Richard Courtemanche, Jean-Pierre Pellerin and Yves Lamarre
J Neurophysiol 88:771-782, 2002.

You might find this additional information useful...

This article cites 36 articles, 20 of which you can access free at:
http://jn.physiology.org/cgi/content/full/88/2/771#BIBL

This article has been cited by 8 other HighWire hosted articles, the first 5 are:

Correcting the Bias of Spike Field Coherence Estimators Due to a Finite Number of Spikes
D. W. Grasse and K. A. Moxon
J Neurophysiol, July 1, 2010; 104 (1): 548-558.
[Abstract] [Full Text] [PDF]

Neocortical Networks Entrain Neuronal Circuits in Cerebellar Cortex
H. Ros, R. N. S. Sachdev, Y. Yu, N. Sestan and D. A. McCormick
J. Neurosci., August 19, 2009; 29 (33): 10309-10320.
[Abstract] [Full Text] [PDF]

Effects of Striatal GABAA-Receptor Blockade on Striatal and Cortical Activity in Monkeys

O. Darbin and T. Wichmann
J Neurophysiol, March 1, 2008; 99 (3): 1294-1305.
[Abstract] [Full Text] [PDF]

Cortico-Cerebellar Coherence During a Precision Grip Task in the Monkey
D. S. Soteropoulos and S. N. Baker
J Neurophysiol, February 1, 2006; 95 (2): 1194-1206.
[Abstract] [Full Text] [PDF]

Widely Distributed Magnetoencephalography Spikes Related to the Planning and Execution of Human Saccades
A. A. Ioannides, P. B. C. Fenwick and L. Liu
J. Neurosci., August 31, 2005; 25 (35): 7950-7967.
[Abstract] [Full Text] [PDF]

Medline items on this article's topics can be found at http://highwire.stanford.edu/lists/artbytopic.dtl on the following topics:

Physiology .. Purkinje Cells
Neuroscience .. Visual Stimulation
Veterinary Science .. Cerebellum
Physiology .. Primates
Physiology .. Monkeys

Updated information and services including high-resolution figures, can be found at:
http://jn.physiology.org/cgi/content/full/88/2/771

Additional material and information about ***Journal of Neurophysiology*** can be found at:
http://www.the-aps.org/publications/jn

This information is current as of August 20, 2010 .

Journal of Neurophysiology publishes original articles on the function of the nervous system. It is published 12 times a year (monthly) by the American Physiological Society, 9650 Rockville Pike, Bethesda MD 20814-3991. Copyright © 2002 by the American Physiological Society. ISSN: 0022-3077, ESSN: 1522-1598. Visit our website at http://www.the-aps.org/.

Downloaded from jn.physiology.org on August 20, 2010

J Neurophysiol
88: 771–782, 2002; 10.1152/jn.00718.2001.

Local Field Potential Oscillations in Primate Cerebellar Cortex: Modulation During Active and Passive Expectancy

RICHARD COURTEMANCHE, JEAN-PIERRE PELLERIN, AND YVES LAMARRE
Département de Physiologie and Centre de Recherche en Sciences Neurologiques, Université de Montréal, Montreal, Quebec H3C 3J7, Canada

Received 27 August 2001; accepted in final form 12 April 2002

Courtemanche, Richard, Jean-Pierre Pellerin, and Yves Lamarre. Local field potential oscillations in primate cerebellar cortex: modulation during active and passive expectancy. *J Neurophysiol* 88: 771–782, 2002; 10.1152/jn.00718.2001. Cerebellar local field potential (LFP) oscillations were recorded in the paramedian lobule of one hemisphere, while monkeys were in two behavioral conditions: actively performing an elbow flexion-extension or a lever-press task in response to an auditory or visual stimulus to get reward (active condition), or waiting quietly for the reward to come in the same time window after the appearance of the stimulus (passive condition). The oscillations in the paramedian lobule were first characterized in four monkeys, and they showed an idiosyncratic frequency for each monkey, between 13 and 25 Hz. The granule cell layer multi-unit activity was phase-locked with the negative phase of the LFP oscillations, while Purkinje cell simple spikes were also sometimes phase-locked with the LFP. Three monkeys were trained to perform the motor tasks: the LFP oscillations were modulated, in the active condition, in a systematic manner in relation to the lever-press or elbow flexion-extension tasks. During periods when the monkey was waiting to initiate movement, LFP oscillations appeared and then stopped with movement initiation. This modulation was valid for the task being executed with either hand. Surprisingly, the LFP oscillations were also systematically modulated during the passive condition; as the monkey was waiting for the usual time to get a reward passively, oscillations appeared stronger and were stopped by the end of the usual delay, whether the monkey was rewarded or not. This type of modulation was not affected by the length of the stimulus, as long as the reward window was known to the monkey. If the monkey had not been previously trained to the active condition, the modulation appeared in the passive condition. These results show that cerebellar LFP oscillations in the paramedian lobule are reliably present when the monkey is involved in a waiting period, whether this period ends with an active or passive event. This study provides electrophysiological evidence for a specific pattern of activity in the cerebellum for the expectancy of events that are known to be bound to happen, either externally, or from voluntary action.

INTRODUCTION

Local field potential (LFP) oscillations in the awake primate brain are well documented in many areas and can be recorded from the low-frequency spectrum of electrical activity in the motor and parietal cortices (Baker et al. 1997; MacKay and Mendonça 1995; Murthy and Fetz 1992, 1996; Rougeul et al. 1979; Sanes and Donoghue 1993). These oscillations are often in the 13–25 Hz range and could be related to motor preparation and to sensorimotor integration prior to movement (Farmer 1998; MacKay 1997). These oscillations were mostly thought to be lacking in the cerebellar cortex (Bullock 1997; Freeman and Skarda 1985); however, recent reports demonstrated the existence of LFP oscillations in the cerebellar cortex of awake primates (Pellerin and Lamarre 1997) and rats (Hartmann and Bower 1998). These oscillations are recorded in the granule cell layer (GCL) of the cerebellar cortex, and in the monkey, these 13–25 Hz oscillations are located mainly in the paramedian lobule of the cerebellar cortex. One particularly salient feature is that the oscillations are seen when the animal is immobile; they are promptly halted by a movement made by the animal. This characteristic of cerebellar LFP oscillations seems to negate a straightforward role in the generation of movement, contrasting with other electrophysiological signals coming from similar regions of the cerebellar cortex, for instance, the Purkinje cell simple spike or complex spike discharge (e.g., Marple-Horvat and Stein 1987; Welsh et al. 1995). Also, these oscillations are related to an optimal arousal level, forecasting a possible contribution to the general state of the animal in relation to its surroundings (Pellerin and Lamarre 1997).

To further differentiate the role of LFP oscillations in the cerebellar cortex in immobility versus movement, recording of oscillatory LFPs was performed in two conditions corresponding to motor and nonmotor behavioral contexts. Findings show a modulation of the cerebellar LFP oscillations in both conditions, with a differential modulation in motor and nonmotor behavioral contexts, which is related to the expectancy of the ensuing movement or reward. Partial results of this study were presented in abstract form (Courtemanche et al. 1999).

METHODS

Subjects, tasks, and behavior

Experiments were conducted on four adult *Macaca mulatta* monkeys: three males (weight: monkey 1, 10.3 kg; monkey 3, 7.8 kg; and monkey 4, 7.0 kg) and one female (monkey 2, 4.7 kg). Each monkey was sitting in a primate chair, and monkeys 1, 3, and 4 were trained to execute a movement in response to a stimulus after waiting for a certain time delay, which was either 1,200 (monkey 1) or 1,500 ms

Address for reprint requests: Y. Lamarre, Département de Physiologie, Université de Montréal, C.P. 6128, Succursale Centre-Ville, Montreal, Quebec H3C 3J7, Canada (E-mail: yves.lamarre@umontreal.ca).

The costs of publication of this article were defrayed in part by the payment of page charges. The article must therefore be hereby marked "*advertisement*" in accordance with 18 U.S.C. Section 1734 solely to indicate this fact.

0022-3077/02 $5.00 Copyright © 2002 The American Physiological Society

Downloaded from jn.physiology.org on August 20, 2010

(monkeys 3 and 4). Monkey 2 was only used for the description of the LFP oscillations, and monkey 4 was also used for recordings prior to training. The stimulus was either a tone (400 Hz, 35 dB; monkeys 1, 3, and 4) or the simultaneous lighting of eight yellow light-emitting diodes (LEDs) placed 1.5 m in front of the monkey's head (monkeys 3 and 4). This signal also served as a temporal guide for the monkey's evaluation of the proper delay to get a reward of a few drops of juice. The reward window for the monkey observing the proper temporal delay was set at values between 900 and 1,200 ms (monkey 1) or 1,100 and 1,500 (monkeys 3 and 4), following the onset of the stimulus. The movement executed by the monkeys was either the pressing of a lever located in front on a small table at waist level (monkeys 3 and 4) or a fast flexion-extension movement of the arm at the elbow (monkey 1). For the lever-press task, the monkey was not restrained, except for the head fixation, and had no physical implements limiting its movements. For the elbow flexion-extension task, in addition to the head fixation, monkey 1 had one arm lying in a shallow trough that was hinged around the elbow joint. For both tasks, a juice dispenser was placed close to the animal's mouth to dispense rewards. The lever-press task and the elbow flexion-extension task were both part of what we call the *active* condition, where the monkey was making a voluntary movement in response to a stimulus to get a reward; this contrasts with the *passive* condition, where the monkey got a reward that was temporally associated with a stimulus, but did not need an active participation to receive reward.

In the elbow flexion-extension task, monkey 1 made a ballistic movement that was measured using a potentiometer to provide angular displacement. This movement was well stereotyped, with the monkey waiting around 1,000 ms prior to movement initiation. In the lever-press task, monkeys 3 and 4 could use many variants of movement as long as they pressed the lever in the target time window. The lever-press was stored as a voltage change and marked as a unitary event for each trial. For monkey 4, the lever was also equipped with a strain gauge to monitor contact of the hand. Analog video (16.6 ms resolution) was also used in some sessions to document the general profile of the monkey's movement (monkeys 3 and 4). Using these means, we saw that even if monkeys were not hindered and could make a variety of movements to press the lever, they adopted a stereotypical movement after training. About 250–300 ms after stimulus onset, the monkey initiated hand displacement toward the lever. This movement to reach the lever lasted around 500 ms, and the monkey waited until the end of the delay period to execute the press. Figure 1 shows one trial of each task for the active condition.

Each trial lasted from 3 (monkey 1) to 5 s (monkeys 3 and 4), with inter-trial delays varying randomly between 1 and 6 s. All three monkeys could perform the task with either hand. Instruction for which hand or arm to use for the task was given at the beginning of a block of trials by placing the lever or the shallow trough either on the left or the right side of the animal. Left and right movements thus composed the active condition. Both the active and passive conditions were presented to the monkey in blocks of trials. In the passive condition, the lever was removed, and the monkey only had to sit quietly, but nonetheless received juice after a 1–1.5 s delay after stimulus onset. During these blocks, the monkey was still rewarded on 60–70% of the trials, which corresponds to the success rate achieved when the active condition was performed by the animal. Variability in juice delivery time in the passive condition was comparable with the variability in the timing of responses performed by the monkey in the active condition.

Database

Monkeys 1, 3, and 4 were all tested during behavioral conditions. Monkey 1 was tested only in the active condition, by performing flexion-extension movements with either hand. Monkeys 3 and 4 were tested in both the active (lever-press) and passive conditions. While monkey 3 was only tested in the passive condition after having been trained to perform the lever-press task, monkey 4 was first tested in the passive condition, trained in the lever-press task, and tested again after training in the active and passive conditions. For characterization of oscillatory activity in relation to behavior, ≥20 different experiments during a period of 6 mo were analyzed in depth for each of the three animals.

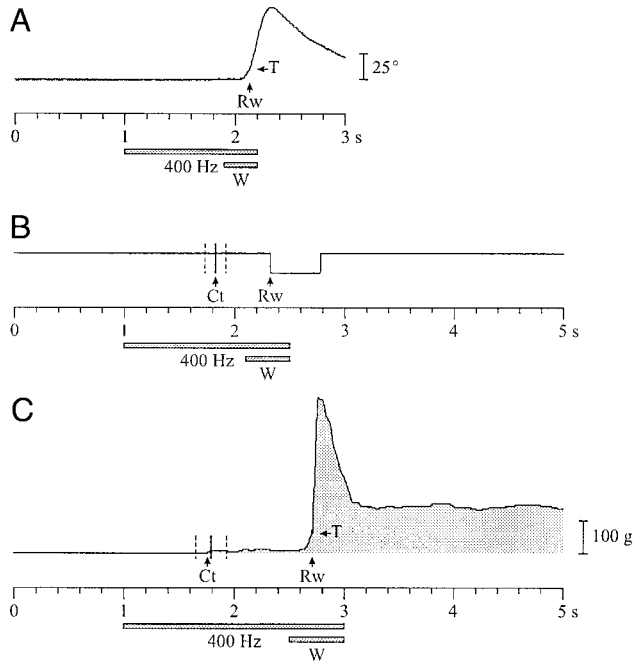

FIG. 1. The 3 tasks making up the active condition. One trial of each task is shown. Periods of stimulus presentation (400-Hz sound) and reward window (W) are shown by horizontal bars. Rw, time of reward delivery. *A*: monkey 1, elbow flexion-extension trial lasting 3 s, with elbow angle given by a potentiometer. Flexion direction is upward. Threshold angle for determination of movement onset is shown (T) and occurs at time Rw. *B*: monkey 3, lever-press trial lasting 5 s. Pressing the lever provokes a voltage change being detected at time Rw. Ct, time of contact (determined using video recordings). Vertical line represents average time of contact; hatched lines represent the ±SD. *C*: monkey 4, lever-press task with a strain gauge to signal pressure on the lever. The strain gauge signal increases with contact, lever-press signal similar as in *B* (not shown). Threshold for reward (T) was dependent on the strain gauge signal, occurring at time Rw. Ct vertical line, average time of contact determined by the signal on strain gauge; hatched lines, ± SD.

Recording of local field potentials and movement signals

Recordings were performed in the left paramedian lobule of the cerebellar cortex of each monkey. The center of the recording chamber was positioned over the left posterior parietal cortex to access the cerebellum. A description of the installation technique is described in Lamarre et al. (1970). Glass-coated tungsten microelectrodes (0.2–0.7 MΩ) were used, and the signal was filtered at two band-pass settings: between 3 and 70 Hz for recording of LFPs and between 0.3 and 10 kHz for monitoring unit activity. Sampling of the LFP signal was at 200 Hz (monkeys 1 and 2) and 1 kHz (monkeys 3 and 4), while movement description signals were sampled at 200 Hz for the potentiometer signal and 1 kHz for the lever-press and strain gauge signal. The LFP signal was also fed on-line to an analog to digital (A/D) discriminator for generation of pulse histograms to evaluate signal rhythmicity through the trials during the experimental session. For monkey 4, prior to the actual training for the active condition, a contact signal from the juice pipette was also fed to the computer, in the form of a voltage variation when the monkey was touching with the mouth or tongue, sampled at 1,000 Hz. On some experiments, data were also recorded directly on a multichannel paper recorder.

Downloaded from jn.physiology.org on August 20, 2010

Data analysis and histology

LFP data were analyzed using Fast Fourier Transforms (FFT) and autocorrelation to evaluate signal rhythmicity. For better isolation of the oscillatory phenomenon, the raw LFP signal was filtered between 13 and 25 Hz, corresponding to the range of frequencies of the cerebellar LFP oscillations in our monkeys (described in RESULTS and Fig. 2). Rhythmicity during certain epochs of the trial was quantified using two methods: with the pulse replicas generated (on-line or off-line) by the A/D discrimination process, in the form of peri-event time histograms and by computing the temporal spectral evolution (TSE) developed by Salmelin and Hari (1994), consisting of filtering the signal according to the frequency band of interest, rectifying this filtered signal, and averaging this new product across trials. The TSE analysis provides information about the occurrence and amplitude of oscillations at different epochs of the behavioral task. Statistical analysis of the significance of task-related changes of LFP oscillatory activity in each experiment was performed in the following way for monkeys 3 and 4. The mean amplitude of the TSE was measured for each trial over a 500-ms time window immediately preceding the onset of the stimulus. The mean and SD of this set of data represented a control value for all trials of a given experiment. The same analysis was repeated for three different time windows corresponding to different epochs of the behavioral task (i.e., 500 ms starting 200 ms after stimulus onset, 500 ms preceding the reward window, and 500 ms following the reward window). The TSE values derived from these windows following the stimulus were expressed in percentage of the control value preceding the stimulus. This allowed us to pool together the results of all experiments repeated in the same experimental conditions in the same animal. Changes after the stimulus were either positive or negative (increased or decreased LFP oscillatory activity) and were considered significant at the 1% level (Student's *t*-test). The same analysis was also performed in monkey 1, but since the data acquisition period was shorter in this animal, 400-ms windows were used instead of 500 ms as in the other two monkeys.

In the last recording session, electrolytic lesions were made in the cerebellar cortex of the monkeys at sites corresponding to recording sessions where oscillations were found, and 2 days later the monkeys were deeply anesthetized and perfused through the heart using a buffered 9% formaline-8% saline solution. Recording sites were controlled on 50-μm frozen sagittal sections of the cerebellum stained with cresyl violet.

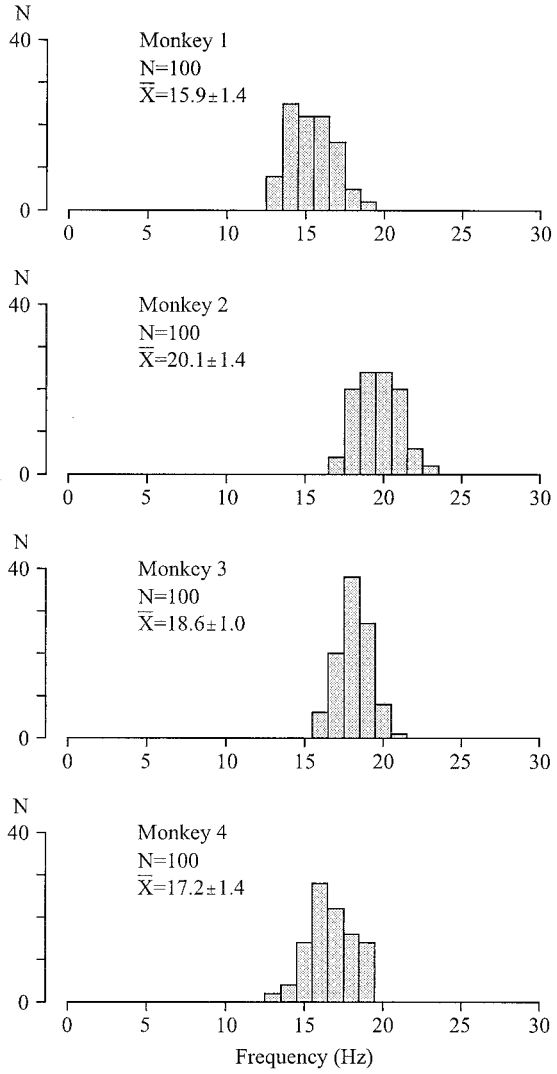

FIG. 2. Frequencies of the local field potential (LFP) oscillations for each monkey. Samples (100 from 30 to 40 trials) were taken from the prestimulus epoch (monkeys 1, 3, and 4) or from periods when the monkey was sitting quietly in the chair (monkey 2). Frequencies were calculated from the inverse of the period determined by the first peak of the autocorrelation of the LFP signal. Each monkey showed an idiosyncratic pattern of frequencies, with a distribution different for each monkey (χ^2, $P < 0.05$). *x* axis, frequency in Hz; *y* axis, number of samples.

RESULTS

LFP oscillations in the cerebellum were recorded in all four monkeys used in this study. From the histology of monkeys 1–3, the recording tracks with oscillations were found to be located mainly in the caudal paramedian lobule. Tracks with oscillations were located between the stereotaxic levels of L4 and L9 in the coronal plane and of P9 and P16 in the sagittal plane. The optimal depth in the cerebellum for finding LFP oscillations was within the last 6 mm of the posterior lobe cortex. The high band-pass filtered signal from the electrode in the four monkeys showed that the electrophysiological activity around the oscillatory foci was made of thin and small spikes with a high frequency of multi-unit activity, indicative of the GCL of the paramedian lobule. These locations and corresponding activity correspond well with the location of previous studies for encountering LFP oscillations in the monkey (Courtemanche and Lamarre 1997; Pellerin and Lamarre 1997). The histology of monkey 4 was not available for this report, but the general location of tracks with reference to the implantation of the chamber was similar to the location listed above for the other monkeys.

Description of the LFP oscillations

One microelectrode positioned clearly in the oscillatory focus would provide sustained 13–25 Hz oscillations as long as the monkey remained immobile. The oscillatory episodes were often comprised of spindles, long episodes of oscillation lasting 2.75 ± 1.46 s during immobile quiet behavior (74 quantified samples). These long episodes could show waxing and waning of the signal, and smaller periods of stable-amplitude oscillations could be made out of long spindles, lasting 592 ± 270 ms (104 quantified samples). For each monkey, an idiosyncratic oscillatory frequency was prevalent during the oscillatory episodes. This is illustrated in Fig. 2, portraying the oscillatory frequency calculated from the autocorrelation period provided by the averaging of 100 samples of 1 s for each

Downloaded from jn.physiology.org on August 20, 2010

monkey. These samples were taken from the period preceding the presentation of the stimulus to the monkey or from periods where the monkey was just sitting quietly in the chair (monkey 2). Overall, the oscillatory frequency was centered around a typical value for each monkey, ranging from 15.9 (monkey 1) to 20.1 Hz (monkey 2), for an average of 18 Hz. Figure 2 also shows that there was some variation of the oscillatory frequency (average SD = 1.3 Hz) for each monkey, but that these frequencies were unimodally distributed around one mean. This idiosyncrasy of the oscillatory frequency was the basis for establishing the filtering boundaries (13–25 Hz) in the further results.

As stated above, location of the microelectrode in the GCL was indicated by multi-unit activity of the very small and thin spikes, with single units extremely difficult to isolate using our type of microelectrode (see also Hartmann and Bower 1998; Morissette and Bower 1996). Nevertheless, characterization of the multi-unit activity was certainly possible, especially in the search for an underlying rhythmicity. This was done by applying autocorrelation to the multi-unit signal coming from the electrode. To compare with the LFP oscillations, the LFP signal was processed by discriminating the amplitude of the LFP according to a certain threshold and marking a unitary event at the top of the ensuing wave maximum. The discriminating threshold was set visually on the computer screen just high enough to avoid the triggering of pulses from low-level activity occurring between oscillatory spindles. In this way, each oscillatory cycle was marked by a pulse replica, much like a spike. The cross-correlation algorithm was applied to verify the synchronization of the multi-unit events with the LFP-related events. The essence of this analysis is presented in Fig. 3 (*top*), showing a 4,000-ms sample of LFP and multi-unit data recorded with one microelectrode located in the GCL of the paramedian lobule of monkey 3. The multi-unit activity is presented in Fig. 3*A* and the LFP signal in Fig. 3*C*; Fig. 3*B* shows the pulse replicas produced by setting the LFP threshold at the level of the horizontal dashed line in Fig. 3*C*. This sample presented a 2,700-ms period of LFP oscillations at the beginning, with the rest being largely nonoscillatory from a movement made by the monkey. The autocorrelation and cross-correlation results of this period are presented in Fig. 3 (*bottom*). The autocorrelation of the multi-unit activity (Autoco A) showed marked rhythmicity at a period around 55 ms (18 Hz). The same goes for the autocorrelation of the pulse replicas generated from the LFPs (Autoco B) at the same period, and with, of course, fewer events than in Autoco A. The exact relation of the multi-unit activity to the LFPs cannot be inferred from only the frequency of rhythmicity; to have a strong grasp of their relation, the cross-correlation needs to establish the synchronization. This is shown in Crossco B-A, which provides evidence for a near-zero lag synchronization between the multi-unit activity and the LFPs. The cross-correlation graph also shows rhythmic peaks at a period near 55 ms. Overall, these results describe a tight relationship between the GCL multi-unit activity and the LFP oscillations coming from the same microelectrode. Another typical observation characterizing the relationship between granule cell multi-unit activity and LFP oscillations is shown in Fig. 3. Indeed, as a rule, we observed that granule cell mean discharge rate was two to three times slower during the periods of LFP oscillations compared with periods without oscillations. This might suggest that some

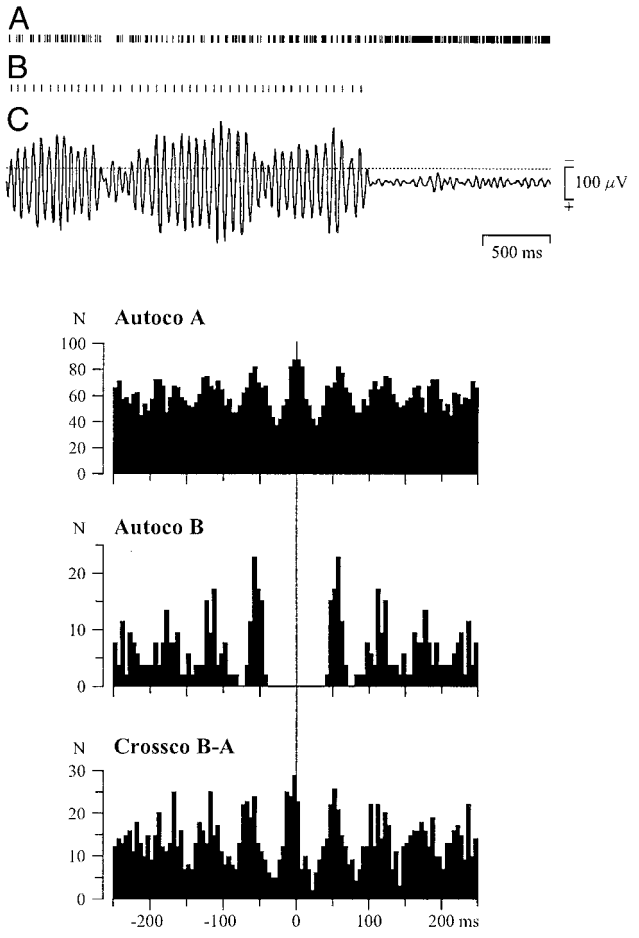

FIG. 3. Relation of LFP oscillations with granule cell layer multi-unit activity. *Top* (*A–C*): neural activity data (total time, 4 s) for 1 trial. *A*: raster plot of multi-unit granule cell layer activity. *B*: pulse replicas generated by the LFP signal reaching the amplitude threshold indicated by the horizontal dotted line in *C*. Threshold was set to capture LFP oscillations during the trial. *C*: band-pass filtered (13–25 Hz) LFP signal recorded from the same microelectrode as multi-unit activity in *A*. *Bottom*: autocorrelations and cross-correlation of signals shown in *top panel*. Autocorrelation of the multi-unit signal in *A* (Autoco A) is shown first, then autocorrelation of the LFP oscillation pulse replicas in *B* (Autoco B), and finally the cross-correlation between *B* and *A* (Crossco B-A). Correlations were calculated on 250-ms windows, which were taken from the period of oscillation on the LFP trace in *C* (0–2,700 ms). Correlations at zero delay are omitted from the computation for both autocorrelations. *Time 0* on the crosscorrelogram abcissa corresponds to the negative peaks of the LFP oscillations (events B).

local inhibitory mechanisms could play a role in the generation of the oscillatory activity.

In monkey 1, it was sometimes possible to record Purkinje cell activity and clear LFP oscillations with the same microelectrode. Simple spikes associated with complex spikes were assumed to be generated by Purkinje cells. The activity of one such cell is shown in Fig. 4. In this case, the simple spike was modulated with the task; first there was a small increase in firing soon after sound onset and then a second, larger increase during movement. The LFP oscillations also showed modulation during this task (Pellerin and Lamarre 1997): the oscillations decreased after sound onset, increased during the delay, and were again strongly reduced during movement. From Fig. 4, it is clear that an increase in simple spike activity corresponds to a decrease in the LFP oscillations. In addition, to

Downloaded from jn.physiology.org on August 20, 2010

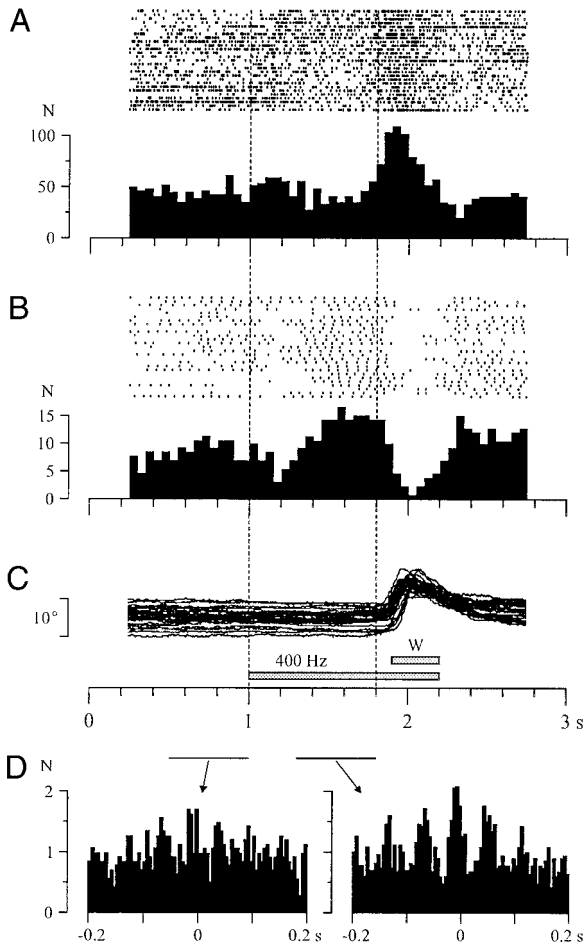

FIG. 4. Relation of LFP oscillations with Purkinje cell simple spike activity, during 1 experiment (30 trials) of the elbow flexion-extension task. *A*: raster plot and histogram of simple spike activity. *B*: raster plot of the LFP-triggered pulse replicas and temporal spectral evolution (TSE) of the LFP activity. *C*: superimposed potentiometer signal for all trials. All traces are aligned on the beginning of the trial. *Left vertical line*, onset of sound; *right vertical line*, mean movement onset. *D, left and right panels*: cross-correlation between simple spikes and the pulse replicas for 500 ms before onset of sound (*left*) and for 500 ms before movement onset (*right*). *Time 0* on the abcissa in *D* corresponds to the occurrence of events B (negative LFP peaks).

determine if Purkinje cell activity is modulated by the LFP oscillations, correlation between the oscillatory activity and the simple spikes was performed in the same manner as for the GCL multi-unit activity. The right inset in Fig. 4*D* shows that simple spike activity is indeed modulated at the LFP frequency during the delay when the oscillations were maximal but poorly modulated, if at all, before the sound when oscillations were not as strong (*left inset*). The central peak in the cross-correlation of Fig. 4*D* (*right*) is off-center by −10 ms, which means that the simple spikes tended to lead the negative peak of the LFP oscillations by 10 ms. The same analysis was performed on 32 Purkinje cells. In 17 cells (53%) there was a clear periodicity, and the mean phase shift was -8.1 ± 5.3 ms. Thus these results show that LFP oscillations can influence the output of the cerebellar cortex. Climbing fiber activity was also recorded in these experiments, particularly in monkey 1, and these results will be detailed in a future publication. However, some observations can be mentioned briefly here concerning instances when both complex spikes and LFP oscillations were recorded with the same microelectrode. As a rule, occurrence of complex spike activity was largely independent of the LFP oscillations and did not modify the amplitude nor the phase of ongoing oscillatory activity. Furthermore, in the paramedian lobule where LFP oscillations were recorded, complex spike activity did not show sustained periodicity in any phase of the behavioral task.

Modulation of the LFP oscillations: active condition

Modulation of the cerebellar LFP 13–25 Hz oscillations with the elbow flexion-extension task is systematic (Pellerin and Lamarre 1997), but to ensure the generality of this pattern, it was interesting to compare with another arm movement task. Hence, the LFP oscillations were recorded in relation to the elbow flexion-extension task and the lever-press task. Even if the monkeys adopted a stereotypical strategy for movement execution, the freedom concerning movement initiation and arm path was greater in the lever-press task than in the elbow flexion-extension task. This represented a good test for the generalization of the movement-related modulation of the LFP oscillations.

The decrease of the LFP oscillations occurs in a systematic stimulus- and movement-related fashion for the elbow flexion-extension task with the ipsilateral hand, but only if the monkey is performing a movement following the signal (Pellerin and Lamarre 1997). A similar modulation was also found for the lever-press task with the ipsilateral (left) hand. The LFP modulation during a series of trials is shown in Fig. 5, displaying the results of a 20-min and 113-trial experiment with monkey 3. In Fig. 5*A*, pulse replicas triggered by an amplitude threshold for the LFPs are presented in the form of a raster plot aligned on stimulus presentation, with the amplitude threshold being adjusted to catch mainly LFP oscillatory cycles, as was done in Fig. 3*C*. The oscillations were better isolated by previously band-pass filtering the LFP signal between 13 and 25 Hz. Thus each LFP oscillation cycle is represented by a raster dot, and each trial corresponds to one line of the raster plot; the 5-s time scale is at the bottom of the figure. During this experiment, the monkey was at first not interested in working to get the reward. This approximately 6-min period (marked on the right with a small b), corresponding to 40 trials, showed that there were oscillations during these trials but without any significant modulation of the pattern of the cycles. However, after approximately 10 min (63 trials, period c), the monkey developed an interest in working to get the reward; the large black dots among the raster represent the time of the lever-press. Juice was delivered instantaneously when the monkey pressed the lever. The raster plot during this period showed some modulation of the amplitude event markers, with a clear reduction of the oscillations around 200–400 ms following the start of the 400-Hz sound, and then an augmentation near the time of the lever-press and another slight reduction after the reward period. Fig. 5, *B* and *C*, corresponds to periods b and c in Fig. 5*A* and shows two types of display of the modulation of the LFP oscillations during the task: the peristimulus time histogram of the oscillation-triggered pulse replicas (black histograms) and the more quantitative TSE (see METHODS). Both these measurements show an identical modulation for each group of trials. Fig. 5*B*, corresponding to period b, when the monkey was less interested, showed no significant

Downloaded from jn.physiology.org on August 20, 2010

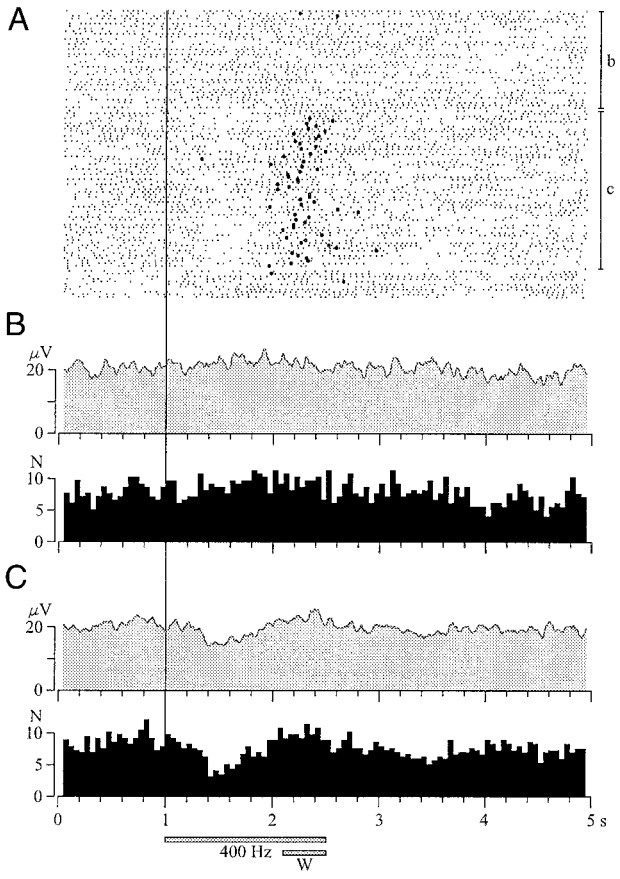

FIG. 5. Modulation of the LFP oscillations, active condition, during the course of 1 experiment, with monkey 3 executing the lever-press task using the left hand. *Bottom*: horizontal bars show the periods of time with sound stimulus (400 Hz) and the reward window (W); vertical line indicates sound stimulus onset. *A*: raster plot of the pulse replicas discriminated from an amplitude threshold based on the LFP signal (band-pass filtered between 13–25 Hz) in the manner shown in Fig. 3. Each trial is represented by 1 raster line. Groups of trials have been separated (periods b and c), based on the monkey's performance. Larger dots represent the time of lever-press onset. *B*: description of the modulation of the LFP oscillations for period b in *A*. *Top*: jagged line representing the average of the rectified LFP signal (TSE) through time. *Bottom*: histogram of the LFP-triggered pulse replicas. *C*: description of the modulation of the LFP oscillations for period c in *A*.

modulation of the LFP oscillations, both in the histogram and in the TSE. This contrasted with the histogram and TSE shown in Fig. 5*C* (period c, monkey at work), which showed clear modulation. Thus both measurements showed a significant decrease of the LFP oscillations (−25% on the TSE), starting about 300–400 ms after the stimulus, followed by a return of the oscillations to the prestimulus level near the lever-press. From the raster plot, the histogram, and the rectified LFP signal, it was clear that the actual performance of the lever-press task was necessary for a modulation of the oscillations to appear. The TSE is used in Figs. 6–10 to describe modulation during a series of trials or experiments. These TSE curves were generally based on 30 or more trials of correct performance by the monkey per experiment. As modulation occurred with task performance, Figs. 6–10 concern only trials where the monkey received a reward (unless otherwise noted); these were the trials with relatively homogeneous timing with respect to the motor response, since the response was occurring within a relatively narrow time window.

Figure 6 summarizes the results in the active condition for the task with the left hand for the three monkeys. Performance and LFP oscillation modulation for monkey 1 is shown on the left side of the figure (Fig. 6, *A–C*); the same for monkey 3 in the middle of the figure (Fig. 6, *D–F*) and also for monkey 4 on the right side of the figure (Fig. 6, *G–I*). For each monkey, the *top* panel shows the filtered LFP signal and movement sensor signal (*A*, potentiometer; *D*, lever switch; *G*, lever strain gauge) during one trial, the *middle* panel shows the TSE and superimposed movement sensor signal for one experiment with a series of trials, and the *bottom* panel shows the TSE for a series of experiments. From this figure, the general aspect of modulation was present in all tasks and could be depicted from the one-trial data; the stimulus-related decrease in the oscillations is present in *A*, *D*, and *G*. Also, the movement-related decrease in oscillations was clearly present in all three monkeys. However, the timing of this movement-related modulation seemed to differ slightly. Comparing Fig. 6, *A* and *D*, the LFP oscillations stop earlier for the elbow flexion-extension task than for the lever-press task; in fact, the oscillations died out before movement initiation in *A*, while the lever had already been pressed in *D* when the oscillations stopped. Fig. 6, *B* and *E*, and also *C* and *F*, shows that this difference in modulation was consistent during a whole experiment or a series of experiments. The TSE clearly peaked prior to movement initiation in the elbow flexion-extension task (*B*), while it seemed to peak right before and nearer to the lever-press (*E*). Since this timing difference could be noticed for a series of trials, the difference in the pattern of modulation must have been task related. The relative freedom of movement that was accorded to the animal in the lever-press task compared with the elbow flexion-extension task must have played a role in this difference.

One element of information was provided by the force signal coming from the strain gauge on the lever. Fig. 6*G* shows the events associated with the timing of the modulation of the oscillations for monkey 4. In this trial, the oscillations did not reappear until contact of the hand on the lever, following the stimulus-related pause; at that time, monkey 4 rested the fingers on the lever and waited for the proper time to fully press the lever to get rewarded. The oscillations reappeared around 150 ms after finger contact, only to decrease again prior to the full press of the lever. This pattern of modulation prior to the actual pressing movement was reminiscent of the modulation for the elbow flexion-extension task, where the oscillations decreased and returned prior to movement initiation. Additionally, a frame by frame analysis of video samples taken during task performance for monkey 3 revealed that the general timing of finger contact to the lever was similar in timing to the data provided by the strain gauge force signal in monkey 4. In essence, monkeys 3 and 4 had similar motor patterns during their task. The TSE shown in Fig. 6*H* also revealed that the return of oscillations is maximal prior to the final lever-press, shown in the superimposed strain gauge signals for each trial. A look at Fig. 6, *C*, *F*, and *I*, provides the most general view of the modulation pattern in the active condition.

For each experiment, statistical analysis of the significance of task-related changes of LFP oscillations was performed as described in METHODS. For the 10 experiments averaged in Fig. 6*C* (monkey 1), a significant decrease of activity soon after stimulus onset was seen in 6 experiments ($X = -31 \pm 15.6\%$)

Downloaded from jn.physiology.org on August 20, 2010

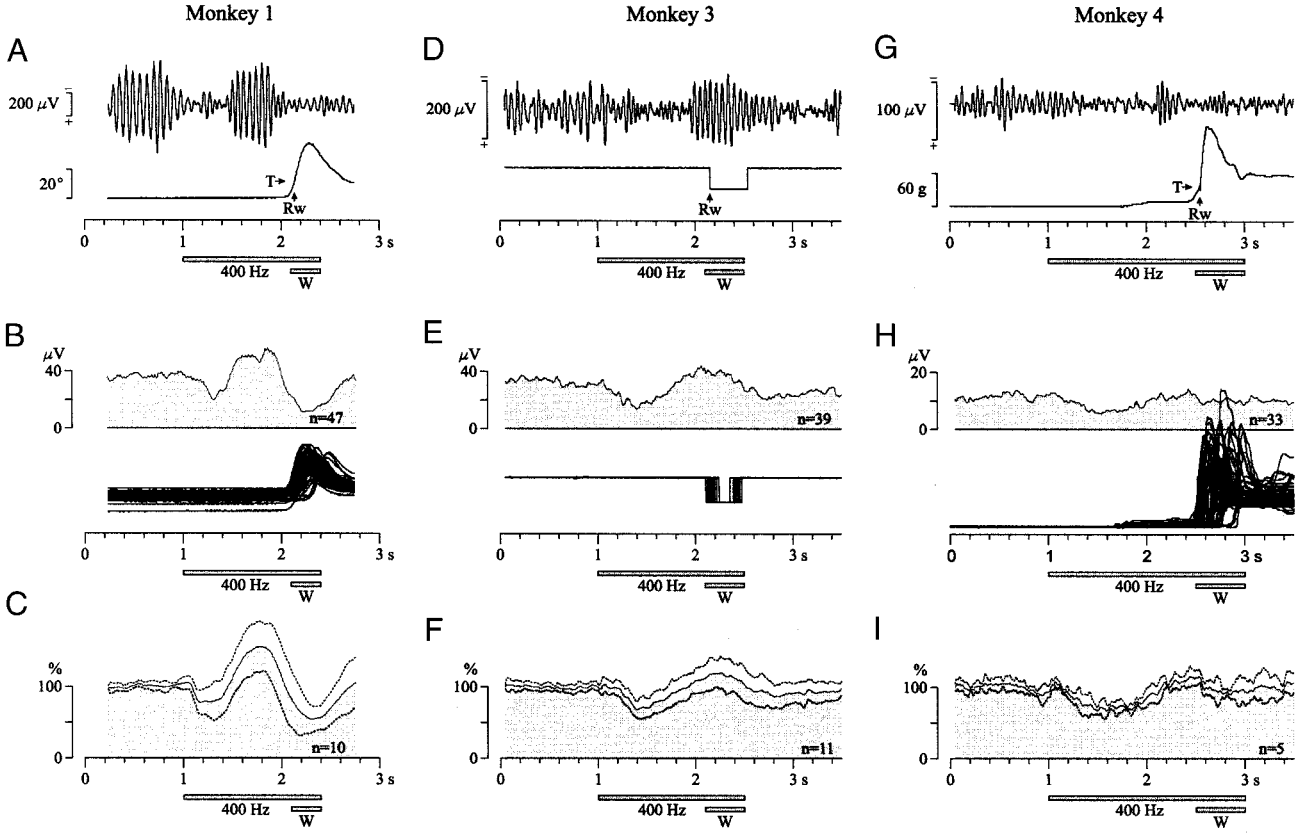

FIG. 6. Modulation of LFP oscillations, active condition, in tasks executed with the left hand, for monkeys 1, 3, and 4. *A*, *D*, and *G*: LFP (band-pass filtered 13–25 Hz) and movement sensor signals during 1 trial. *B*, *E*, and *H*: TSE and superimposed movement sensor signals for 1 experiment. Number of trials is indicated on each panel. *C*, *F*, and *I*: normalized TSE for a series of experiments, with the average ±SD. Each TSE was normalized with respect to the mean signal amplitude in the prestimulus period (100%). Number of experiments is indicated on each panel. Movement sensor signals: *A* and *B*, potentiometer; *D* and *E*, lever contact; *G* and *H*, strain gauge. Sound stimulus and reward window periods are at the bottom of each panel. T, threshold for strain gauge to give reward; Rw, reward time.

while there was no significant change in 4 experiments. Later on in the delay preceding movement, a significant increase occurred in eight experiments ($X = 59 \pm 30.7\%$) while in the other two experiments, the TSE level simply returned to prestimulus activity. A significant decrease was seen in all experiments during movement ($X = -44 \pm 14.9\%$). In the 11 TSE averaged in Fig 6*F* (monkey 3), 8 showed a significant decrease soon after stimulus onset ($X = -25 \pm 9.1\%$) and there was no change in 3. Later on in the delay preceding reward, significant changes were seen in four experiments: two showing an increase ($X = 23 \pm 2.8\%$) and two showing a decrease ($X = -14 \pm 2.1\%$). After the reward, significant changes occurred in seven experiments: increases in five ($X = 18 \pm 5.7\%$) and decreases in two ($X = -23 \pm 2.0\%$). Finally, in the five experiments averaged in Fig. 6*I* (monkey 4), a significant decrease in the first part of the delay was seen in all experiments ($X = -28 \pm 6.4\%$). In the second part of the delay before reward, the activity returned to prestimulus control value in four experiments and remained lower (−23%) in the other experiment. After reward, there was a significant change in only two experiments: one showing an increase of 22% and the other a decrease of 23%. In essence, for all three monkeys, the general pattern of modulation emerging from these results was that the oscillations seemed to be more potent when the monkey was actually immobile waiting for the stimulus and when the monkey was in active expectation to execute the movement enabling reward.

To verify if this pattern of modulation was restricted to performance using only the left (ipsilateral) hand, we had the monkey also perform with the right hand. One experiment where the task was performed with each hand is shown in Fig. 7, where monkey 3 pressed the lever in blocks of trials first with the left hand (*A* and *B*) and then with the right hand (*C* and *D*). The TSE is shown for the times when the monkey was either working properly and getting reward (*A* and *C*) or not working at all (*B* and *D*). A comparison of these groups of trials clearly shows again that actual task performance was necessary for any modulation in the TSE to occur; Fig. 7, *B* and *D* shows no modulation. What was even more interesting was that the modulation was very similar for the left and right hands; both Fig. 7*A* and Fig. 7*C* show a clear transitory decrease prior to lever-press. This indicated that the task-related modulation was not restricted to performance of the lever-press task by the ipsilateral hand; in fact, the performance using the contralateral hand provided at least a similar level of modulation. This pattern of modulation was present for all experiments where both hands were tested. A summary of this left and right hand similarity in terms of modulation is shown in Fig. 8 (*A* and *B*). This summary shows the TSE signal for the 14 experiments where both the left and right hands were tested

Downloaded from jn.physiology.org on August 20, 2010

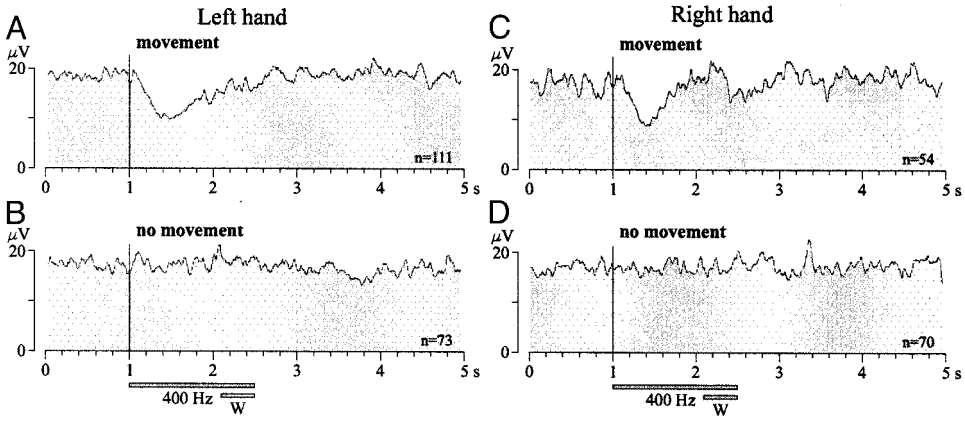

FIG. 7. Comparison between the left and right hand in the active condition, lever-press task: one experiment where both hands were tested for monkey 3. TSE signal (band-pass filtered 13–25 Hz) shown for the trials where the monkey performed the task correctly (movement), or didn't press the lever at all (no movement). *A*, *B*: task executed with the left hand; *C*, *D*: task executed with the right hand. Number of trials indicated on each panel. Sound stimulus and reward window periods at the bottom of *B* and *D*. Vertical line indicates sound stimulus onset.

(*A*: left hand; *B*: right hand, monkey 3). Statistical analysis revealed no difference between the two tasks. This suggested that the modulation of the LFP oscillations was actually hinting at a more general mechanism than strict limb-related afferent information.

Modulation of the LFP oscillations: passive condition

The generality of the modulation of the LFP oscillations for both limbs meant that the modulation could also be extended to even more abstract variables. The oscillations were modulated by the expectancy in a stimulus-response-reward situation; what about a stimulus-reward situation? To test this, the passive condition was introduced to monkeys 3 and 4, with blocks of trials given to the monkey containing a stimulus followed by the same reward, with the same delays as in the active condition (1,100–1,500 ms). In this condition, the oscillations were also clearly modulated during the task. This is shown in Fig. 8, *C* and *D*, which shows the modulation of the TSE for a group of nine experiments in the passive condition for monkey 3. The rewarded trials are shown in Fig. 8*C* and the unrewarded trials are shown in Fig. 8*D*. The TSE was clearly modulated in this condition, with LFP oscillations increasing after stimulus presentation, for the whole stimulus-reward delay, and decreasing after the reward had been given. This showed a tendency of the oscillations to increase when the monkey was actively expecting the reward to be given in the next instant. Another important observation was that the oscillations were clearly increased only to stop after the reward window had expired, even when the reward had not been given (Fig. 8*D*). This was an indication that, as long as the reward was expected to be given, the oscillations were present. But, as the time after the stimulus increased and the reward had not been given, the monkey estimated that reward would not follow and stopped expecting the reward in itself. This translated into a more gradual decrease in the oscillations than when the reward was given (cf. Fig. 8*C* and Fig. 8*D*).

Thus the modulation of the oscillations was strikingly different when the monkey was simply waiting for the expected reward (passive condition) compared with waiting for the correct time to move (active condition). In the passive condition, the TSE, as a rule, did not show any decrease following stimulus onset contrary to the active condition (active, $X = -32 \pm 9.4\%$; passive, $X = 8 \pm 10.8\%$; $P < 0.001$). In the second part of the delay preceding reward, the TSE increased systematically in the passive condition, while it simply tended to return to prestimulus control value in the active condition (active, $X = -15 \pm 15.4\%$; passive, $X = 33 \pm 12.9\%$; $P < 0.001$).

In the passive condition, the observed increase in the oscillations could have been related to the persistence of the stimulus during the whole delay period. The experiments on Fig. 9 show that the persistence of the sound in itself was not necessary for the increase in the oscillations. Figure 9*A* shows an experiment with monkey 3 where the sound stimulus was present throughout the delay until the end of the reward window (W). The pattern of the TSE is similar to Fig. 7*C*, with the oscillations increasing after the stimulus and lasting during the whole delay. Figure 9*B* shows the TSE when sound lasted only 200 ms, while the reward was given at the same delay as before. This variation in the task showed no difference in the TSE, with the sound lasting the whole delay. Figure 9, *C* and *D*, demonstrates another experiment that confirmed the lack of relationship between persistence of sound and increase in oscillations. Figure 9*C* shows the passive condition in monkey 4,

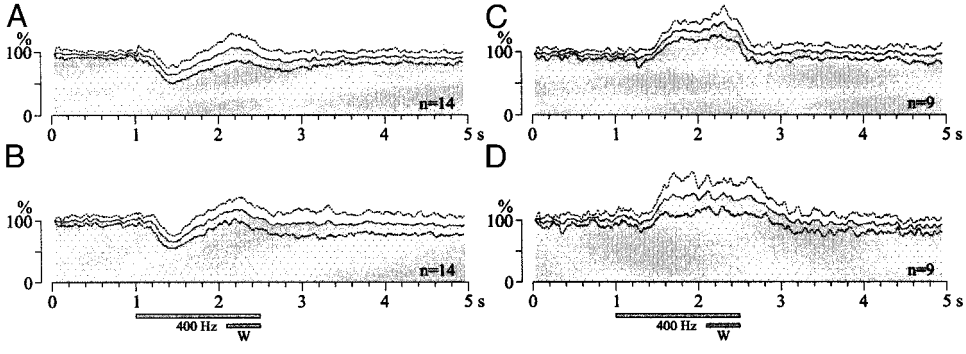

FIG. 8. Modulation of the LFP oscillations in monkey 3 for a group of experiments according to the active (left and right hands) and passive conditions. Normalized TSE is shown for a series of experiments. *A*: active condition, left hand. *B*: active condition, right hand. *C*: passive condition, trials with reward. *D*: passive condition, trials without reward. In *A* and *B*, the 14 experiments compiled were those where both hands were tested. Out of these 14, 9 were also tested for the passive condition and are shown in *C* and *D*. Number of experiments is indicated for each panel.

Downloaded from jn.physiology.org on August 20, 2010

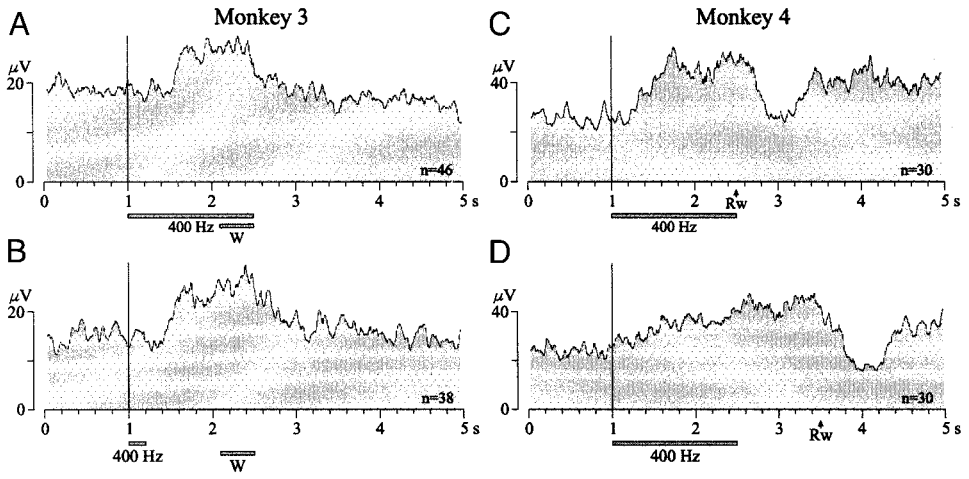

FIG. 9. Modulation of the LFP oscillations with 2 different sound stimuli durations (*A* and *B*: TSE from monkey 3) and different reward delays (*C* and *D*: TSE from monkey 4). In *A* and *B*, the reward window is the same but the sound stimulus lasts 1.5 s (*A*) and 0.2 s (*B*). In *C* and *D*, the sound stimulus duration is the same (1.5 s), but the reward is delivered at the end of the stimulus in *C* and 1 s after the end of the stimulus in *D*. Number of trials is indicated on each panel. Sound stimulus and reward periods are indicated. W, reward window; Rw, time of reward. Vertical line indicates stimulus onset.

with the usual 1,500 ms delay between stimulus onset and reward, displaying again the typical increase of LFP oscillations following presentation of the stimulus, lasting until the end of the delay, and a further increase 600 ms after the reward (Rw). Figure 9*D* shows the TSE when the delay between stimulus onset and reward had been lengthened from 1,500 to 2,500 ms, while the sound still lasted only 1,500 ms. The pattern of the TSE changed in this task variation, with a gradual increase in the oscillations lasting until reward presentation, i.e., 1 s after the end of the sound. These patterns of modulation of the LFP oscillations clearly showed that the modulation in the passive condition was independent of the length of the sound and was really affected by the length of the waiting period to get a reward.

One important aspect to consider with respect to the modulation of the LFP oscillations was the possibility that the modulation seen in the passive condition only occurred in animals trained to wait for the correct time to move. Indeed, the monkey could have been in some way inhibiting a motor response to the stimulus if it had been previously trained to move. One way of testing this was to present the passive condition to a completely naive animal. This was done in monkey 4, which was systematically rewarded at the end of a sound stimulus lasting 1.5 s. The TSE corresponding to two different periods of testing in this condition is shown in Fig. 10. For this set of experiments, each contact made by the monkey on the pipette, most often with the mouth or tongue, was recorded as unitary events, as described in METHODS. A peristimulus time histogram of these contacts made on the pipette is shown at the bottom of Fig. 10, *A* and *B*, in addition to the TSE shown at the top. Figure 10*A* shows the behavior and oscillations corresponding to an early stage in the training (3rd session). The sound stimulus lasted 1,500 ms, with reward given simultaneously with the end of the sound. It is clear from the histogram that contacts on the pipette increased only after reward had been given (around 300 ms after); the number of pipette contacts was the same during the delay as in the prestimulus period. From this we could presume that the monkey had not yet made the relation that a reward would follow the stimulus in a predictable fashion, with no sign of anticipation of the imminent reward. At this stage, the TSE showed no modulation during the delay. In fact, there was some increase in the oscillations, but only 600 ms after the reward had been given (apart from the short-latency evoked response to the reward). Figure 10*B* shows the behavior and oscillations from a later stage of training, when the monkey had presumably made the association between the stimulus and the reward. The stimulus-reward delay had been constant throughout the training regimen. At this stage, the histogram shows a clear increase in pipette contacts during the delay starting around 500 ms after the onset of the sound. This could be interpreted as an anticipation of the reward ≥1 s before its delivery. The corresponding TSE also showed a clear modulation during the delay, starting about 300 ms after sound onset, i.e., about 1.2 s before reward delivery. This modulation was identical to the one observed in monkey 3 in the passive condition. These

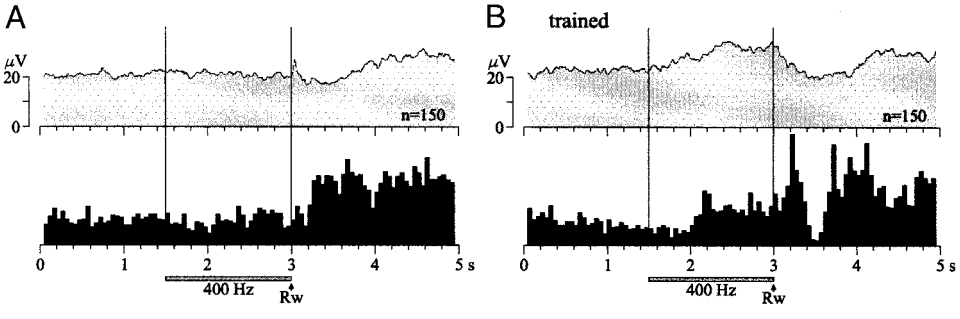

FIG. 10. Modulation of the LFP oscillations, passive condition, in monkey 4 at 2 different stages of learning the association between the sound stimulus and reward. TSE signal (band-pass filtered 13–25 Hz) shown, with the histogram of the signal coming from contact on the juice pipette. The juice pipette had been equipped with a contact sensor that generates unitary events when the monkey touched it. *A*: naive stage, before any exposure to the sound or reward. *B*: after 5 days of exposure to the sound with a stable temporal relation to the reward. Number of trials is indicated for each panel. Sound stimulus period shown; Rw, time of reward.

Downloaded from jn.physiology.org on August 20, 2010

results thus showed a learning-dependent change in the modulation of the TSE. This change in the modulation of the oscillations also gave evidence that the monkey did not need to be previously trained to move for a modulation in the passive condition to occur. Thus the modulation of the oscillations seemed to be related solely with the predictability of the reward delivery after stimulus had been given. This confirmed a relationship between the oscillatory phenomenon and passive expectancy. One interesting aspect here was the fact that pipette contacts with mouth or hand during the delay was not accompanied with a decrease in the oscillations.

DISCUSSION

Our results show an involvement of the cerebellum in both active and passive expectancy. This involvement is exemplified by the episodes of 13–25 Hz oscillations in the GCL of the paramedian lobule during periods of immobility when the monkey was actively waiting for the appropriate time to depress a lever or initiate a flexion of the elbow, or oscillatory episodes seen during the delay when the monkey was passively waiting to receive an expected reward. These oscillations are thus present when the animal is waiting for an event to occur, whether this event is internally or externally regulated. In the active condition, oscillations were systematically modulated during the task performed by either hand. In the passive condition, oscillations were systematically modulated with the administration of reward or the passage of the expected time of reward. These types of modulation suggest that cerebellar cortex oscillations in the paramedian lobule are involved in information processing relevant to an expected outcome.

Putative mechanisms for the genesis of cerebellar LFP oscillations

As shown by examples in Pellerin and Lamarre (1997) and reported in Courtemanche and Lamarre (1997), LFP oscillations around 13–25 Hz in the cerebellar cortex are especially prominent in the paramedian lobule; all of the data presented here comes from sites located in the GCL of the paramedian lobule. The GCL is the input layer for mossy fiber afferents to the cerebellum and is made up of the very small but numerous granule cells, along with the Golgi and Lugaro interneurons, and also the unipolar brush cells. The mechanism for the generation of the cerebellar LFP oscillations could consist of extra-cerebellar sources, intra-cerebellar intrinsic mechanisms, or a combination of both (Courtemanche 1999). One point of reference is that cortical regions like the motor and parietal cortices project to the paramedian lobule (Sasaki 1979) via the pons (Brodal 1978), and that these can exhibit oscillations in the same frequency range (see INTRODUCTION). This observation points to possible cerebro-cerebellar influences on the cerebellar LFPs, and the cerebellar oscillations could be a reflection of mossy fiber input. Alternatively, neuronal elements could in fact readily account for loops that can subserve the LFP oscillations, namely an excitatory-inhibitory feedback (or feedforward) loop involving the granule and Golgi cells (Bell and Dow 1967, Eccles et al. 1967, Llinás 1981). The granule cell-Golgi interaction has been successfully modeled to promote oscillations (Maex and De Schutter 1998), and Golgi cell properties can be favorable to rhythm genesis (Dieudonné 1998). The Lugaro cell is less known but is also thought of as being inhibitory like the Golgi cell (Lainé and Axelrad 1996). Alternatively, the unipolar brush cells (Mugnaini and Floris 1994) could also be involved in the generation of LFP oscillations, forming an excitatory feedback loop to the granule cell (Nunzi and Mugnaini 1999). Indeed, both excitatory and inhibitory feedback loops could subserve rhythmicity in local circuits (Jefferys et al. 1996; Ritz and Sejnowski 1997). Finally, the rhythm in the cerebellar LFPs could stem from both extra- and intra-cerebellar interactions. For example, the input coming from the cerebro-cerebellar or spino-cerebellar connections could strongly influence this circuitry and modulate its entry into an oscillatory mode. The only definitive test would be to inactivate the pontine nuclei, cut the peripheral afferents going to the cerebellum, and see what happens with an oscillatory locus, but these methods fall outside the scope of this paper.

Our current data do point to a progressive decrease of the oscillatory content when the signal stems from elements further away from the mossy input, i.e., oscillations in the LFPs, less obvious in the granule cell firing, and even less obvious in the Purkinje cell firing. Our type of microelectrode and preparation does not permit single granule cell isolation or the definition of mossy fiber terminals versus granule cell soma spikes. However, as shown in Fig. 4, Purkinje cell firing can sometimes be related to the cerebellar LFP oscillations. While these LFP oscillations are poorer in the Purkinje cell layer, there were instances when both oscillations and reliable spike activity from Purkinje cells could be recorded. In these cases, simple spike activity and LFP oscillations often changed in opposite directions over time, e.g., oscillations are stronger during the delay when there is less Purkinje cell firing, and they decrease right before movement, while Purkinje cell firing increases. Also, the phase-locking of the simple spikes with the peak of the LFP wave during periods of robust oscillations is another hint at the possible influence of the GCL rhythm on the output of the cerebellar cortex. Our current understanding of these results is that during the delay, the input-output relations within the cerebellar cortex are more influenced by the oscillatory process, while movement disturbs these relations, quite possibly a result of the barrage of movement-related sensory inputs.

Ipsilateral and contralateral modulation

The modulation of LFP oscillatory activity according to movements made with either limb suggests that the oscillations are involved with some factor other than movement itself. Indeed, when it comes to arm movements, as neural discharge in the cerebellar cortex is generally more related to movement production of the ipsilateral arm (e.g., Brooks 1984), our results are somewhat surprising. The more general nature of this modulation that is present in both limbs could be related to a preparatory mechanism for the imminent release of the movement. The oscillations themselves could participate in evaluating the steady-state of the information coming in the system necessary to establish the proper conditions for the initiation of movement. In this sense, the oscillations would support the activity of other cerebellar elements involved in movement initiation (Chapman et al. 1986; Lamarre and Jacks 1978; Meyer-Lohmann et al. 1977). The more general aspect of this information processing would probably be related to surveying

Downloaded from jn.physiology.org on August 20, 2010

a more extended region of the body for the proper states to perform an optimal movement initiation, since gross receptive fields displayed by evoked potentials in the paramedian lobule often encompass ipsilateral and contralateral limbs (Snider and Stowell 1944).

Modulation during nonmotor behavior

There is, however, an even more general manifestation revealed by the modulation of LFP oscillations, as was shown by the results in the passive condition. The oscillations are more prevalent when the monkey is waiting for the expected reward than when waiting for the correct time to move. As the stimulus is paired with the reward at a fixed interval, the oscillations get more potent during the interval leading from the stimulus to the reward and weaken after the reward administration or after the delay to usually get the reward as elapsed (see Fig. 8). This type of modulation is different from during the active condition but nonetheless is very robust. This type of modulation seems tightly related to expectancy, and would seem to entail an analysis of the incoming information to subserve a "steady-state", checking for an entry into the system. This information could again be somatosensory, but this is impossible to infer with certainty from our results. However, as the monkey is expecting the reward to come, there is a continuous probing of the system to evaluate a change of environmental status, to check the arrival of the reward. The paramedian lobule might then be part of a greater system evaluating the expectancy of an incoming input, particularly in the temporal domain.

Functional role of the cerebellar LFP oscillations

The modulation of LFP oscillations in the cerebellum is tightly related to expectancy in both conditions, with each showing potent oscillations during the poststimulus onset waiting period; in the active condition, the waiting period is ended by the internal "movement trigger" of the monkey, and in the passive condition, the waiting period is ended by the calculated delay that the monkey is observing in expecting the reward. The exact nature of this expectancy modulation is still speculative, as more testing will be necessary to dissect the sensory, motor, or cognitive aspects warranting the presence of LFP oscillations in the cerebellar cortex. Current propositions in light of the task performed by our monkeys could include, in the "sensorimotor" realm, some support to sensory acquisition for evaluating an internal steady-state, in preparation for future incoming inputs (Bower 1997a,b; Hartmann and Bower 1998). This steady-state could be the proper baseline operation for accurately portraying inputs from the periphery or from the cortex. LFP oscillations in the GCL of the paramedian lobule could segment the pattern of sensory inputs into predictable values for regular chunks of time, by rhythmic cycles of excitation and inhibition. Support of sensory processing is an important aspect of cerebellar function in species where the precise determination of anticipated events is crucial for survival, such as in the electric fish, where cerebellum-like structures play a determining role in the quantitative determination of an efference copy to permit differentiation from regular sensory input (Bell et al. 1997). The cerebellum could possibly contribute to cognitive aspects of the task (Schmahmann 1997); within this realm, cerebellar LFP oscillations could support timing functions (Braitenberg 1967; Ivry and Keele 1989; Jueptner et al. 1995), with oscillatory cycles acting as a discrete unit. Another timing mechanism might be the rhythmic activity of the climbing fibers originating from the inferior olive (Lang et al. 1999; Pellerin et al. 1997), which could act as a clock, though the clock hypothesis has been disputed (Keating and Thach 1995). In our task, however, climbing fiber activity seemed unrelated to the LFP oscillations. An even more general mental "set" function like the set-related activity in the premotor cortex (Weinrich and Wise 1982) could be postulated: in the present task, the increase of the TSE during the delay in the passive condition could signal a steady-state of expectancy mediated by the characteristic 13–25 Hz LFP oscillations. As all these propositions remain to be tested, a more global view of the expectancy phenomenon we observe, which somewhat comprises both the sensorimotor and cognitive aspects, consists of how the cerebellum could support prediction and preparation (Courchesne and Allen 1997). In both the active and passive conditions, whether this prediction and preparation are implemented in a movement context within the cerebellum (Thach 1996) remains to be determined.

Nevertheless, the present experiments do support a role for the oscillations in both motor and nonmotor situations, possibly aiding in the processing by other structures that are involved in the proper timing of motor actions and of simple expectancy. This role is in some ways similar and complementary to the types of modulation of oscillations in other areas involved in motor control (MacKay 1997), with the oscillations being mostly related to movement preparation, although motor cortex LFPs can in some cases be related more closely with the peripheral activity (Baker et al. 1997; Farmer 1998). The cerebellar LFP oscillations in the paramedian lobule do compare favorably with those from the parietal cortex (MacKay and Mendonça 1995; Rougeul et al. 1979), a brain region concerned with more abstract elements of the motor output. In fact, the modulation of oscillations during both active and passive conditions hints at a more general expectancy mechanism than only for the generation of movement.

The authors thank M.-T. Parent for excellent work with the monkeys and data analysis, C. Valiquette and G. Richard for technical assistance, and T. Drew and A. Smith for technical help and discussions.

This work was supported by a Group Grant from the Canadian Institutes of Health Research and by grants from the Fonds pour la Formation de Chercheurs et d'Aide à la Recherche (FCAR, Quebec) and National Alliance for Autism Research (NAAR, USA) to Y. Lamarre; R. Courtmanche received support from the National Sciences and Engineering Research Council of Canada (NSERC; Canada) and Fonds de la Recherche en Santé du Québec–FCAR-Santé (Quebec).

Present address of R. Courtmanche: E25-618, Dept. of Brain and Cognitive Sciences, Massachusetts Institute of Technology, Cambridge, MA 02139 (E-mail: rcourt@mit.edu).

REFERENCES

BAKER SN, OLIVIER E, AND LEMON RN. Coherent oscillations in monkey motor cortex and hand muscle EMG show task-dependent modulation. *J Physiol (Lond)* 501: 225–241, 1997.

BELL CC, BODZNICK D, MONTGOMERY JC, AND BASTIAN J. The generation and subtraction of sensory expectations within cerebellum-like structures. *Brain Behav Evol* 50: 17–31, 1997.

BELL CC AND DOW RS. Cerebellar circuitry. *Neurosci Res Prog Bull* 5: 121–222, 1967.

Downloaded from jn.physiology.org on August 20, 2010

BOWER JM. Control of sensory data acquisition. In: *The Cerebellum and Cognition-International Review of Neurobiology*, edited by Schmahmann JD. San Diego: Academic, 1997a, vol. 41, p. 489–513.

BOWER JM. Is the cerebellum sensory for motor's sake, or motor for sensory's sake: the view from the whiskers of a rat? In: *Progress in Brain Research. The Cerebellum: From Structure to Function*, edited by de Zeeuw CI, Strata P, and Voogd J. Amsterdam: Elsevier Science, 1997b, p. 463–496.

BRAITENBERG V. Is the cerebellar cortex a biological clock in the millisecond range? *Prog Brain Res* 25: 334–346, 1967.

BRODAL P. The corticopontine projection in the rhesus monkey. Origin and principles of organization. *Brain* 101: 251–283, 1978.

BROOKS VB. Cerebellar functions in motor control. *Hum Neurobiol* 2: 251–260, 1984.

BULLOCK TH. Signals and signs in the nervous system: the dynamic anatomy of electrical activity is probably information-rich. *Proc Natl Acad Sci USA* 94: 1–6, 1997.

CHAPMAN CE, SPIDALIERI G, AND LAMARRE Y. Activity of dentate neurons during arm movements triggered by visual, auditory, and somesthetic stimuli in the monkey. *J Neurophysiol* 55: 203–226, 1986.

COURCHESNE E AND ALLEN G. Prediction and preparation, fundamental functions of the cerebellum. *Learn Memory* 4: 1–35, 1997.

COURTEMANCHE R. *Oscillations Locales Dans le Cervelet: Organisation, Modulation et Synchronisation Avec le Cortex Cérébral Lors du Mouvement* (PhD Thesis). Montreal, Canada: Université de Montréal, 1999.

COURTEMANCHE R AND LAMARRE Y. Localization of cerebellar oscillatory activity of the awake monkey and relation with cortical rhythms. *Soc Neurosci Abstr* 23: 1286, 1997.

COURTEMANCHE R, PARENT MT, AND LAMARRE Y. Cerebro-cerebellar and intracerebellar synchronization of local field potential oscillations in the monkey performing a behavioral task. *Soc Neurosci Abstr* 25: 373, 1999.

DIEUDONNÉ S. Submillisecond kinetics and low efficacy of parallel fibre-Golgi cell synaptic currents in the rat cerebellum. *J Physiol (Lond)* 510: 845–866, 1998.

ECCLES JC, ITO M, AND SZENTÁGOTHAI J. *The Cerebellum as a Neuronal Machine.* New York: Spinger-Verlag, 1967.

FARMER SF. Rhythmicity, synchronization and binding in human and primate motor systems. *J Physiol (Lond)* 509: 3–14, 1998.

FREEMAN WJ AND SKARDA C. A. Spatial EEG patterns, non-linear dynamics and perception: the Neo-Sherringtonian view. *Brain Res Rev* 10: 147–175, 1985.

HARTMANN MJ AND BOWER JM. Oscillatory activity in the cerebellar hemispheres of unrestrained rats. *J Neurophysiol* 80: 1598–1604, 1998.

IVRY RB AND KEELE SW. Timing functions of the cerebellum. *J Cogn Neurosci* 1: 136–152, 1989.

JEFFERYS JGR, TRAUB RD, AND WHITTINGTON MA. Neural networks for induced "40 Hz" rhythms. *Trends Neurosci* 19: 202–208, 1996.

JUEPTNER M, RIJNTJES M, WEILLER C, FAISS JH, TIMMANN D, MUELLER SP, AND DIENER HC. Localization of a cerebellar timing process using PET. *Neurology* 45: 1540–1545, 1995.

KEATING JG AND THACH WT. Nonclock behavior of inferior olive neurons: interspike interval of Purkinje cell complex spike discharge in the awake behaving monkey is random. *J Neurophysiol* 73: 1329–1340, 1995.

LAINÉ J AND AXELRAD H. Morphology of the Golgi-impregnated Lugaro cell in the rat cerebellar cortex: a reappraisal with a description of its axon. *J Comp Neurol* 375: 618–640, 1996.

LAMARRE Y AND JACKS B. Involvement of the cerebellum in the initiation of fast ballistic movement in the monkey. In: *Contemporary Clinical Neurophysiology*, edited by Cobb WA and Van Duijn H. Amsterdam: Elsevier, 1978, p. 441–447.

LAMARRE Y, JOFFROY AJ, FILION M, AND BOUCHOUX R. A stereotaxic method for repeated sessions of central unit recording in the paralyzed or moving animal. *Rev Can Biol* 29: 371–376, 1970.

LANG EJ, SUGIHARA I, WELSH JP, AND LLINÁS R. Patterns of spontaneous Purkinje cell complex spike activity in the awake rat. *J Neurosci* 19: 2728–2739, 1999.

LLINÁS RR. Electrophysiology of the cerebellar networks. In: *Handbook of Physiology—The Nervous System II*, edited by Brookhart JM and Mountcastle VB. Bethesda, MD: American Physiological Society, 1981, p. 831–876.

MACKAY WA. Synchronized neuronal oscillations and their role in motor processes. *Trends Cogn Sci* 1: 176–183, 1997.

MACKAY WA AND MENDONÇA AJ. Field potential oscillatory bursts in parietal cortex before and during reach. *Brain Res* 704: 167–174, 1995.

MAEX R AND DE SCHUTTER E. Synchronization of Golgi and granule cell firing in a detailed network model of the cerebellar granule cell layer. *J Neurophysiol* 80: 2521–2537, 1998.

MARPLE-HORVAT DE AND STEIN JF. Cerebellar neuronal activity related to arm movements in trained rhesus monkeys. *J Physiol (Lond)* 394: 351–366, 1987.

MEYER-LOHMANN J, HORE J, AND BROOKS VB. Cerebellar participation in generation of prompt arm movements. *J Neurophysiol* 40: 1038–1050, 1977.

MORISSETTE J AND BOWER JM. Contribution of somatosensory cortex to responses in the rat cerebellar granule cell layer following peripheral tactile stimulation. *Exp Brain Res* 109: 240–250, 1996.

MUGNAINI E AND FLORIS A. The unipolar brush cell: a neglected neuron of the mammalian cerebellar cortex. *J Comp Neurol* 339: 174–180, 1994.

MURTHY V AND FETZ EE. Coherent 25- to 35-Hz. oscillations in the sensorimotor cortex of awake behaving monkeys. *Proc Natl Acad Sci USA* 89: 5670–5674, 1992.

MURTHY V AND FETZ EE. Oscillatory activity in sensorimotor cortex of awake monkeys: synchronization of local field potentials and relation to behavior. *J Neurophysiol* 76: 3949–3967, 1996.

NUNZI M-G AND MUGNAINI E. UBCs axons form a sizeable portion of the mossy fibers in the vestibulocerebellum. *Soc Neurosci Abstr* 25: 1403, 1999.

PELLERIN J-P AND LAMARRE Y. Local field potential oscillations in primate cerebellar cortex during voluntary movement. *J Neurophysiol* 78: 3502–3507, 1997.

PELLERIN J-P, PARENT M-T, VALIQUETTE C, AND LAMARRE Y. Rhythmic climbing fiber responses in the cerebellum of the awake behaving monkey. *Soc Neurosci Abstr* 23: 1286, 1997.

RITZ R AND SEJNOWSKI TJ. Synchronous oscillatory activity in sensory systems: new vistas on mechanisms. *Curr Opin Neurobiol* 7: 536–546, 1997.

ROUGEUL A, BOUYER JJ, DEDET L, AND DEBRAY O. Fast somato-parietal rhythms during combined focal attention and immobility in baboon and squirrel monkey. *Electroenceph Clin Neurophysiol* 46: 310–319, 1979.

SALMELIN R AND HARI R. Spatiotemporal characteristics of sensorimotor neuromagnetic rhythms related to thumb movement. *Neuroscience* 60: 537–550, 1994.

SANES JN AND DONOGHUE JP. Oscillations in local field potentials of the primate motor cortex during voluntary movement. *Proc Natl Acad Sci USA* 90: 4470–4474, 1993.

SASAKI K. Cerebro-cerebellar interconnections in cats and monkeys. In: *Cerebro-Cerebellar Interactions*, edited by Massion J and Sasaki K. Amsterdam: Elsevier/North-Holland Biomedical Press, 1979, p. 105–124.

SCHMAHMANN JD. *The Cerebellum and Cognition—International Review of Neurobiology*, vol. 41. San Diego: Academic, 1997.

SNIDER RS AND STOWELL A. Receiving areas of the tactile, auditory, and visual systems in the cerebellum. *J Neurophysiol* 7: 331–357, 1944.

THACH WT. On the specific role of the cerebellum in motor learning and cognition: clues from PET activation and lesion studies in man. *Behav Brain Sci* 19: 411–431, 1996.

WEINRICH M AND WISE SP. The premotor cortex of the monkey. *J Neurosci* 2: 1329–1345, 1982.

WELSH JP, LANG EJ, SUGIHARA I, AND LLINÁS R. Dynamic organization of motor control within the olivocerebellar system. *Nature* 374: 453–457, 1995.

Downloaded from jn.physiology.org on August 20, 2010