No Clock Signal in the Discharge of Neurons in the Deep Cerebellar Nuclei

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Keating, J. G. and W. T. Thach. No clock signal in the discharge of neurons in the deep cerebellar nuclei. J. Neurophysiol. 77: 2232–2234, 1997. We examined the spike activity of deep cerebellar nuclear cells recorded from awake, behaving monkeys to determine if there was a tendency for periodic discharge at or near 10 Hz. Data were obtained from four Rhesus monkeys trained to perform either targeted flexions and extensions of the wrist in relation to a visual cue (2 monkeys) or instrumented digit movements and natural reaches (2 monkeys). We determined the interspike intervals of 274 isolated cells. We looked for periodicity by autocorrelating the interval data and Fourier transforming the resulting autocorrelation function. The autocorrelograms and the Fourier transforms failed to reveal periodicity at or near 10 Hz for any cell. This lack of oscillatory discharge in deep nuclear cells of the cerebellum is consistent with our previously reported results that the complex spike of the Purkinje cell is aperiodic. Our failure to observe a clocklike timing signal in awake, behaving animals in either the Purkinje cell complex spike or the deep nuclear cell discharge argues against a popular idea that the inferior olive may act through the cerebellum as a motor clock.

INTRODUCTION

What the inferior olive contributes to the cerebellum is controversial. One idea is that cerebellar coordination of movement is timed by the oscillation of populations of inferior olivary cells (Welsh and Llinas 1993; Welsh et al. 1995). The proposal is that inferior olivary neurons fire during the depolarizing phase of an underlying membrane oscillation (Llinas and Yarom 1986) “on the beat” of a 10-Hz clock. We previously examined Purkinje cell complex spike activity in awake, behaving monkeys and found no tendency for periodic discharge (Keating and Thach 1995).

It is conceivable that in awake animals a tendency for 10-Hz periodicity in inferior olivary cells is too weak to be seen in single inferior olive or Purkinje cells. Purkinje cells project to the deep nuclei of the cerebellum, with an average of 860 Purkinje cells (cats, Palkovits et al. 1977; similar or greater in macaques, Chan-Palay 1977) converging on a single deep nuclear cell. One might expect a synchronous periodic signal to be enhanced in the discharge of the deep nuclear cells. We therefore have examined the discharge of these cells for evidence of periodicity.

METHODS

Data from four Rhesus monkeys were examined. Two of the four (Ba and Y) (Thach et al. 1992) were trained to track a visual target by flexing or extending their right wrist. Initially, they held the wrist position within a target window. The window then moved at an unpredictable time to a different position, and the monkeys made a ballistic wrist movement (“jump”) to the window (Thach et al. 1992). Isolated single unit discharge data were obtained from cells in the right fastigial (13 cells), interposed (31 cells), and dentate (45 cells) nuclei of the cerebellum during the hold and movement time of these tasks. In these two monkeys, spike data were recorded only during the trial periods. In our previous paper (Keating and Thach 1995), data for 2/3 monkeys were obtained in the same way. There we calculated interspike intervals for each trial and then concatenated these data for autocorrelation analysis. It has been pointed out to us that this method of analysis may obscure a weak oscillatory signal, because each data gap and concatenation introduces a small amount of randomness in the interspike interval sequence. Here we autocorrelated the interspike interval data (1-ms bins) and then summed the autocorrelation functions. Summation avoids the small amount of randomness that may be introduced by concatenation and the data gaps. The resulting summed autocorrelation functions were then Fourier transformed to reveal the spectral frequency of the discharge. (Autocorrelations and Fourier transforms were performed with Spike2 Data Analysis Software from Cambridge Electronic Design.)

For the other two monkeys (Be and E) (Goodkin and Thach 1993), we analyzed nuclear cell discharge that was recorded continuously across trials of several tasks and the waiting intervals in between. In the first task, the animals held their hand around a pistol-like grip and were required to follow a visual cue to flex either thumb or index or both simultaneously to close switches. In the second task, the animals performed a natural reach to pick bits of food off a pin. Isolated single unit discharge data were obtained from cells in the right interposed (37 cells) and dentate (190 cells) nuclei recorded from awake, behaving monkeys to determine the depolarizing phase of an underlying membrane oscillation (Llinas and Yarom 1986) “on the beat” of a 10-Hz clock. We previously examined Purkinje cell complex spike activity in awake, behaving monkeys and found no tendency for periodic discharge (Keating and Thach 1995).

It is conceivable that in awake animals a tendency for 10-Hz periodicity in inferior olivary cells is too weak to be seen in single inferior olive or Purkinje cells. Purkinje cells project to the deep nuclei of the cerebellum, with an average of 860 Purkinje cells (cats, Palkovits et al. 1977; similar or greater in macaques, Chan-Palay 1977) converging on a single deep nuclear cell. One might expect a synchronous periodic signal to be enhanced in the discharge of the deep nuclear cells. We therefore have examined the discharge of these cells for evidence of periodicity.

RESULTS

We examined the timing of spike data taken from 274 units in the four monkeys. The results for units from monkeys Ba and Y are shown in Fig. 1 (according to the nucleus in which they were located) (Thach et al. 1992). In all the figures, we have plotted the maximum power seen for any unit (top) and the average power for all units (bottom). There was no tendency for the spikes to occur at any particular frequency near 10 Hz, as can be seen by the absence of any peaks. There was some lower frequency activity near 2 Hz. This was most prominent for cells in the dentate nucleus (Figs. 1A and 3A). A peak near 2 Hz was also seen for cells in the fastigial and interposed nuclei (Fig. 1B and C). A signal near 2 Hz (Fig. 2A) also was seen in the wrist movement during the performance of the jump task (Fig. 2B).

Nor did the deep nuclear cells in monkeys Be and E...
FIG. 1. Spectral frequency plots of data from monkeys Ba and Y. Top: maximum power found for any cell in group. Bottom: average frequency seen across all cells in group. A: spectral frequency plots for cells in dentate nucleus of monkeys Ba (8 units) and Y (37 units). B: cells in interpositus nucleus of monkeys Ba (11 units) and Y (20 units). C: cells found in fastigius nucleus of monkey Y (13 units).

FIG. 2. A: spectral frequency of average position trace (shown in B) for behavior of monkeys Ba and Y. B: average wrist position vs. time for 32 trials of a targeted ballistic wrist extension movement. Flexor wrist positions are plotted as positive values. Instruction to move was given at time 0. Monkey made movements from a initial hold position of 40° flexed to 25° extended (—25° on plot).

We have discussed elsewhere the inferior olive motor clock hypothesis (Kane and Thach 1989; Keating and Thach 1995). Tremor of the palate often is accompanied by a degenerative hypertrophy of the inferior olive (Gautier and Blackwood 1961). This led to the assumption that the diseased olive was the generator of the tremor, which in turn led to the use of harmaline as a tool to generate tremor from the olive. We previously concluded that harmaline tremor and palatal tremor probably involve different generators mechanisms (Kane and Thach 1989). We have shown that the Purkinje cell complex spike (the result of olivary discharge) does not show preferential discharge at 10 Hz or any other frequency (≤100 Hz) in the awake, behaving monkey (Keating and Thach 1995). The interspike interval of the complex spike was of random duration.

In our previous report (Keating and Thach 1995), complex spike data were collected continuously in one monkey and discontinuously in two. Because of the gaps in the data stream, the analysis could have missed a weak oscillatory signal in those two monkeys. Nevertheless, the data from the third animal were recorded continuously (for some cells, >1 h). There was no periodicity seen in this animal’s data, and the process was unencumbered by the above criticism. Furthermore, there was no evidence of complex spikes time-aligned specifically on the onset of movement nor of...
complex spikes time-locked to other complex spikes occurring around the start of movement (the critical period for ‘‘clocking’’ hypotheses). These results were valid for all three animals, independently of whether the data were collected as blocked trials or continuously.

It is conceivable that an apparent absence of periodic discharge of the complex spike in single Purkinje cells is because the tendency is weak in any one cell. It is further conceivable that the weak signal is amplified through the convergence of Purkinje cells onto the nuclear cells. To address this possibility, we examined the unit discharge of the deep cerebellar nuclei. Because the deep nuclei are the only output pathway from the cerebellum, any signal arising from the inferior olive or the Purkinje cells must go through the deep nuclei to affect movement. In our examination of deep nuclear cell discharge, not one cell showed a periodic signal at or near 10 Hz signal.

We have looked for periodicity in cerebellar neural discharge in seven different monkeys and have failed to detect any periodicity except in the frequency range where it also is seen in movement (position) records. The correlation of both Purkinje cell discharge and deep nuclear cell discharge with movement is well established (Thach 1968). Periodic discharge during periodic movement is not in itself evidence that the olive acts as a ‘‘motor clock’’ (e.g., Welsh et al. 1995).

Our data do not address the more recent addition to the clock hypothesis of a tendency across inferior olive and Purkinje cells for synchronized discharge. However, the absence of periodic discharge in any one cell argues against oscillation within the inferior olivary nuclei as being a general determinant of normal movement.

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