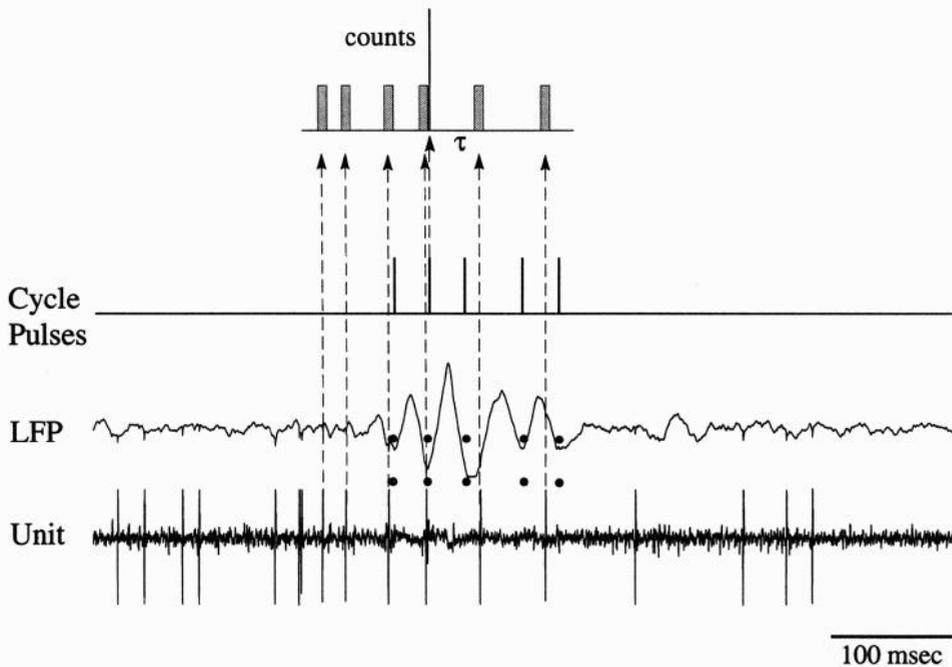


FIG. 1. Method for compiling cycle-triggered averages (CTAs). Local field potential (LFP) signal was passed through a time-amplitude window discriminator to generate cycle pulses (●: window levels). Averages of analog signals such as LFP and rectified electromyogram (EMG) were aligned with the cycle pulses. Similarly, cycle-triggered histograms of unit activity compiled counts in appropriate bins when spikes occurred (*top*). CTA analysis interval typically straddled ± 125 ms.

electrode socket, and LFPs could be monitored simultaneously in all the electrodes. The nearest stainless steel chamber served as the indifferent electrode for recordings.

RECORDING SESSIONS. For each recording session, the monkey was chaired and one arm was restrained in a cast. The head was stabilized and the working arm was placed in a trough that held the elbow at $\sim 90^\circ$. The hand was inserted into a torque manipulandum and the monkey performed alternating flexion and extension movements of the wrist. Then the working arm was released and recordings were made while the monkey reached for pieces of food as described above. In some sessions, recordings were obtained not only while the monkey manipulated food pieces with either hand alone and with both hands, but also while the monkey sat quietly with no overt movements. In each session, recordings from the same sites in the cortex were obtained during different behaviors so that we could compare the occurrence and characteristics of the oscillations under different conditions. A total of 124 recording sessions were conducted: 81 with *monkey 1*, 26 with *monkey 2*, and 17 with *monkey 3*.

Data analysis

All neural data were recorded on a 21-channel FM tape recorder (XR-7000, TEAC, bandwidth DC 2.5 kHz) for off-line analysis. LFPs, EMGs, and the torque signal were digitized at 1-ms resolution on a PDP 11/73 computer (Plessey Systems) and transferred to a Sun 4/260 computer for further analysis.

CYCLE-TRIGGERED AVERAGES. To document the activity associated with oscillatory cycles, we calculated cycle-triggered averages (CTAs) of LFPs and of unit and rectified EMG activity (Fig. 1). The LFP signal was passed through a time-amplitude window discriminator (BAK Electronics) to generate trigger pulses. The threshold and the window were adjusted so that triggers were generated when the LFP signal had an oscillatory cycle with a period between 10 and 40 Hz. Trigger pulses were rarely generated by clearly identifiable artifacts, and isolated pulses were rejected by the software program. Cycle pulses triggered a multichannel averager to compile CTAs of 1) LFPs at all sites, 2) time histograms of unit activity, and 3) rectified EMG activity. CTAs usually had a binwidth of 1 ms and a duration of 250 ms, centered about the

trigger. The phase of the oscillatory cycle (relative to the peak) at which the triggers occurred had a slight uncertainty, which was estimated as follows. Segments of LFP recordings were digitized at 1-ms resolution and the times of cycle triggers were calculated by an algorithm that simulated the hardware time-amplitude discriminator. The LFP peaks were also determined by zero-slope calculations. Histograms of the time between cycle triggers and cycle peaks were fitted to Gaussians. In 10 of 10 randomly chosen segments from different cortical sites, the SD of the fitted Gaussians was < 1.8 ms, indicating that 95% of triggers had errors of < 2.4 ms. This estimate includes the effect of variance in the duration of the cycle period, i.e., in the cycle frequency. The phase shifts introduced by preamplifiers were determined empirically and numerical values were corrected accordingly. The figures, however, are displayed without such corrections.

To determine whether the oscillatory episodes were related to movements in a consistent way, we also compiled episode-triggered averages of EMGs with a coarser binning (binwidth 2–5 ms) and longer pre- and posttrigger durations (1–2 s). An episode of LFP oscillation was defined as three or more consecutive triggers from cycles of oscillations with intertrigger separation of < 50 ms; the first trigger was taken to be the onset of the oscillatory episode.

POWER SPECTRA. To monitor changes in oscillatory activity, we calculated power spectra of LFPs for 256-ms windows, which were shifted successively by 100 ms. Power spectra were computed with a fast Fourier transform algorithm (Press et al. 1990). Average power in different bands was plotted as a time series along with LFPs (and EMGs if available), allowing changes in power to be correlated with behavior.

CROSS-CORRELATIONS. To quantify the extent of synchronization of LFPs, we computed pairwise cross-correlations of LFPs (digitized at 1 kHz) from different sites with the use of the formula

$$C(\tau) = \frac{\sum_{i=1}^n [x(i) - \bar{x}][y(i - \tau) - \bar{y}]}{\frac{1}{n} \sqrt{\sum_{i=1}^n [x(i) - \bar{x}]^2 \sum_{i=1}^n [y(i - \tau) - \bar{y}]^2}} \quad (1)$$

where τ is the delay, $x(i)$ and $y(i)$ are two LFP signals at time i , and \bar{x} and \bar{y} are averages of $x(i)$ and $y(i)$ across n time bins (Gray

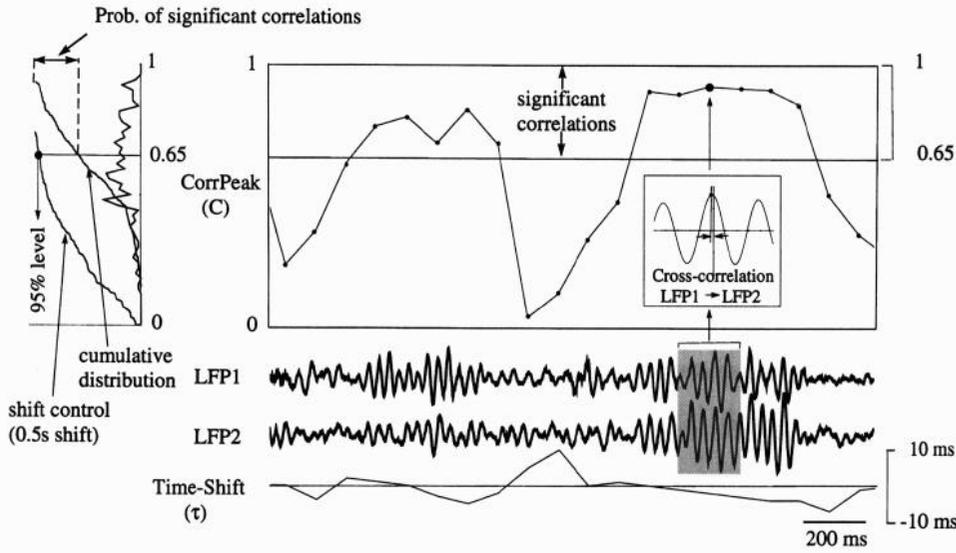


FIG. 2. Assessment of significant cross-correlations. Cross-correlation of 2 LFPs was computed for 200-ms windows (e.g., for the shaded interval). The correlogram peak value closest to origin (C) and the corresponding time shift (τ) were determined for successive windows shifted by 100 ms. C and τ were plotted continuously with corresponding LFPs. A probability distribution of the peak correlations (C) was made from 20-s data segments, which, on integration, provided a cumulative distribution (left). A control distribution (shift control) was obtained by repeating this procedure with 1 of the LFPs shifted by 0.5 s. The value below which 95% of the shift control correlations lay was used as the significance level for the actual correlations.

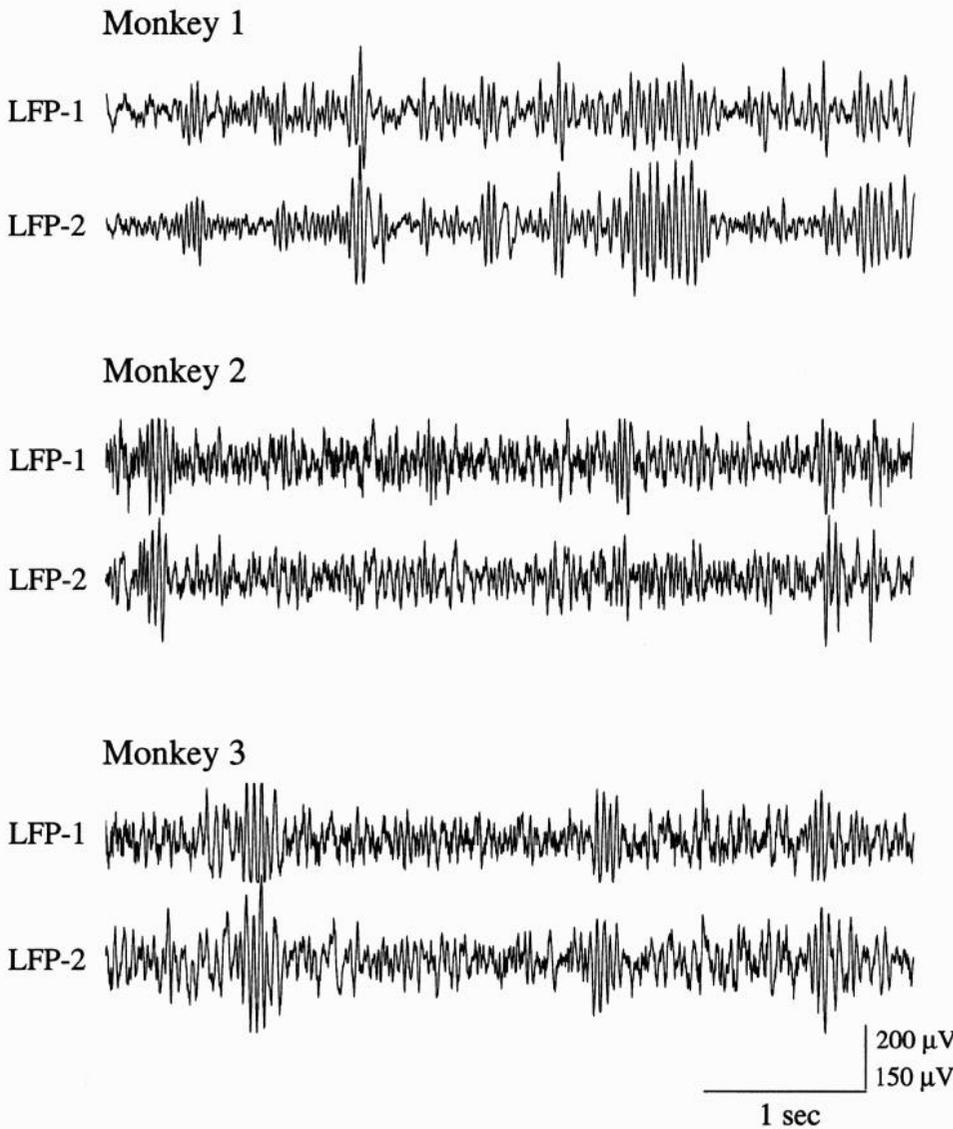


FIG. 3. Sample episodes of oscillations from each of the 3 monkeys. LFPs were recorded simultaneously from 2 precentral sites separated by ~ 2 mm while each monkey reached to the side of its head to retrieve a raisin from the experimenter's hand. Top voltage calibration is for monkey 1; bottom is for monkeys 2 and 3.

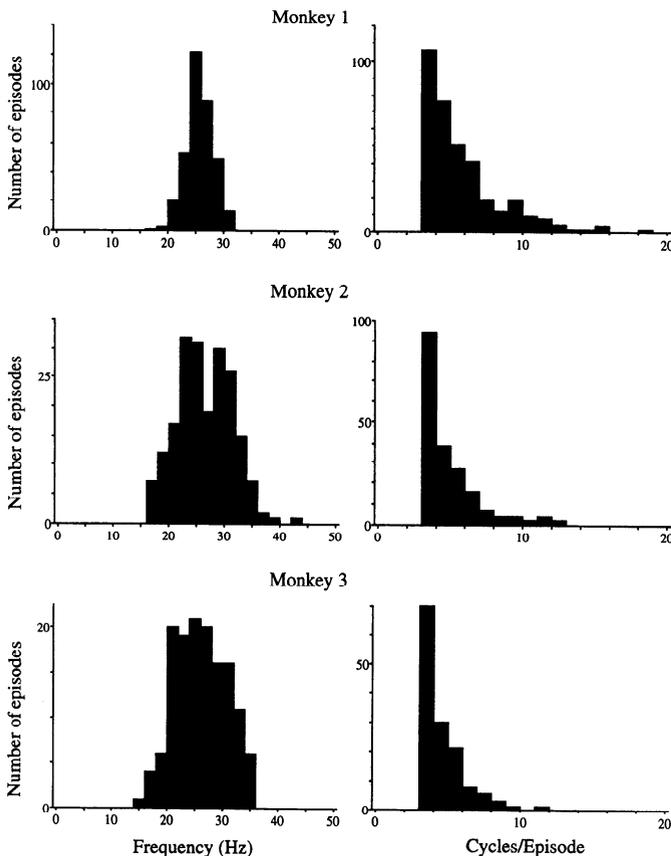


FIG. 4. Parameters of LFP oscillations for a typical recording session. Pulses were generated from cycles of LFP oscillations as described in METHODS. At least 3 pulses with separations of <60 ms were required to identify an oscillatory episode. Frequency of each episode was calculated as the reciprocal of the average interpulse intervals. Distribution of frequency of episodes (*left*) and number of cycles per episode (*right*) for typical recordings from each monkey are shown. Recordings were made in the hand area of the precentral cortex while the monkey retrieved a raisin offered at the side of its head.

of the average of all such values over a period of 50 s yielded the “average correlation during oscillations” (ACO).

Histology

To identify the location of recording sites, at the conclusion of the experiments we perfused the monkeys and determined the coordinates of the recording chamber by referring to india ink marks made at specific chamber coordinates. The sites of the pin electrodes were evident on close inspection of the cortex.

RESULTS

Characterization of LFP oscillations

PARAMETERS OF THE OSCILLATORY LFP. Examples of intracortical LFP recordings in pairs of motor cortex sites of each of the three monkeys are shown in Fig. 3. Recognizable oscillations increased in amplitude above baseline and decreased after a variable number of cycles. Power spectra of LFPs confirmed that power in the range of 20–40 Hz could increase up to 10 times above baseline power. The shape of the oscillatory bursts varied considerably; some episodes were spindle shaped, others started or ended abruptly, and some were sustained continuously for many cycles. The number of cycles within an episode varied from 3 (the minimum required to identify an oscillation) to 30 successive cycles, with an average of 4.2 ± 0.5 (SE) (Fig. 4). The rate of occurrence of oscillatory episodes varied with behavior (see below). The frequency of the oscillations varied slightly from one episode to the next (Fig. 4), and the average frequency was slightly different for each animal (*monkey 1*: 27.4 ± 3.1 Hz; *monkey 2*: 24.7 ± 1.7 Hz; *monkey 3*: 25.7 ± 1.0 Hz). (Note: all \pm values represent SD unless otherwise noted.)

PHASE CHANGE IN CORTICAL DEPTH. Evoked field potential responses in the cortex typically show transitions in polarity at certain layers of the cortex, usually indicative of synaptic current flows at corresponding depths. Alpha rhythms also show phase gradients in the superficial layers (Lopes da Silva and Storm van Leeuwen 1977; Spencer and Brookhart 1961). To determine whether such phase changes occur for the 20- to 40-Hz oscillations in the sensorimotor cortex, we recorded with dual microelectrodes. A reference electrode inserted into the motor cortex recorded LFPs at a depth of 2 mm. A movable electrode, inserted in a track close to the reference electrode ($<500 \mu\text{m}$), recorded simultaneous LFPs at different depths from the surface of the cortex in steps of 250 or 500 μm . CTAs revealed the phase relation between oscillations recorded in the two electrodes as a function of depth. Near the surface of the cortex, LFPs had small amplitudes and were 180° out of phase with oscillations recorded from the deep electrode. As the movable electrode was advanced, the phase of the LFP oscillations changed with depth; below 1,000 μm the oscillations remained in phase with oscillations in the reference electrode (Fig. 5). The depth of the phase reversal varied slightly, probably because of slight differences in the extent to which the electrodes dimpled the cortex. However, oscillations consistently reversed phase by 1,000 μm . The occurrence of potential gradients in the superficial layers suggests the presence of intracortical sources of LFP oscillations (as opposed to remote sources whose signals are volume-conducted to the recording site). The reversal of phase was observed in all

et al. 1992). Correlations were most commonly calculated for time windows of 200 ms, successively shifted by 100 ms. For each window, the peak correlation closest to the origin (0 delay) and the corresponding time shift were obtained (Fig. 2). Peak amplitudes of correlation were distributed (1 point from each 200-ms segment) for recording epochs of 2–50 s. This distribution was integrated and normalized to 100%, thereby yielding a cumulative probability distribution (Fig. 2, *left*). Because high correlations could occur purely by chance, especially if the two correlated signals have similar frequencies, a significance level was determined as follows. For the same recording epochs, cross-correlations were recalculated with one of the records shifted by a time interval much larger than the duration of oscillatory episodes, usually 1 s. From the cumulative distribution of the “shifted” correlations, the significance level for the actual correlations was taken as the level below which 95% of the shifted correlations lay (Fig. 2). The probability of synchronization was calculated as the proportion of peak correlations that were above the 95% significance level (e.g., 11 significant/20 total = 55% in Fig. 2). The average value of the significant peak correlations (above the 95% significance level) was also calculated (e.g., 0.79 in Fig. 2). An estimate of average synchronization specifically during oscillations was obtained by the following procedure. If either site or both sites exhibited LFP oscillations, as judged by the autocorrelations (magnitude of the secondary peak $> 50\%$ of central peak), the cross-correlation peak for the corresponding window was measured; calculation

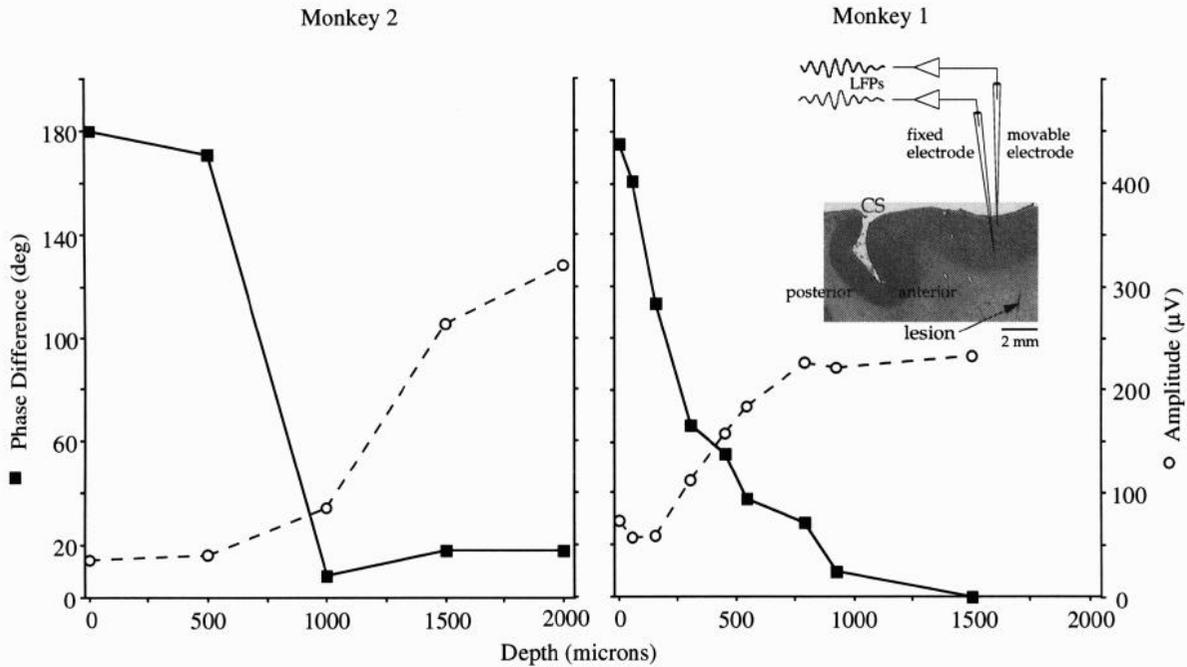


FIG. 5. Change in phase and amplitude of LFP oscillations through the depth of the cortex in 2 monkeys. The fixed electrode was positioned at 2 mm depth in the cortex. The movable electrode was advanced in steps of 500 mm (left) or 250 mm (right), and oscillations were recorded from both electrodes. From CTAs the phase shift between the 2 LFPs (■) and the peak-to-peak amplitude of the averaged LFPs from the movable electrode (○) were determined at each depth. Inset: cortical section from *monkey 1* with the electrodes drawn at the estimated location from which recordings were made to construct the right panel figure.

four measurements in *monkey 1* and both of two measurements in *monkey 2*, and was not tested in *monkey 3*.

BEHAVIORAL CORRELATES. For each of the four behavioral conditions we documented the rate of occurrence of the oscillatory episodes, the duration of single episodes, and the mean frequency. The parameter of oscillations that changed the most with behavioral condition was the rate of occurrence of oscillatory episodes (Fig. 6). The intrinsic frequency and the number of cycles per oscillatory episode changed relatively little with different behaviors ($P < 0.01$ for Side/Klüver compared with F-Ex/Spont). The frequency and number of cycles per episode were unrelated to maximum amplitude.

When the monkey was sitting at rest and making no overt movements, a few spontaneous oscillations occurred infrequently (0.23 ± 0.17 episodes per s, average across all 3 monkeys); they occurred significantly more often during the Klüver and Side tasks (0.62 ± 0.12 ; $P < 0.001$; Fig. 6). This difference was not related to active movement per se: when the monkey performed a routine, overtrained step tracking task, generating ramp-and-hold flexion and extension torques about the wrist, the cortical oscillations occurred as infrequently as when the monkey was at rest and less often than during free arm movements (Fig. 6). With the flexion-extension movements, oscillations tended to occur during the tonic hold period of the isometric force production and decreased at the onset of force production. Power spectral analysis indicated that a signal in the 10- to 25-Hz range increased in the tonic-hold period and was attenuated during the phasic period. In contrast, power in the 25- to 40-Hz band did not exhibit much reduction at the onset of movement. Oscillations occurred with equal likelihood during extension

and flexion periods of the task, independently of whether the cortical site had cells related to flexion or to extension. In *monkeys 2* and *3*, the cycle frequency of spontaneous oscillations at rest and during F-Ex was slightly lower than the frequency of oscillations during performance of other behaviors ($P < 0.01$, Fig. 6).

The behaviors that elicited the oscillations most robustly were exploratory arm and hand movements, which involved attention to sensorimotor coordination. For instance, oscillations appeared often when the monkeys retrieved raisins from an unseen container, with the use of tactile and proprioceptive cues to explore the container. In a similar task, the monkey was offered raisins at the side of its restrained head, beyond the range of peripheral vision. The monkey had to palpate the raisin in the investigators' hands and wrest it free. In this task, oscillations appeared very reliably in the precentral areas. Retrieving raisins from slots in a Klüver board visible in front of the monkey also evoked oscillations. Even when raisins were simply placed in the slots of the board while the monkey's arms were restrained, oscillations often appeared for variable durations. Oscillations also occurred during manipulative movements that did not involve food, such as removing adhesive tape from the contralateral arm or manipulating inedible objects. Oscillatory episodes occurred ~ 3 times more often during exploratory reaching movements (0.62 ± 0.12 episodes per s, average for all 3 monkeys) than during trained flexion-extension movements (0.22 ± 0.04 episodes per s, average for all 3 monkeys); the difference was significant at $P < 0.001$ (t -test).

The correlation of LFP oscillations with movement was documented by means of video recordings while *monkey*

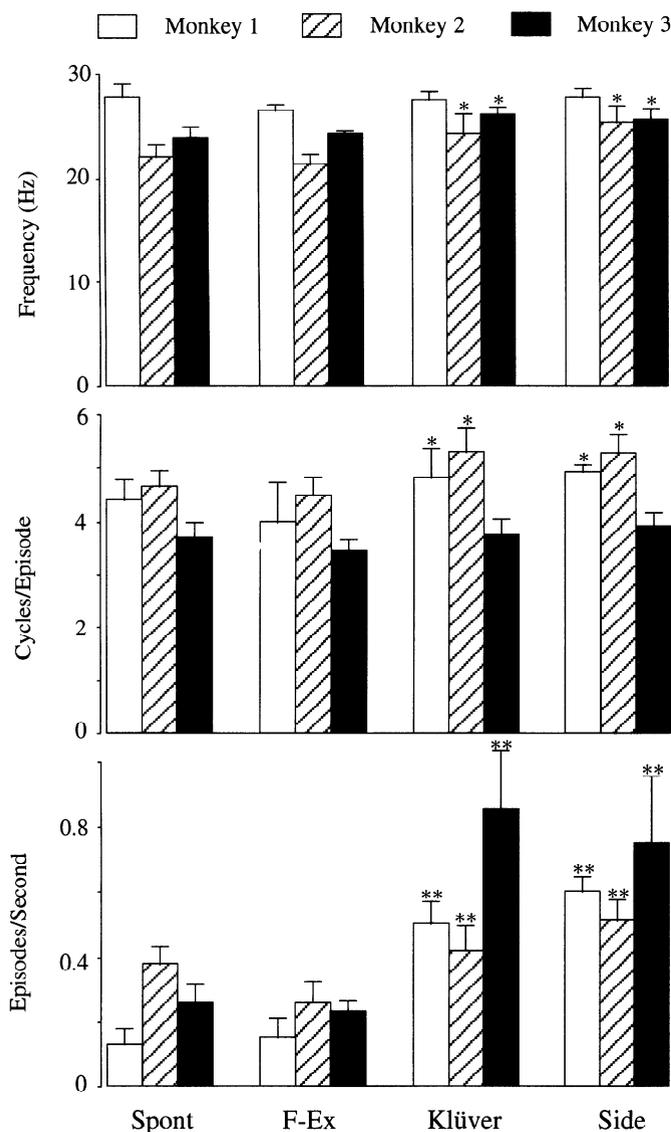


FIG. 6. Parameters of LFP oscillations during 4 behaviors. Cycle frequency of oscillations (*top*), number of cycles per episode (*middle*), and rate of occurrence of oscillatory episodes (*bottom*) were documented during different motor activities for 3 monkeys (number of sessions with 4 behaviors: 13, 6, and 4 for monkeys 1–3). Error bars: mean \pm SE. Spont, quiet sitting, no overt movement; F-Ex, alternating flexion-extension of wrist; Klüver, retrieving raisins from slots of Klüver board in front of the monkey; Side, wrestling raisins from experimenter's hand at the side of monkey's head. Frequency and cycles/episode for Klüver and Side were greater than for F-Ex and Spont (* $P < 0.01$). The number of episodes per second was significantly greater for Klüver and Side than for F-Ex and Spont for all 3 monkeys (** $P < 0.001$); 1 exception was when *monkey 2* Spont was used as the baseline for comparison; in that case, the significance level was 0.01.

I performed different behaviors. Pictures from two video cameras, one recording the monkey and the other monitoring LFP traces on an oscilloscope, were mixed electronically and recorded simultaneously with audio clicks generated from cycles of oscillations. These recordings confirmed that oscillations occurred most frequently during exploratory behaviors involving fine control of the hand. However, no consistent relation between instantaneous movements and occurrence of oscillations could be identified. This lack of consistent temporal relation was further confirmed with EMG recordings.

Oscillations were also elicited sometimes by cutaneous stimulation of the wrist and hand. Such stimulus-evoked oscillations occurred less reliably on succeeding days, and appeared to be related to the monkey's alertness or its motor behaviors. Moving objects away from the monkey's head sometimes evoked oscillations. A particularly effective way of eliciting oscillations was to show the monkeys a leather glove that had been used to capture them. Although these methods of evoking oscillations were too uncontrolled and qualitative to allow specific characterization, they do suggest that such oscillations may be related to increased attention or arousal.

Correlation between LFP oscillations and movements

The relation between LFP oscillations and arm movements is illustrated by an example of simultaneously recorded LFPs and EMGs (Fig. 7). During the premovement period, when the monkey sat with its arm unrestrained and the EMGs were silent, LFPs showed little oscillatory activity. When the monkey was presented with a raisin at the side of its head, it attempted to wrest the raisin from the experimenter's hand and oscillations appeared at both pre- and postcentral recording sites. Individual oscillatory episodes were not time locked to the occurrence of EMG bursts. During this period of exploratory movements, there was no consistent relation between the occurrence of EMG bursts and LFP oscillations on a subsecond time scale. This was further confirmed by the fact that averages of rectified EMGs triggered from oscillatory episodes usually showed flat EMGs (Murthy and Fetz 1992). Such episode-triggered averages are illustrated in Fig. 8, *left*, for bimanual movements. In some cases there was a slight reduction in EMG activity during the episodes (e.g., FDP-R in Fig. 8), but the episodes were never associated with an increase in average EMG. However, CTAs of rectified EMGs often revealed a periodic modulation synchronized with the LFP oscillations, as shown for representative flexor and extensor muscles in Fig. 8, *right*. This suggests that cortical output cells were entrained with the LFP cycles (Murthy and Fetz 1992).

Correlation between LFP oscillations at different cortical sites

SYNCHRONIZATION OF OSCILLATIONS IN PRECENTRAL CORTEX. Simultaneous recordings were made in pairs of precentral cortex sites to determine the spatial extent of the oscillations, their synchronization, and their relation to behavior. Cortical sites were functionally identified by the movements evoked by intracortical microstimulation and the discharge properties of recorded cells. Recordings were made from precentral areas covering 18 mm in the mediolateral direction, which included the entire arm representation (and, in 1 monkey, part of the facial representation). A total of 31 paired recordings was made in the precentral cortices of all three monkeys. Of these, nine penetrations were made at nearly identical pairs of sites on different days, and these data were averaged and plotted as a single pair. In four other recordings, reconstruction showed that penetrations were close to the precentral sulcus and therefore not perpendicular to the surface of the cortex. To avoid the confounding effects of depth of recording, which affects

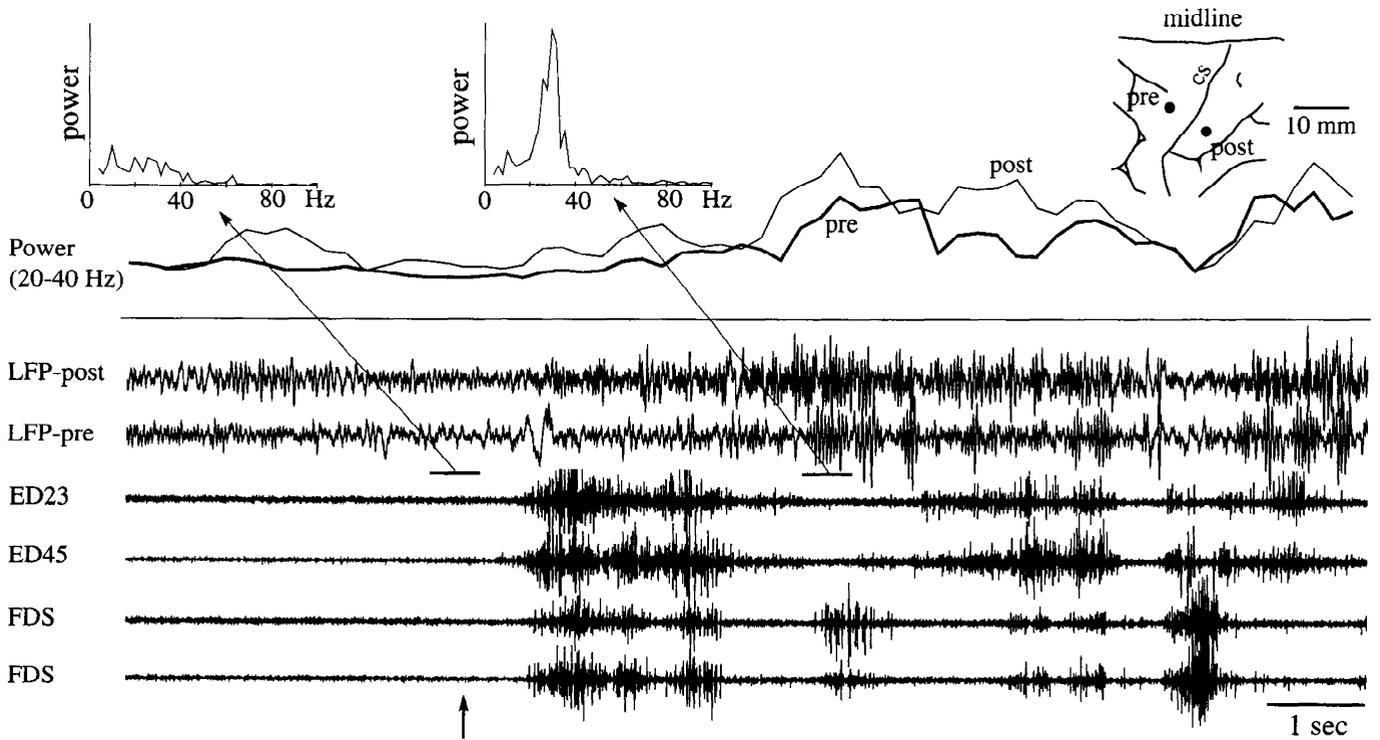


FIG. 7. Plot of LFP oscillations recorded at pre- and postcentral sites, power in the 20- to 40-Hz band, and EMGs (*monkey 1*). Recordings begin with monkey at rest. At the time marked by the arrow a raisin was offered to the side and the monkey reached for it. LFP oscillations were small during the quiet period and increased during the reaching period. However, the LFP oscillations began after the onset of the movement. Power spectra were calculated for 256-ms windows successively shifted by 100 ms. *Top*: sample power spectra for comparison of oscillatory period with quiet period. Power in the 20- to 40-Hz band (obtained by integrating the power spectrum) increased after the onset of movement (*top traces*).

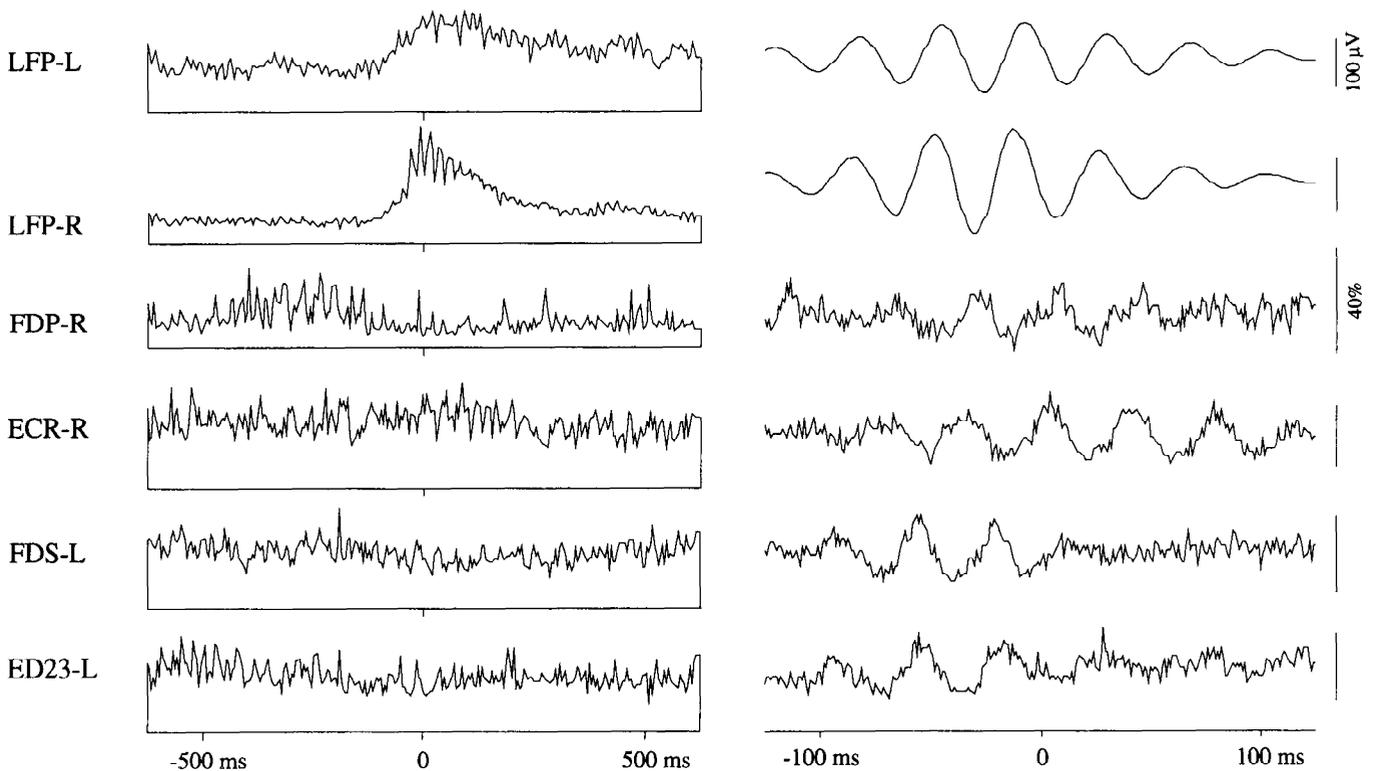


FIG. 8. Averages of rectified EMG from flexor and extensor forearm muscles triggered from oscillatory episodes (*left*) and from oscillatory cycles (*right*). Triggers were generated from LFP oscillations in right hemisphere during bimanual movements. Records show LFP and EMG recorded from left (L) and right (R) sides. EMG recordings of all muscles were shown to be independent by cross-correlation (Fetz and Cheney 1980). Recordings from *monkey 1*.

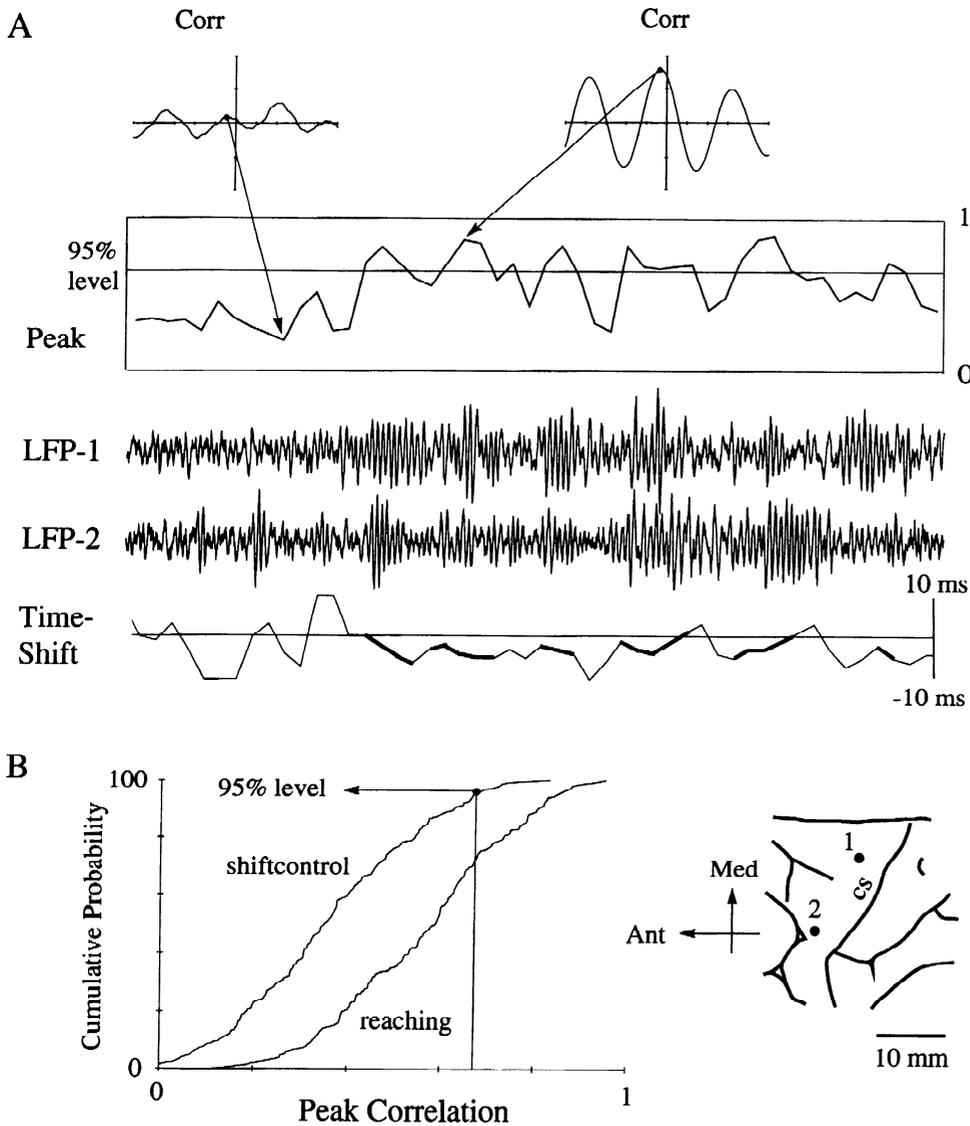


FIG. 9. Correlation between LFPs recorded at 2 precentral sites separated by 14 mm (see bottom right). A: correlation peaks (Peak) and corresponding delays (Time-Shift) computed for 200-ms windows, shifted successively by 100 ms. Top: sample correlations for 2 windows. Time shifts corresponding to significant correlations are highlighted. The monkey was reaching for a raisin offered at the side of its head. B: cumulative probability distribution of correlation peaks for the reaching period and the shifted control distribution.

phase of oscillations, we excluded these four recordings from the analysis. Thus, of the 31 pairs of sites recorded in the precentral cortex, 19 were included in the analysis. A representative recording from electrodes in the proximal and distal arm representation of the motor cortex is shown in Fig. 9. Multiunit activity in the proximal location (site 1) was responsive during active shoulder extension and pressure on the right biceps; units at site 2 were active with wrist movements. While the monkey attempted to retrieve a raisin from the experimenter's hand at the side of its head, oscillations could occur at both sites, but these were not always correlated. Peak correlations and corresponding time shifts calculated for 200-ms windows (with 100-ms overlap) are shown. Oscillations at the two sites could become highly synchronized, but not every episode at a particular site was accompanied by oscillations in the other site. The cumulative distribution of correlation peaks is shown in Fig. 9B, along with the shifted distribution used to determine the 95% significance level for correlations. In this example, 25% of the correlation values were significant, giving a probability of significant correlation of 0.25. The average value of the significant correlations was 0.81.

In general, strong correlations between LFPs at pairs of sites occurred predominantly during periods of oscillations. Although it was possible for any particular pair of sites to exhibit highly synchronized oscillations, the incidence of significant correlations generally decreased with increasing separation of the sites in the mediolateral extent of the primary motor cortex. The relation between correlation parameters and electrode separation was similar for all three monkeys and is shown collectively in Fig. 10. Each point represents the correlation between a pair of motor cortex sites with a mediolateral separation, approximately parallel to the central sulcus. The probability of occurrence of significant correlations decreased with horizontal separation (Fig. 10A). This was not due simply to a change in the threshold for significant correlations, because the significance level did not change with separation (Fig. 10C). The average correlation strength (calculated with only the significant correlations) also decreased slightly with horizontal separation of ≤ 6 mm (Fig. 10B). For separation of >6 mm, the correlation strength appeared to increase again. This increase was not related to the cortical location of the sites (e.g., medial vs. lateral). These results suggest that strong synchronization

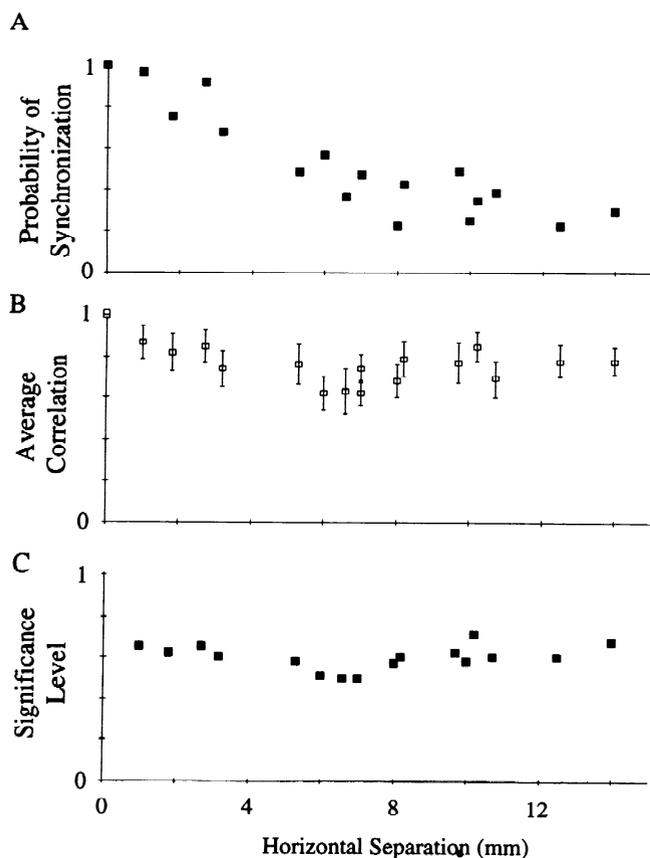


FIG. 10. Dependence of correlation parameters on horizontal separation of precentral sites. *A*: probability of observing significant correlation peaks decreased with horizontal separation of the recording sites. *B*: average of significant correlations (above the 95% significance level) showed a decrease up to a separation of 6 mm. Bars: SE. *C*: significance level (95% of shifted correlations below this level) did not change appreciably with horizontal separation.

was possible between remote cortical sites, but their probability of occurrence was lower than that for nearby sites.

It was also of interest to determine the phase shifts of oscillation with separation of sites. To avoid the confounding effects of changing phase with cortical depth, we used only recordings at depths of >1 mm for this analysis. For a given pair of LFP recordings, plots of the time shift against the peak correlation showed that time shifts usually were widely scattered for periods of low correlation values (Fig. 11*A*). However, when the correlations were high, they were tightly grouped around a particular time shift. The average time shift was calculated for those points with above-chance correlations (the 5% chance level for the example shown was 0.6). All time shifts were calculated with the lateral electrode as reference and then converted to phase shifts with the use of the corresponding average frequency of oscillations. Because cross-correlations included contributions from multiple-frequency components, phase shifts calculated in this manner were averaged over all component frequencies. The resulting average phase shifts appeared to increase slightly with increasing separation (Fig. 11*B*). However, the large variation in phase shifts for higher separation caused a low r^2 value that was not statistically significant ($P > 0.05$). A more parsimonious explanation would be that there was no systematic or consistent change in phase shift with distance.

Simultaneous recordings from 4–10 electrodes allowed us to observe the occurrence and synchronization of oscillations over a large area simultaneously. Figure 12 shows data recorded from six sites in the precentral cortex and one postcentral site while *monkey 1* retrieved a piece of apple offered at the side of its head. Oscillations occurred at all sites, although with different rates of occurrence. Cross-correlations were compiled with the most lateral site as reference. The probability of occurrence of significant correlations decreased with increasing separation, consistent with the findings from paired recordings. The ACO also decreased with increasing separation (Fig. 12*C*). Time shifts for significant correlations were not different across the different precentral sites (Fig. 12*D*). The single postcentral site (labeled 7) had a time shift that was comparable with that of other sites and was not proportionally greater despite the significantly greater intracortical separation. Recordings from the same locations on six different days yielded similar results.

Synchrony and behavior. To test the hypothesis that oscillations in the proximal and distal arm representation sites could become synchronized more often when the monkeys made exploratory movements requiring coordination of the arm and hand, we recorded LFPs at paired sites simultaneously when the monkey 1) rested quietly without making any overt movement, 2) performed the stereotyped wrist

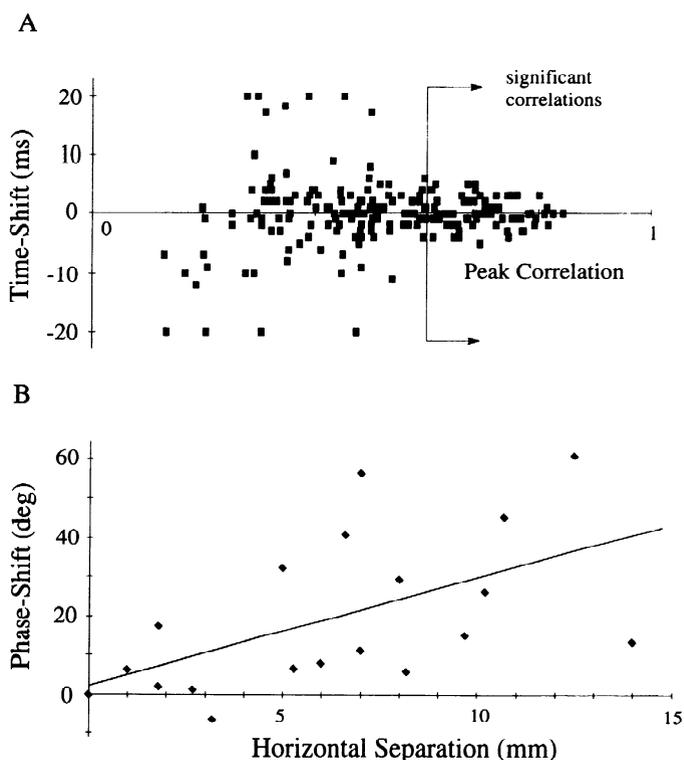


FIG. 11. Method for calculating average phase shift. *Top*: for a 40-s recording of simultaneous LFPs from 2 precentral sites, a plot of time shift against peak correlation shows that significant correlations were associated with more tightly clustered time shifts. The average of time shifts corresponding to significant peak correlations was calculated and converted to phase shift with the use of the average frequency of oscillations. *Bottom*: phase shifts calculated with the use of the above method as a function of horizontal separation of simultaneously recorded sites in the mediolateral direction. Phase shifts tended to increase with increasing horizontal separation. The least-squares regression line had a slope of $2.71^\circ/\text{mm}$ and an offset of 2.2° ($r^2 = 0.30$; $P > 0.05$, F test).

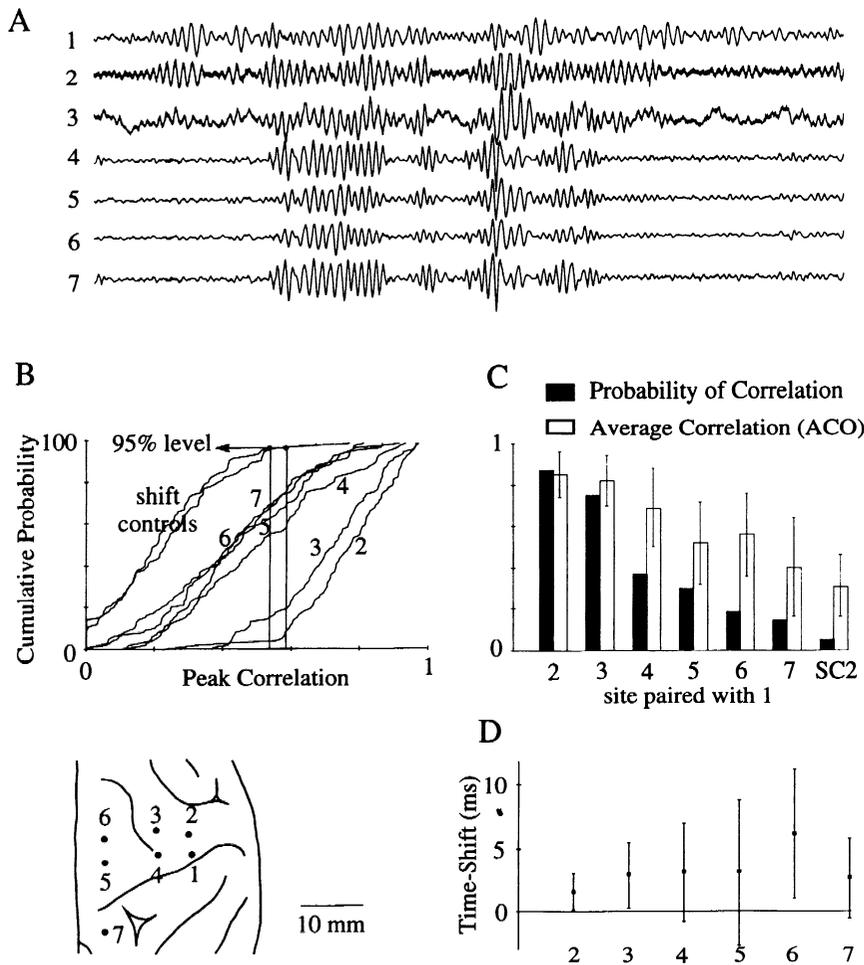


FIG. 12. Simultaneous recordings from 6 sites in precentral and 1 in postcentral cortex. *A*: sample LFPs recorded while the monkey retrieved raisins from a Klüver board. *B*: pairwise correlations computed with site 1 as the reference; cumulative distributions are shown along with shift control distributions for sites 2 and 7. Shift control distributions for the other sites were within the range covered by sites 2 and 7. Numbers on traces refer to target LFP (reference was always site 1). Bars in this and subsequent figures: SDs. *C*: probability of observing peak correlations >95% level, and average correlations for 6 pairs (all referred to site 1). Average correlations were calculated from correlation peaks for which the corresponding secondary autocorrelation peak of either or both LFPs was >0.5. SC2 refers to shift control for site 2. *D*: average time shift for significant correlations.

flexion and extension movements, 3) performed reaching movements to retrieve raisins from slots of a Klüver board, and 4) retrieved raisins offered at the side of its head.

As described above (Fig. 6), oscillations occurred more often during unconstrained reaching movements than during repetitive trained movements. For the same recordings, cross-correlations between pairs of LFPs and the autocorrelations of both LFPs were calculated for each behavior. The cumulative probability distribution of peak correlations showed that there was a higher incidence of strong correlations during unconstrained exploratory movements than during trained movements or quiet sitting (see the rightward shift in the distribution for Klüver and Side in Fig. 13A). Mean ACOs from four recording sessions with electrodes in similar cortical locations are shown in Fig. 13B. The proportion of correlations that were above the 95% level was also estimated for each behavior, and the average values for the same four sessions are shown in Fig. 13B. ACOs and probability of correlation were greater for Klüver and Side than for Spont and F-Ex.

SYNCHRONY BETWEEN SENSORY AND MOTOR CORTEX LFPs. LFP oscillations at pre- and postcentral sites could also become synchronized, as confirmed for 11 pairs of recordings made with one electrode each in pre- and postcentral cortex (*monkey 1*). Simultaneous recordings with up to 12 electrodes were also made in some sessions. Precentral sites exhibited robust oscillations that were synchronized with

each other (Fig. 14). Oscillations also occurred at postcentral sites and could become synchronized with precentral oscillations, although to a lesser extent. The strength of synchronization with precentral oscillations did not change in any systematic manner from anterior to posterior sites in the postcentral cortex, nor was there a consistently better correlation with sites that were immediately posterior (e.g., 2-4, 2-5, 3-5, etc.). The possibility that oscillations recorded at postcentral sites were merely volume-conducted signals from precentral cortex was ruled out by the fact that they could occur independently and that action potentials of units at both sites could become synchronized with the LFPs and with each other (Murthy and Fetz 1996).

Synchrony and behavior. If oscillations play a role in mediating interactions between cells in specific sensory and motor areas, the synchronization of oscillations at different sites should depend on the behavioral context. This associational hypothesis would predict that different cortical sites may exhibit independent oscillations that become synchronized preferentially during behaviors involving the coordination of neural responses at these sites. To test this hypothesis, we obtained simultaneous recordings of LFPs from the pre- and postcentral cortex in the distal arm representation area while the monkey performed the four tasks described above. As before, oscillations occurred more often during unconstrained reaching movements than during repetitive trained movements. The probability of synchronization and the ACO were calculated over five

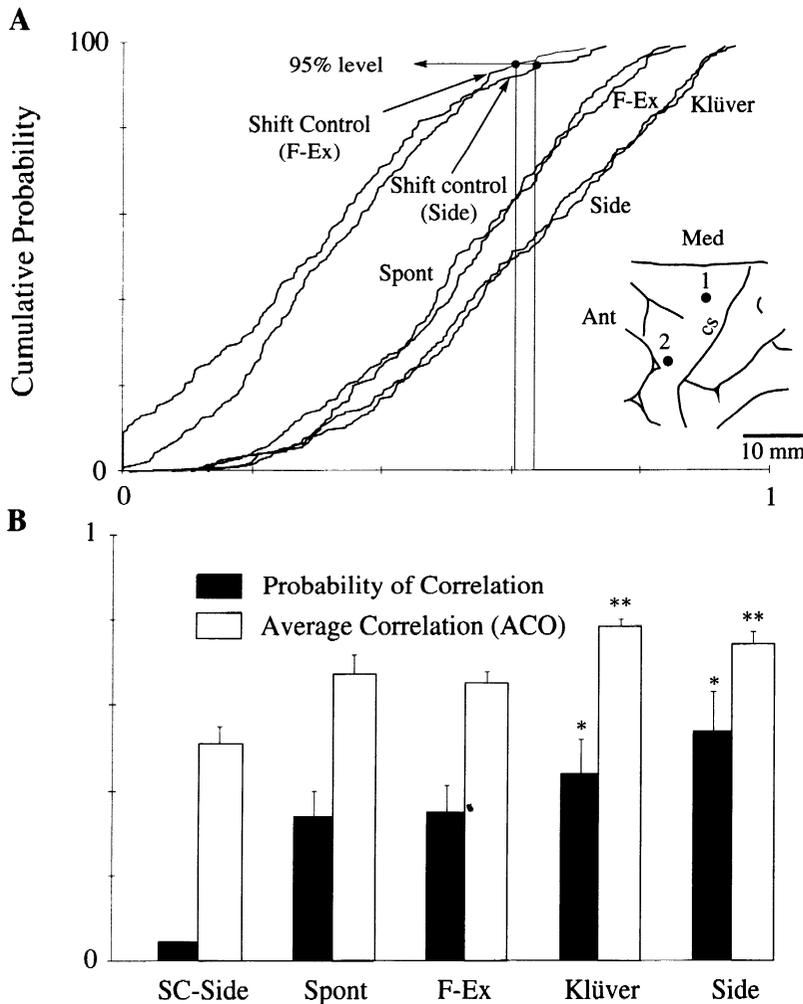


FIG. 13. Synchronization of LFP oscillations recorded at 2 precentral sites (1 and 2) during different behaviors. *A*: cumulative probability distribution of correlation peaks for 40-s recording periods for 4 different behaviors. For sake of clarity, shift control distributions are shown for only 2 behaviors. *B*: probability of observing peak correlations that were greater than the 95% level, and average correlations calculated for 4 different recording sessions. Average correlations were calculated from correlation peaks for which the corresponding secondary autocorrelation peak of either or both LFPs was >0.5 . SC-Side refers to shift control for Side; the shift control for other behaviors was not significantly different from that for Side. Single asterisk: probability of synchronization was greater for Klüver and Side than for Spont and F-Ex at $P < 0.01$. Double asterisk: average correlations for Klüver and Side greater than those for Spont and F-Ex at $P < 0.005$.

similar recording sessions. Both parameters were greater for the reaching movements than for the overtrained movements or for periods of rest ($P < 0.01$, Fig. 15).

To determine whether synchronization of LFPs in pre- and postcentral sites was related to movement, EMGs were recorded from forearm muscles. A typical recording of LFPs and EMGs obtained when the monkey reached to retrieve a raisin from a Klüver board is shown in Fig. 16. In the pre-movement waiting period, oscillations were infrequent. Oscillations and their synchronization decreased immediately after the onset of movement, but then increased significantly (note when the correlation trace crosses the 95% significance level in Fig. 16). However, there was no consistent relation between the occurrence of synchronization and EMG activity. This lack of consistent relation was observed in 11 recording sessions involving pre- and postcentral cortex sites; it was also confirmed for synchronization within the precentral cortex.

INTERHEMISPHERIC SYNCHRONY. Primates commonly perform synergistic bimanual movements, which could be expected to involve interhemispheric cortical interactions. To test whether oscillations in the sensorimotor cortex are involved in mediating such interaction, we obtained bilateral recordings while *monkey 1* manipulated unshelled peanuts with either hand alone and with both hands together. LFPs

and multiunit activity were recorded simultaneously at two homologous sites bilaterally in the hand representation of the motor cortex. The occurrences and parameters of the LFP oscillations at both cortical sites were documented, as was the synchrony between them. EMGs were also recorded from a flexor and extensor muscle in each forearm.

Oscillations occurred in both hemispheres when the monkey made bimanual movements (Fig. 17*A*) but also when it moved either hand alone (Fig. 17*B*). The probability of occurrence of oscillatory episodes in either hemisphere during bimanual movements was the same as during unimanual activity. Synchronization of LFPs was determined by calculating cross-correlations for 200-ms windows shifted by 100 ms. The cumulative distributions of correlation peaks over a period of 40 s each when the monkey was actively making manipulatory movements with the left hand, the right hand, and both hands were very similar (Fig. 17*C*). If synchronization of LFPs had increased preferentially during the bimanual task, the distribution of correlations during this task would have shifted to the right compared with those for either hand alone. The probability of occurrence of significant correlations and ACO did not differ between unimanual and bimanual movements (Fig. 17*D*). Phase shifts were not statistically different from zero, for either unimanual or bimanual movements (-1.9 ± 2.9 ms and -1.3 ± 3.8 ms, respectively).

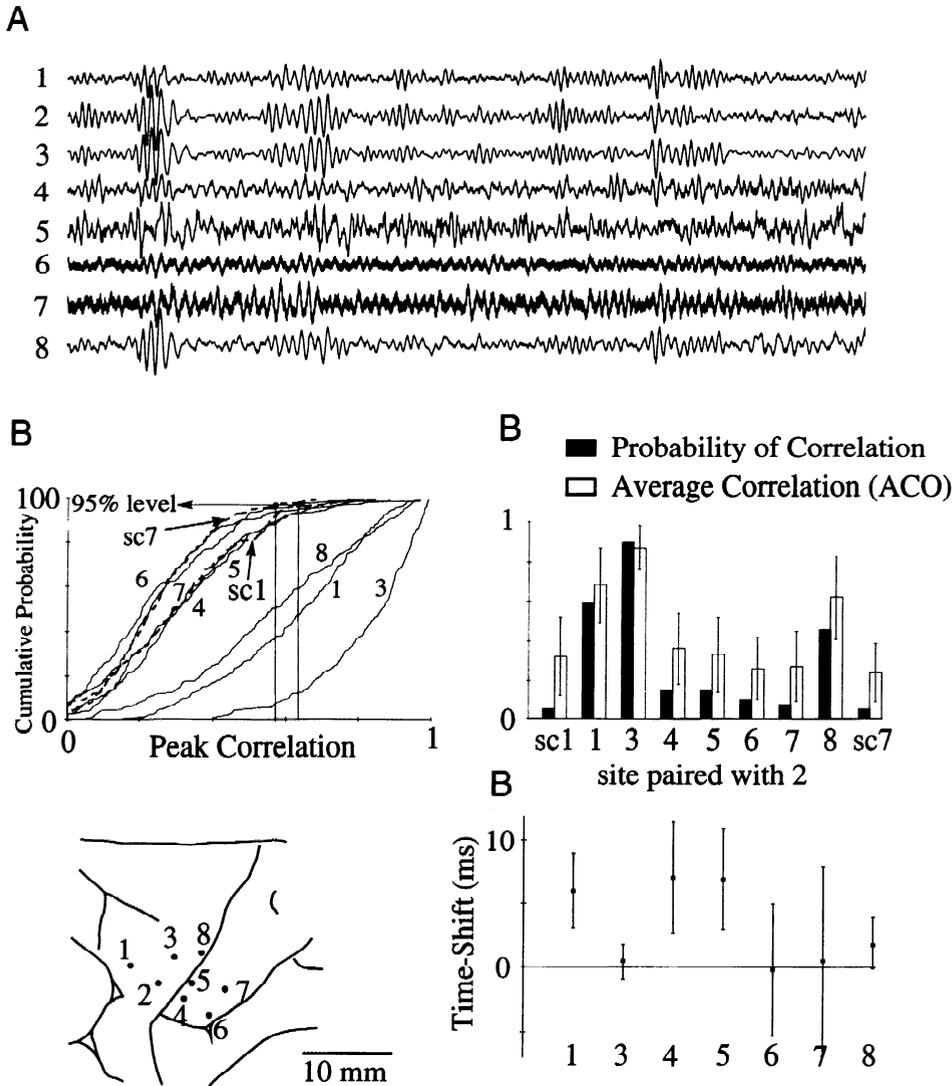


FIG. 14. Synchronization of LFP oscillations recorded at 8 sites in the sensorimotor cortex. *A*: sample LFPs recorded while the monkey retrieved raisins from a Klüver board. *B*: pairwise correlations computed with the use of site 2 as the reference; cumulative distribution is shown along with shift control distributions for sites 1 and 7. The other shift control distributions were within the range of those for sites 1 and 7. Numbers on traces refer to the target LFP (with the reference always being site 2). *C*: probability of significant correlations (using the corresponding significance level for each pair) and average correlations for the 7 pairs calculated as in Fig. 13. *D*: average time shift for significant correlations.

The fact that the recordings at bilateral sites were independent and not contaminated by common mode signals is shown by CTAs of neurons recorded at both sites, aligned on the cycles of LFP oscillations at one site. In 34 of 43 pairs of recordings, averages indicated oscillatory modulation of units at both sites, confirming the presence of local generators of synchronized rhythmic activity in each hemisphere (Murthy and Fetz 1996). Moreover, the output neurons in left and right motor cortex are also transiently synchronized; CTAs of rectified EMG of both left and right forearm muscles show modulation in relation to oscillatory cycles recorded in the left hemisphere (Fig. 8).

DISCUSSION

The results above confirm previous findings that the monkey's motor and somatosensory cortex exhibit intermittent oscillatory activity at 20–40 Hz, especially while the animal performs tasks that require fine finger movements and focused attention. It seems significant that the oscillations occurred preferentially during demanding sensorimotor tasks such as retrieving raisins from unseen lo-

cations and occurred much less often during relatively "automatic" motor activity such as overtrained alternating wrist movements. This suggests that these oscillations may play a role in attended motor behavior and/or sensorimotor integration. These intermittent oscillations represent a mode of neural activity that clearly differs from the modulated firing rates of units that covary with sensory and motor parameters. Most neurons in sensorimotor cortex discharge reliably in relation to specific somatic stimuli or particular motor responses. In contrast, the oscillations were not consistently related to particular movement parameters or to episodes of forearm muscle activity in the behaviors explored so far. Nevertheless, CTAs of EMG suggest that oscillatory activity can influence corticofugal cells whose activity influences motoneurons (Murthy and Fetz 1992) (Fig. 8). Similar correlations have been reported between the magnetoencephalogram and EMG of human subjects (Conway et al. 1995).

Sources of oscillation

The polarity of the oscillations reversed completely between the cortical surface and a depth of ~1,000 μm,

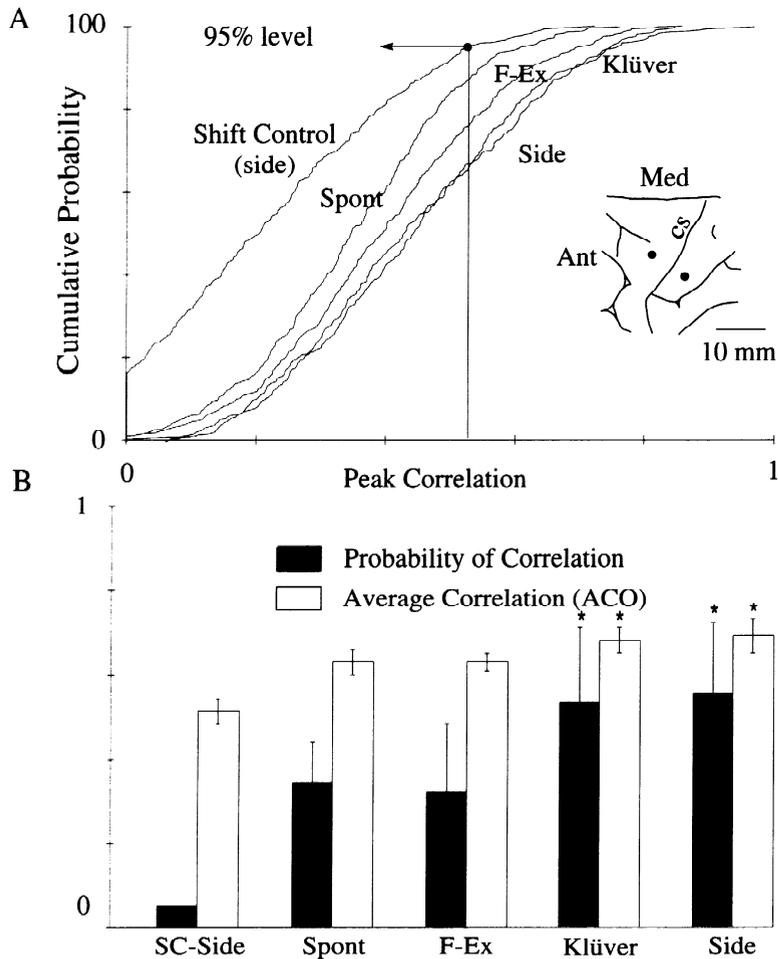


FIG. 15. Synchronization of LFP oscillations between pre- and postcentral sites during different behaviors. Microstimulation of the precentral site caused wrist extension; neurons at the postcentral site responded to passive and active flexion of wrist. *A*: cumulative probability distribution of peak correlations for 40-s recording periods for 4 different behaviors. Shift controls were essentially identical for the different behaviors; only that for Side is shown. *B*: probability of observing significant correlation peaks and average correlations calculated for 5 recording sessions. Procedure for estimating these parameters was the same as for Fig. 13. SC-Side refers to shift control for the Side task. Asterisk: both parameters were significantly higher for Side and Klüver than for F-Ex and Spont ($P < 0.01$).

indicating that the source of LFP signals was in the superficial cortical layers. These layers are particularly involved in corticocortical transmission (e.g., Felleman and Van Essen 1991; Jones 1986). This would suggest that corticocortical connections may participate in the generation and synchronization of oscillations. However, input from extrinsic structures such as the thalamus could also contribute to the generation of the oscillations (Llinás and Ribary 1993). It is becoming increasingly evident that oscillatory activity in thalamocortical circuits arises through a combination of intrinsic properties of neurons and the interaction between circuits (Steriade et al. 1993a,b). At the cellular level, cortical and subcortical neurons are intrinsically capable of generating oscillations in the 40-Hz range (Chagnac-Amitai et al. 1990; Chen and Fetz 1993; Gutfreund et al. 1995; Llinás et al. 1991; Steriade et al. 1991, 1993a). However, even if single neurons exhibit tendencies toward intrinsic oscillations, circuit interactions are likely to be necessary for synchronization of oscillations across large cortical areas. Indeed, synchronization in networks of neurons has been amply demonstrated by simulation studies (e.g., König and Schillen 1991; Sompolinsky et al. 1990; Sporns et al. 1989; Wilson and Bower 1991). Still unresolved are the relative contributions of intrinsic oscillatory properties of neurons and circuit interactions to the generation of 20- to 40-Hz oscillations in the sensorimotor cortex *in vivo*.

Synchronization with zero delay

The phase shift between LFP oscillations recorded at paired sites had a slight tendency to increase with their mediolateral separation. However, there was considerable variability across the sample, as seen by the scatter in Fig. 11*B*. This variability implies that although perfect synchronization occurs often for nearby sites, synchronization is more variable for remote sites. Synchronization over long distances without significant phase shifts was also seen in recordings between pre- and postcentral sites and in bilateral recordings. This is of interest because the major subcortical sources of input to the sensorimotor cortex, the thalamic nuclei, do not have common projections over distances of >6 mm (Deschênes and Hammond 1980). It is possible that nonspecific thalamic nuclei such as the intralaminar nuclei, which project to large areas of cortex (Cunningham and LeVay 1986), play a role in synchronizing remote cortical areas. In fact, neurons in the intralaminar centrolateral nucleus are known to exhibit 40-Hz oscillations, which can trigger rapid bursts of action potentials (Steriade et al. 1993a,b). These neurons could, in principle, synchronize cortical targets over a large area. In addition to subcortical structures, it seems likely that corticocortical connections also play a role in synchronization. The bilateral synchronization of oscillations in the left and right motor cortex would probably involve callosal interactions, because there are no known sub-

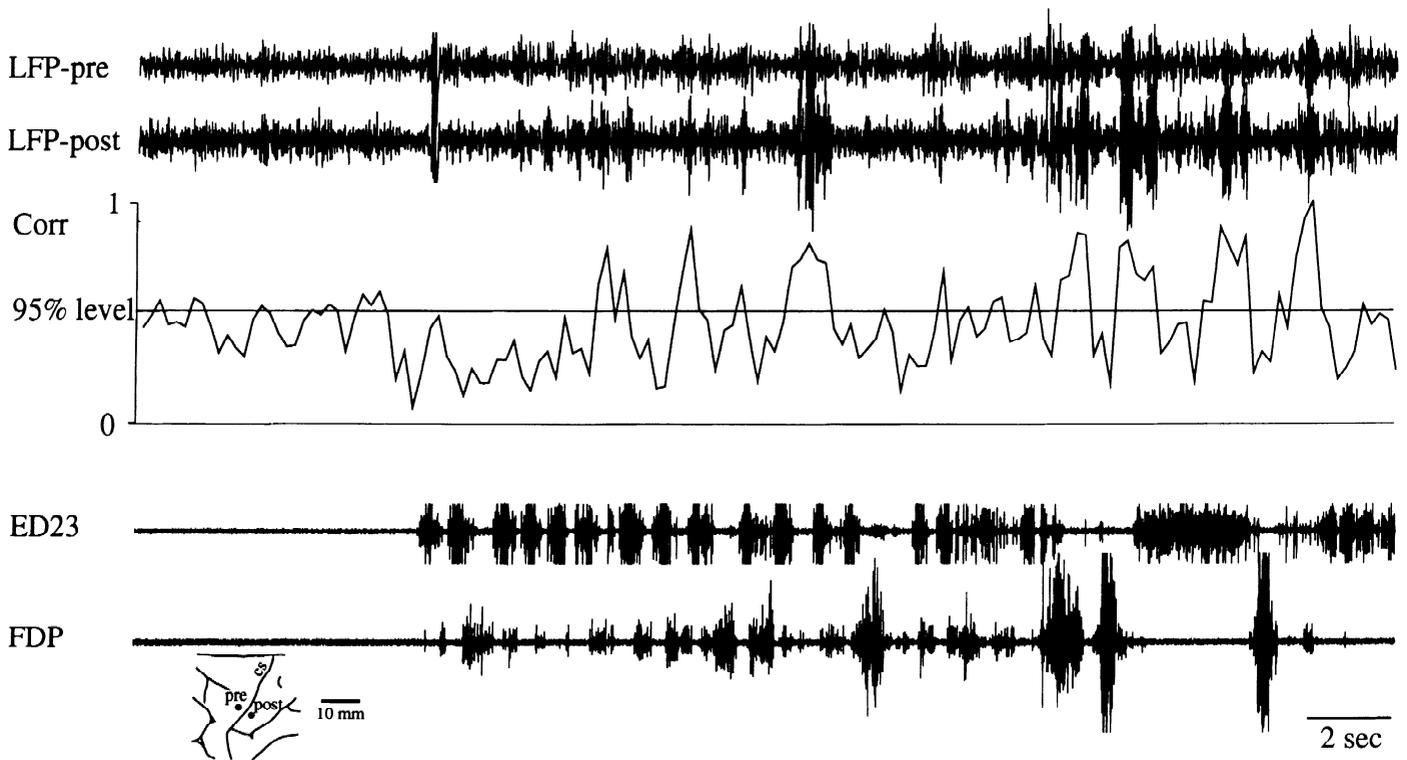


FIG. 16. LFPs recorded at pre- and postcentral sites (marked in the sketch of the cortex), peak correlations (Corr) between them, and EMGs recorded when the monkey reached to pick a raisin from slots of a Klüver board. In the premovement period (when the EMGs were silent) correlations were low. Just after the onset of movement, correlations decreased. However, later in the movement period, when the monkey was attempting to pick the raisin out of the slot, correlation increased intermittently to significantly higher values. Note the absence of any systematic relation between timing of peak correlation and EMGs.

cortical structures that project bilaterally to the cortex. Indeed, in the visual cortex, bilateral synchronization is abolished by sectioning the corpus callosum (Engel et al. 1991a).

It is of interest to understand how zero delay synchronization is possible over large cortical distances with axons that have finite conduction delays. Simulations have demonstrated that periodic activity can be synchronized with zero phase shift in the presence of conduction delays for conduction delays of up to one third of the period of oscillations (i.e., ~ 10 ms for the present study) (König and Schillen 1991). In addition, simulations of cortical networks with the use of compartmental models of neurons have shown that synchronization can occur for delays of < 5 ms (Bush and Sejnowski 1996). This limiting delay value is likely to increase for frequencies of < 40 Hz. Our data indicate that synchronization can occur between sites separated by large intracortical distances, and that synchronization occurs more frequently during periods of oscillations. This lends support to the idea that oscillations may facilitate synchronization between distant neural sites (König and Schillen 1991; König et al. 1995), an idea that is confirmed by increased synchronization of spikes during oscillation (Murthy and Fetz 1996).

It has been reported that 40-Hz oscillations in humans occur as traveling waves across the cortex in the anterior-posterior direction (Ribary et al. 1991). Our experiments revealed no systematic change in the phase of oscillations

from anterior to posterior sites (e.g., Fig. 14D). However, traveling waves of oscillations with velocities similar to those suggested to occur in humans (Llinás and Ribary 1993) would generate time shifts of < 1 ms for the spatial separations of our electrodes, below our level of resolution.

Synchronized oscillations and sensorimotor binding

Despite ample evidence for the widespread existence of 20- to 80-Hz oscillatory activity in cerebral cortex of behaving animals, there is little agreement about its possible function. High-frequency (20- to 70-Hz) cortical oscillations in sensory areas have been proposed as a binding mechanism in perception (Freeman 1978; Singer 1993). The hypothesis that synchronous oscillations play a role in "sensorimotor binding" was tested by simultaneous recordings from paired sites in the precentral cortex and from sites in the pre- and postcentral cortex and in the left and right hemispheres. In each case, synchronization was examined in relation to behaviors that coactivated neurons in the paired cortical sites.

Within the precentral cortex, the association hypothesis was tested by determining whether oscillations could become synchronized between medial and lateral sites preferentially during performance of a task that coactivated the two sites. The reaching (Klüver and Side) tasks used in the study involved the activation of neurons controlling proximal and distal muscles. In contrast, during wrist movements the arm was restrained and movements of the elbow and

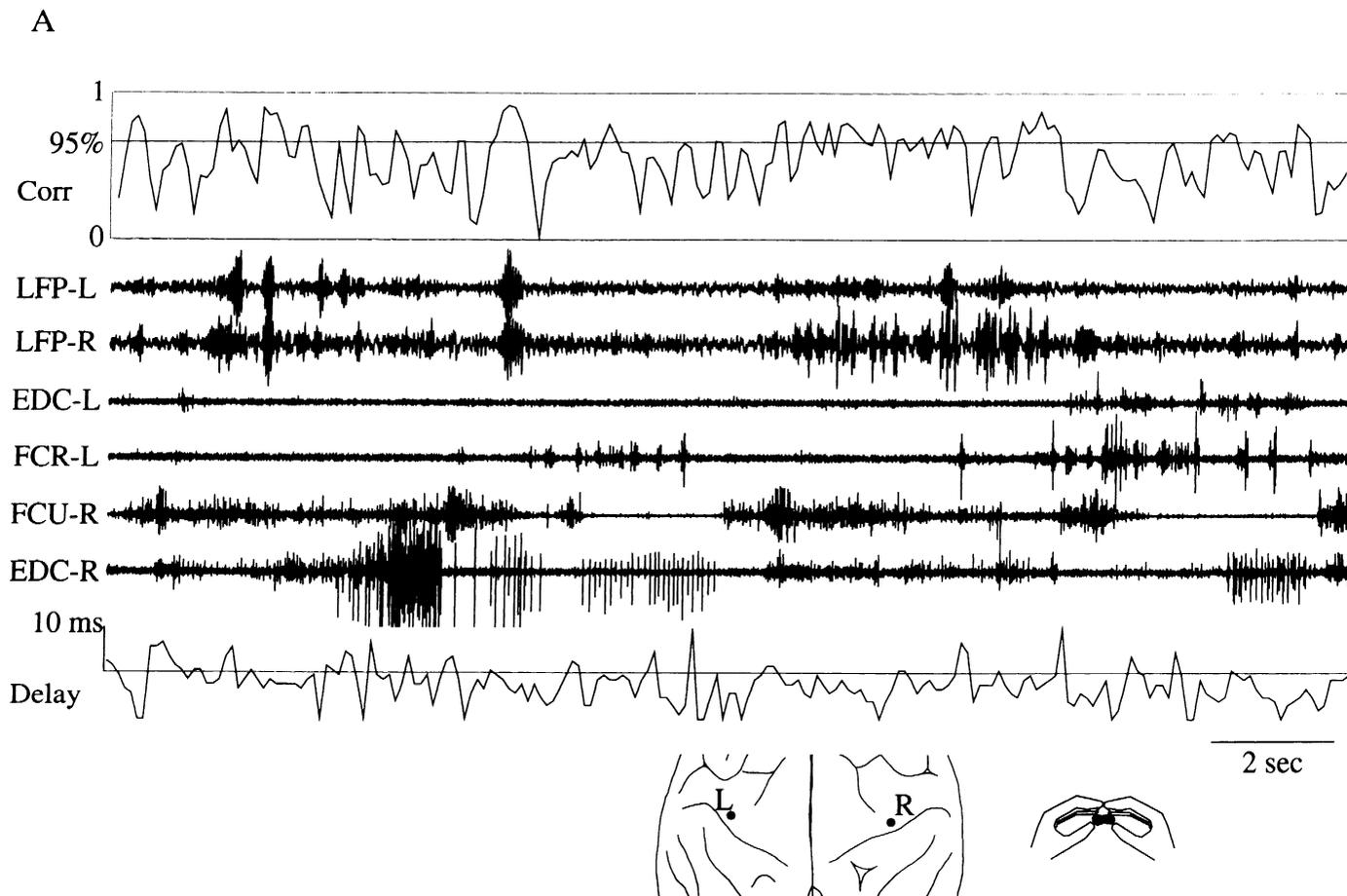


FIG. 17. *A* and *B*: bilaterally recorded LFPs, EMGs, correlation peaks, and delays when monkey was manipulating objects with both hands (*A*) and with the right hand alone (*B*). Oscillations occurred in both hemispheres under all 3 conditions and could become strongly synchronized with each other. *C*: cumulative probabilities of synchronization for the 3 conditions were similar. Shift control was the average for the 3 movement periods. *D*: probability of observing peak correlations that exceeded 95%, and average correlations. There were no significant differences in the parameters during unimanual and bimanual movements. Parameter values for the shifted distribution are shown at *left*.

shoulder were minimal. In addition to the obvious difference in the number of muscles involved, the two tasks also differed in the complexity of sensorimotor integration. Oscillations did become synchronized between medial and lateral sites more frequently during exploratory tasks than during overtrained wrist movements or inactive periods. The strength of synchronization (i.e., the average amplitude of significant correlations) was also greater during unconstrained movements than during trained and constrained movements. However, there was no precise relation between synchronization of LFPs and the occurrence of movements or bursts of EMG activity.

LFP oscillations could become synchronized between somatosensory and motor cortex, particularly during performance of manipulatory tasks (Side and Klüver, Fig. 10) requiring sensory feedback. During exploratory tasks, sensory feedback is essential to guiding precise movements (Asanuma and Arissian 1984). Therefore synchronized LFP and multiunit oscillations in pre- and postcentral sites could be a possible substrate for sensorimotor integration. The anatomic substrate for such synchronization could be provided by the abundant connections between pre- and postcentral cortex (DeFelipe et al. 1986). A close functional link between the two areas is also supported by similarities

in response properties of pre- and postcentral neurons, with regard to sensory input and motor-related activity (e.g., Fetz 1984). Although synchronization occurred between pre- and postcentral sites, it was not temporally associated with onsets of movements. Furthermore, neither the occurrence nor the synchronization of oscillations was preferentially related to task-related sites in the sensorimotor cortex (cf. Murthy and Fetz 1996).

The association hypothesis was further tested in one monkey by recording simultaneously in the left and right hemispheres while the monkey made unimanual and bimanual movements. The supplementary motor area is often considered to play a role in bimanual synergies (Brinkman 1984; Wiesendanger et al. 1992), but there is clear evidence that the primary motor cortex could also play an active role: some motor cortex neurons respond with ipsilateral movements (Tanji et al. 1988), and stimulating certain sites in the motor cortex elicits bilateral hand movements (Aizawa et al. 1990). We found that LFP oscillations occurred simultaneously at bilateral sites for unimanual as well as bimanual movements. LFP oscillations at bilateral sites could become synchronized with negligible phase shifts during these manipulations. Interestingly, synchronization of LFP oscillations was just as likely and just as strong for unimanual as

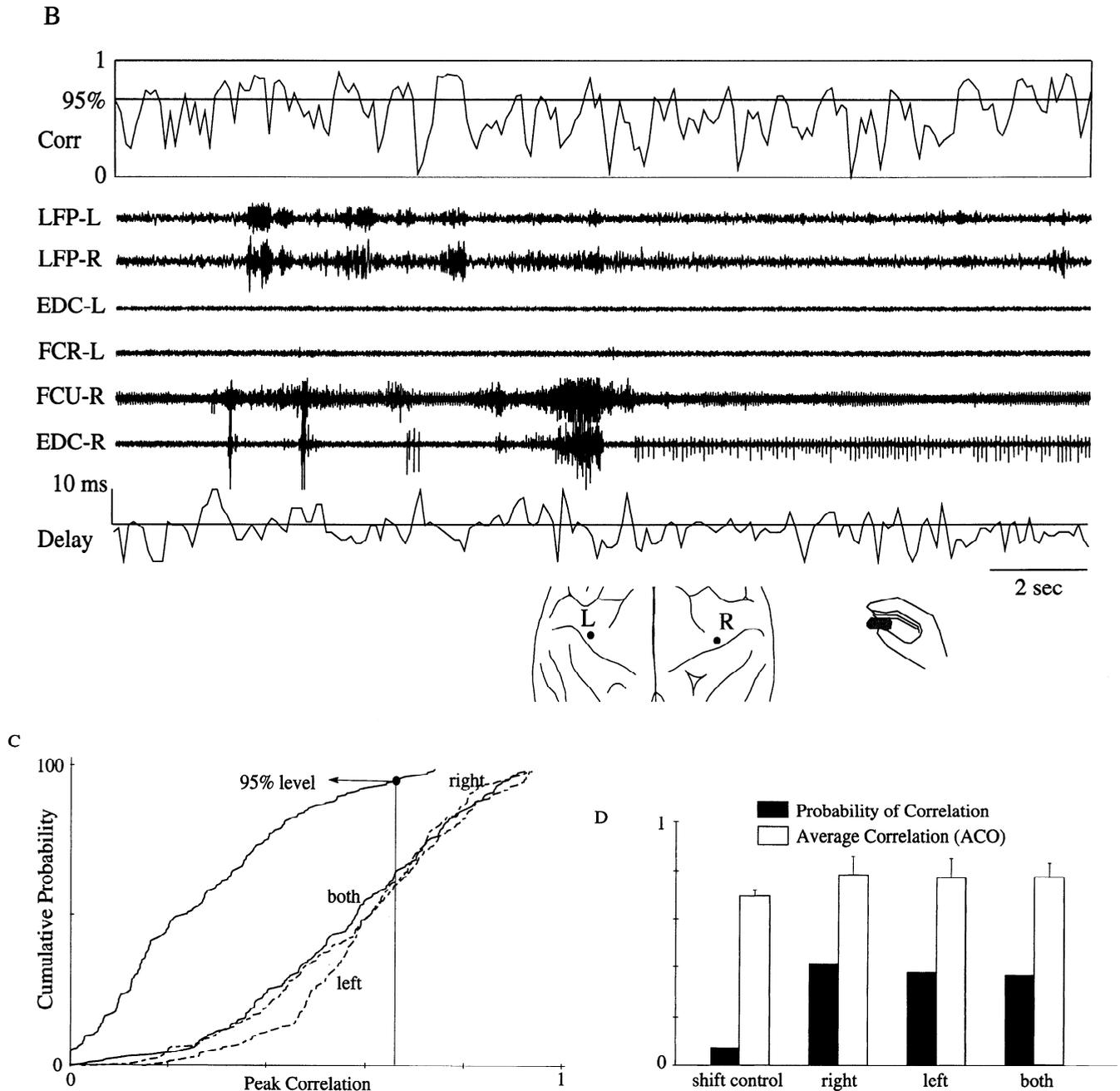


FIG. 17. (continued)

for bimanual manipulations, suggesting that synchronization did not occur preferentially with bimanual coordination. However, because LFPs are complex resultants of underlying synaptic activity, they may not reflect transient and specific synchronization of smaller groups of neurons. As with the ipsilateral recordings, interhemispheric synchronization was also poorly correlated with components of the movements or with episodes of EMG activity.

Widespread synchronization of LFP oscillations in the sensorimotor cortex appears to be too nonspecific and episodic to be directly involved in mediating motor control. Indeed, they have been observed to occur before trained movements and to disappear during movements (Sanes and Donogue 1993). Therefore it seems unlikely that oscillations play a specific role in the control or execution of movements.

In the three different types of paired recordings discussed above, synchronization did not occur more often or more strongly when the sensorimotor task involved the two recording sites. However, cross-correlation of single neurons with known response properties could determine more effectively whether synchronization occurred between coordinated sets of neurons. The companion paper provides more specific evidence on the synchronization of neurons with defined response properties (Murthy and Fetz 1996).

Oscillations may be involved in attention

In the absence of evidence that synchronous oscillations have a specific relation to coordinated movements, one can consider a more general role in higher-order stages of move-

ment preparation or in increased attention. For instance, during attentive periods before execution of a movement, synchronous oscillations could help bring functionally related neurons closer to firing threshold and facilitate their interactions. Such a widespread increase in excitability could help in recruiting diverse groups of neurons for an intended sensorimotor behavior. Oscillations in sensorimotor cortex have been suggested to play a role in attention (MacKay and Mendonca 1995; Rougeul et al. 1979; Rougeul-Buser 1994) when they may facilitate the responsiveness of neurons. Indeed, synchronized oscillations have been generated by electrical stimulation of brain stem sites (Munk et al. 1996; Steriade et al. 1991). Our data are consistent with an attentional role because oscillations were less prominent during the overtrained flexion-extension movements, which involved minimal attention to peripheral stimuli. In contrast, oscillations occurred more often during the retrieving tasks, when the monkeys had to use sensory feedback continually to execute appropriate movements. The attention hypothesis is also supported by our observation that oscillations increased dramatically when the monkey was shown the capture glove. Further behavioral experiments should be designed to test this hypothesis more directly.

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Present address of V. N. Murthy: CNL, The Salk Institute, 10010 N. Torrey Pines Rd., La Jolla, CA 92037.

Address for reprint requests: E. E. Fetz, Regional Primate Research Center, Box 357330, University of Washington, Seattle, WA 98195-7330.

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