Local Field Potential Oscillations in Primate Cerebellar Cortex During Voluntary Movement

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Pellerin, Jean-Pierre and Yves Lamarre. Local field potential oscillations in primate cerebellar cortex during voluntary movement. J. Neurophysiol. 78: 3502–3507, 1997. Sustained oscillations of 13–18 Hz were observed in local field potentials (LFPs) in the cerebellar cortex of a behaving monkey. These oscillations, which appeared to be generated in the granular cell layer, were particularly prominent in the paramedian lobule. The oscillatory activity decreased during drowsiness or extreme arousal and occurred most often when the animal was immobile but alert. In a task requiring the animal to move the arm ~1 s after an auditory cue, the oscillations stopped some 150–200 ms after the cue, resumed 200–300 ms later, and stopped again 50–100 ms before movement onset. This modulation pattern was observed with consistency only when the animal responded reliably to the auditory cue. The results suggest that the cerebellum could be involved in some higher level of integration particularly during complex sensorimotor behavior.

INTRODUCTION

State-dependent oscillations in local field potentials (LFPs) in the frequency range of 12–90 Hz have been recorded from different regions of the mammalian cerebral cortex during performance of a variety of tasks (Singer 1994, for a review). More specifically, a number of studies were concerned with the relationship of fast LFP oscillations to motor behavior, and in all these studies, the oscillatory activity was derived from the sensorimotor cortex and thalamus (Bouyer et al. 1981; Conway et al. 1995; MacKay and Mendonca 1995; Murthy and Fetz 1996; Pfurtscheller and Neuper 1997; Rougeul et al. 1979; Rougeul-Buser et al. 1983; Samelin and Hari 1994; Sanes and Donoghue 1993; Toro et al. 1994). To our knowledge, the occurrence of fast LFP oscillations in association with behavior never has been reported in the cerebellum. Here, we describe the occurrence and characteristics of 13- to 18-Hz oscillatory activity in the cerebellar cortex of a awake behaving monkey trained to respond to an auditory cue after a delay of ~1 s. The oscillatory activity that occurred preferentially when the animal was immobile and attentive to its environment showed a consistent and characteristic modulation during the behavioral motor task. A preliminary account of these results has been published (Pellerin et al. 1995).

METHODS

The experiments were performed in one male adult monkey (Macaca mulatta, weighing 7.8 kg) seated in a primate chair with one arm lying in a shallow trough that was hinged about the elbow joint. During training, the animal learned to perform a flexion of the elbow in response to an auditory cue (400 Hz, 35 dB, 100 ms). The movements had to reach a preset amplitude (usually 10°) within a specified time window to be rewarded by a drop of fruit juice. For most of the experiments reported here, we have used a window of 900–1,200 ms so that movement onset occurred on the average ~1 s after the auditory signal. Microelectrode recordings were obtained in the left cerebellar hemisphere using a technique described elsewhere (Lamarre et al. 1970). The signal from the microelectrode (glass-coated tungsten, impedance 0.5–1.0 MΩ) was filtered at two band-pass settings: between 3 and 70 Hz for LFPs and between 0.3 and 10 kHz for unit activity. Angular displacement at the elbow was measured by a potentiometer. LFP and movement signals were digitized on-line at 200 Hz. Routinely, the LFP signal also was fed to an amplitude discriminator to generate a pulse from each oscillatory cycle, and the interpulse intervals were measured with a resolution of 1 ms. The discriminator threshold was set so that no pulse was triggered when the oscillatory activity was absent or very low in amplitude. Selected data also were recorded directly on a multichannel paper recorder (Gould, ES-2000).

Recordings were performed during a 6-mo period mainly throughout the paramedian lobule but also in some parts of crus I, crus II, and simple lobule. Sampling of the data during each behavioral trial lasted 3 s, including 1 s of prestimulus activity. Recordings also were performed outside the behavioral context of the motor task, i.e., while the animal remained sitting in the chair with the operant arm free and the fruit juice dispenser and manipulation removed. Records thus were obtained selectively during different stages of vigilance such as drowsiness, quiet wakefulness, or intense arousal.

The oscillatory activity was analyzed using either the raw analogue signal or its pulse replica. Power spectra of the LFPs were calculated for each trial using a fast-Fourier transform (FFT) algorithm (Press et al. 1990) and averaged across all trials for any one condition. Change in oscillatory activity during behavioral trials was assessed by calculating the power spectrum for 160-ms windows, which were shifted successively by 40 ms. The pulse replicas of the oscillatory activity from each trial were displayed in the form of rasters and peri-event time histograms, which could be aligned with any of the behavioral events.

At the end of the recording period, a selected recording site was marked with an electrolytic lesion (50 μA, 10 s) and verified on serial 10-μm parasagittal sections of the cerebellum. This paper reports data obtained in one monkey, but the observations presented here have been confirmed recently in a second animal that still is being investigated.

RESULTS

Description and localization of the oscillatory activity

Oscillatory activity at 13–18 Hz was observed throughout the paramedian lobule. This activity was characterized by
episodes of oscillations of variable amplitude (100–300 μV) and duration (range: 0.2–6 s; mean: 1.3 s) separated by intervals of 0.2–3 s (mean: 0.6 s). These episodes often were spindle-shaped but they could also start and stop abruptly. Figure 1A illustrates a 7-s sample of oscillatory activity at 15 Hz recorded while the monkey was sitting quietly and immobile. Figure 1C shows the orientation of four electrode penetrations drawn on a sagittal section of the cerebellum, 6 mm lateral to the midline. Recordings were performed at different levels from the surface to the bottom of the cerebellum. Oscillations such as those illustrated in Fig. 1A were observed only in the paramedian lobule (square). In all instances, the amplitude of the oscillations decreased sharply when the tip of the electrode reached past the bottom of the cerebellum. At the bottom of the most anterior electrode penetration (Fig. 1C), the recording site was marked with an electrolytic lesion. The photomicrograph shows that the tip of the electrode was in the granular layer. In our recording conditions, we could not determine with certainty the exact cortical layer of all the sites where the oscillatory activity was recorded. However, we believe that the oscillations were recorded mostly in the granular layer because they were largest at sites where rhythmic bursting of thin, small spikes occurred at the same frequency as the LFP oscillations. This is illustrated in Fig. 1B, where the two traces are derived from the same microelectrode. In many instances, a small microelectrode displacement of the order of 0.5 mm could produce a sharp change in the amplitude of the oscillations. In addition, at recording sites yielding large amplitude oscillations, we rarely saw climbing fiber responses nor did we record large, well isolated simple spikes.

Correlation with the general behavior of the animal

The most obvious correlation between the oscillatory activity and the animal’s behavior was that movement of any part of the body was usually associated with complete cessation of the oscillations. This is shown in Fig. 2A (top) where the 16 Hz oscillations stopped rather abruptly ~100 ms before a spontaneous flexion of the ipsilateral arm (bottom). The oscillations were present, however, whatever the posture assumed by the animal as long as it remained immobile. On the other hand, we did not observe any obvious correlation with eye movements. We further correlated the oscillatory activity with respect to various stages of vigilance as shown in Fig. 2, B–D. When the animal was sitting quietly and immobile but alert, the oscillations were quite sustained as confirmed by the power spectra of LFPs, showing a significant increase of power in the range of 12–18 Hz (Fig. 2B). When the monkey was aroused provocatively by the experimenter standing close by and staring directly into the animal’s eyes, the oscillations decreased significantly (Fig. 2C) despite the fact that the animal remained immobile. Finally, during episodes of reduced vigilance or slight drowsiness, the frequency range of LFPs shifted between 3 and 12 Hz with the occurrence of bursts of large irregular waves (Fig. 2D).

Correlation with the motor task

To perform the task, the animal’s arm had to be strapped onto the manipulandum and the fruit juice dispenser positioned near its mouth (task context). We observed that when the arm was free and the juice dispenser was taken away (nontask context), the episodes of oscillations were less sustained (mean duration: 1.1 s; range: 0.2–3 s) than in the task context (mean duration: 1.5 s; range: 0.2–6 s). Most remarkable was the fact that the oscillations showed a consistent and characteristic phasic modulation during the behavioral motor task as illustrated in Fig. 3 with data derived from a block of 320 successive trials. Each trial lasted 3 s with a mean intertrial interval of 9 s. Figure 3A illustrates one of these trials with a sample LFP recorded from the left paramedian lobule (top) and left arm displacement (bottom). The animal responded with a 15° elbow flexion (M) ~1 s after the onset of the sound (S). To obtain some quantification of the modulation of LFP oscillations during the task, we performed FFT in short 320-ms epochs (64 points) at four different moments during each behavioral trial, and the spectra were averaged over the number of trials. Even though such short epochs reduced considerably the frequency resolution of the spectral analysis, this was sufficient to document major changes in the power of the oscillations.
tory process within our frequency range of interest (13–18 Hz). The results of this analysis are illustrated in Fig. 3A. The four epochs labeled a–d are indicated by horizontal lines underneath the sample LFP trace. The FFT performed before the onset of the sound (epoch a) yielded large values in the bins corresponding to 12.5 and 15.6 Hz. The power in those two bins was considerably reduced between 150–470 ms after the onset of the sound (epoch b). The FFT again showed large values preceding movement onset (epoch c), particularly in the 15.6 Hz bin, and this disappeared during movement (epoch d). No other large peaks were ever observed in the 30- to 50-Hz range.

The phasic modulation of the LFP oscillations during the behavioral task also is illustrated in Fig. 3B with greater time resolution using 160-ms windows successively shifted by 40 ms and using either the stimulus (left) or the onset of movement (right) as the time reference. In this particular experiment, there was a slight tendency for the oscillations to increase during the 1-s period preceding the onset of the stimulus (Fig. 3B, left). This, however, was not observed systematically (see Fig. 4) in contrast to the modulation seen after the stimulus.

Figure 4, from another experiment, shows that the modulation of LFP oscillations depend on the performance of the animal. In this experiment, 142 successive trials were recorded during an about half-hour period. Each trial lasted 3 s with a mean intertrial interval of 9 s (range: 6–10 s). Figure 4A illustrates one of these trials with specimen of LFP recorded in the paramedian lobule (top) and left arm displacement (bottom). The dotted line across the LFP trace indicates the set level of the amplitude discriminator that generated trigger pulses from individual oscillatory cycle. These pulses were treated in the same manner as neural spike trains and displayed in raster form.

Figure 4B (left) shows such a raster for the block of 142 trials presented in order of acquisition (top to bottom).
FIG. 4. Modulation of LFP oscillations and performance of the animal. A: LFPs and movement trace during a 3-s behavioral trial where the monkey responded with a flexion of the arm (M) ~1 s after the onset of the auditory cue (S). Dotted line, threshold of the amplitude discriminator used to generate pulses from individual cycle of oscillations as represented in B and C. B, left: raster plot of 142 consecutive trials obtained during a period of ~30 min. Trials are aligned with respect to stimulus onset (S) and presented in order of acquisition from top to bottom. Small dots are pulse replicas of the oscillatory activity, and the larger dots indicate movement onset. Right: perievent time histograms (20-ms binwidth) and power plots (obtained as in Fig. 3B) constructed from each of 3 epochs (1–3) corresponding to different levels of the monkey performance. Characteristic modulation of LFP oscillations was observed only when the monkey responded reliably to the stimulus (1 and 3). C: same as in B with trials aligned with respect to movement onset (M).

and aligned with the stimulus. The heavier dots indicate the onset of movement. During the first 12 min (Fig. 4B1, 57 trials), the animal responded regularly after the sound cue (S). For these trials, one can notice that the number of dots decreased markedly some 150–200 ms after the onset of the sound, indicating that the LFP amplitude fell below the discriminator level. LFP amplitude remained low for ~300–400 ms, then became large again for ~400 ms, decreased a second time with movement execution, and finally recovered toward the end of the trials. This characteristic modulation of the amplitude of LFP oscillations disappeared during the following 8 min of acquisition (Fig. 4B2, 44 trials) when the monkey spontaneously stopped responding to the cue most of the time. The modulation reappeared during the last period of acquisition when the animal spontaneously resumed its performance (Fig. 4B3, 41 trials). The presence or absence of LFP modulation depending on the performance of the animal is also evident (Fig. 4B, right) in the perievent time histograms constructed for each of the three periods of acquisition and in the power plots obtained in the same way as in Fig. 3B. In Fig. 4C, the data from the first and third period of acquisition are aligned with movement onset (M) to define more accurately the timing of the modulation of the oscillations with respect to the movement.

**Discussion**

The results presented in this paper indicate that intermittent LFP oscillatory activity at 13–18 Hz is present at least in some regions of the primate cerebellar cortex and in particular in the paramedian lobule. The oscillations clearly are modulated with respect to the general behavior of the animal and also within the context of a specific motor task. To our knowledge, such cerebellar oscillatory activity has never been reported before, and it appears to be more sustained and more precisely related to motor behavior than the sensorimotor cortex oscillations at 20–40 Hz studied recently in the awake monkey (MacKay and Mendonca 1995; Murthy and Fetz 1996; Sanes and Donoghue 1993). However, one group of investigators (Bouyer et al. 1981, 1983; Rougeul et al. 1979) have described, in cats, cerebral cortical (and thalamic) oscillatory activity in the 12- to 18-Hz band primarily localized in the parietal cortex and that are very similar to the oscillations recorded in the cerebellar cortex and described in this paper. The most striking behavioral correlate of these rhythms is the fact that the oscillations occur only when the animal is immobile and apparently waiting for some external event to occur. They are not present during drowsiness or in situations when the animal is aroused with its attention focused on something precise. Similar activity termed "mu" rhythms already has been observed in humans.
with scalp recordings over the central region of the brain (Gastaut et al. 1957).

Cerebellar sources of oscillations

From a number of indirect arguments, we are led to postulate that LFP oscillations are generated primarily in the granular layer of the cerebellar cortex. This is based on the fact that we never recorded presumed Purkinje cell spikes or climbing fiber responses that showed clear phasic relationship with the oscillations. Whenever rhythmic unitary activity was found synchronized with LFP oscillations, this was always in the form of high-frequency bursts of thin, small spikes (Fig. 1B) presumably recorded in the granular layer. Because the vast majority of neurons in the granular layer are granule cells, it is somewhat surprising that this rhythmic activity does not seem to produce overt modulation of the Purkinje cells via the parallel fiber system. However, if the granule cells that are active rhythmically were located most superficially in the granular layer, they then would contact the more distal portion of the Purkinje cells dendrites (Eccles et al. 1967), and their synaptic influence might be so remote that it could not readily be observed in our experimental conditions. It is also possible that the oscillatory process involves mainly a special type of granule cells that do not directly influence Purkinje cells (Arshavskii 1972). Finally, the rhythmic unitary activity recorded in the granular layer could be generated by Golgi cells and by neuronal elements that do not ascend into the molecular layer, such as unipolar brush cells (Mugnaini and Floris 1994) and mossy fiber terminals.

At this point in time, it is not possible to speculate whether the oscillations arise solely from the intrinsic properties of neuronal elements and circuitry within the cerebellar cortex itself or if they involve extracerebellar circuit interaction. There is some evidence, however, that circuits in the cerebellar cortex and particularly in the granular cell layer are intrinsically capable of generating oscillations (Maex et al. 1996).

Contrary to the cerebral cortex, the structure and organization of the cerebellar cortex are virtually the same for all parts of the cerebellum. It is thus quite surprising to find that the 13- to 18-Hz oscillations were present mainly in the paramedian lobule. Even though we did not perform a systematic investigation of the whole cerebellar cortex, these oscillations were not observed in the regions traversed by the microelectrode on the way to the paramedian lobule, namely in the simple lobule, crus I laterally, and lobule V and VI medially. The dorsal paraflocculus and crus II were not systematically investigated, and we cannot rule out the possibility that some oscillations are present in these lobules as well particularly in the regions adjacent to the paramedian lobule. A systematic mapping of the oscillations throughout most of the cerebellum is now being performed in another animal (female M. mulatta, 4.4 kg). In this second monkey, the frequency range of LFP oscillations is somewhat higher (16–22 Hz) then what is reported in this paper. This is the only difference between the two animals. Indeed, the oscillations are found in the same region of the cerebellum and show the same modulation with behavior as reported here.

The paramedian lobule has not been investigated system-

atically in primates during voluntary movements but it likely plays an important role in sensorimotor control of limb movements. In our experiments, Purkinje cell activity in the paramedian lobule was strongly modulated with the animal’s behavior. Simple spikes increased frequency on the average 55 ms before the onset of movement (n = 45) but no response to the stimulus was observed. All these cells responded only to deep stimulation of the limbs with large receptive fields, often involving both upper and lower ipsilateral limbs and sometimes contralateral as well. Passive displacement of the elbow by a torque motor generated a response with a mean latency of 28 ms (n = 14). Most complex spikes that were recorded (n = 46) also were modulated in the task. Half responded only with movement (~25 ms before onset), 20% only with the stimulus (mean latency of 150 ms), and 10% with both stimulus and movement. So far we were not able to demonstrate any obvious precise phasic relationship between Purkinje cell activity and LFP oscillations, but this will require further experiments and analysis before any definitive statement can be made.

Functional considerations

The possible function of these newly discovered oscillations in the cerebellar cortex remains as obscure as the role of the oscillatory activity, which has been studied for some time in the cerebral cortex. The particular behavioral task that we have used was designed to search for some electrophysiological correlates of “time measurement” in the cerebellum. The systematic modulation of the oscillatory activity in the period of 1 s between the external cue and the motor response is quite impressive. Indeed, this modulation could be interpreted along the hypothesis put forward by Rougeul, namely that the oscillations could be related to a “conditioning expectation of something significant that has a high probability to happen” (Rougeul-Buser and Buser 1994). While the trained animal is sitting in the chair with the arm fixed to the manipulandum and the juice dispenser near its mouth, it is most likely waiting for the occurrence of the expected cue if it is in a mood to respond. The oscillatory process shuts down some 150–200 ms after the occurrence of the cue, possibly signaling the end of this first waiting period. This is followed by a second waiting period in which the oscillations resume to finally end again shortly before the motor response and reward delivery. The end of the first waiting period is determined by an external event (the sound cue) and the oscillations stop after a delay after the occurrence of the event. The second waiting period is terminated by an “internal” event, i.e. the decision to move, and this internal event must precede the actual instrumental motor response. In this case, indeed, the oscillations terminate some 60–80 ms before the onset of arm displacement and resume sometime later presumably when the animal is again waiting for the next cue. The external cue by itself does not influence the oscillatory process when the animal is not prepared to respond to it as is clearly shown in Fig. 4B. In this case, the animal still must be aware that the sound cue will come at some time but it is not “expecting” it because the cue has no more significance in terms of a timing event. Whether the oscillatory activity described here has indeed some specific timing function relevant to the task requirement is not
known. Even though the oscillations tend to be larger and more coherent in the 500-ms period preceding the movement, we have not been able to document any precise phase relationship between the oscillatory process and the motor response. This particular aspect is now being investigated using conditions in which the motor response onset can be measured more accurately.

During recent years, much attention has been devoted to oscillatory activity in the cerebral cortex of behaving animals, and it has been proposed that synchronization of oscillations between different cortical areas could play a role in sensorimotor integration (Singer 1993). The findings reported here support the idea that the cerebellum also could be involved in some higher level of sensorimotor integration perhaps by synchronizing its oscillatory activity with certain regions of the cerebral cortex in specific motor performances.

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REFERENCES


