Does the Cerebellum Provide a Common Computation for Diverse Tasks?

A Timing Hypothesis[a]

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OVERVIEW

The cerebellum provides a temporal computation for a number of tasks. We have found that the accuracy in timing motor responses is correlated across different motor effectors. Moreover, perceptual acuity in judging durations of auditory intervals is correlated with motoric measures of timing. These results suggest a common process underlying timing of different sorts, and that this process may depend on a specific neural system. Our data indicate that damage to the cerebellum impairs motor and perceptual timing. Patients with cerebellar lesions are also impaired at judging the velocity of a moving visual stimulus, a process that would appear to require precise timing. Furthermore, the lateral cerebellum has been implicated in classical "eyeblink" conditioning of the rabbit's nictitating membrane response. Because classical conditioning of discrete, adaptive responses is precisely timed, we argue that the cerebellum is the conditioning site for this response because of the need for temporal computation. Classical conditioning of responses such as of heart rate, which is not so precisely timed, does not depend on the cerebellum. The cerebellar influence on locomotion may also be one of providing temporal information. Clumsy children appear as a group to have poor timing, not only on motor production but on perception as well, as would be expected if a general computation is impaired. Because of the importance of the discovery of a cerebellar role in classical conditioning, we begin our argument with respect to classical conditioning.

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INTRODUCTION

A notable discovery of recent years is that some forms of classical conditioning are localized to the cerebellum. Thompson and his colleagues (see Woodruff-Pak, Logan & Thompson, this volume, and Thompson, 1986, for reviews; also Glickstein, Yeo & Stein, 1986) and Yeo, Hardiman, and Glickstein (1985a,b,c) have studied conditioning of the nictitating membrane in rabbits. Cerebellar lesions eliminate the learned, conditioned responses of the membrane to light and tone stimuli while leaving intact the unconditioned response to mild shock or air puffs. Therefore, even after damage to the cerebellum, rabbits still blink in response to shock or to a jet of air blown at their eyes, but they no longer blink in response to a light or a tone that had been paired with the shock or airpuff; that is, the conditioned response is abolished.

The critical site of this conditioning remains a point of debate. While some studies have found that lesions restricted to the cerebellar cortex may impair but not abolish learning (McCormick & Thompson, 1984; Woodruff-Pak, Lavond & Thompson, 1985; Lavond, Steinmetz, Yokaitis & Thompson, 1987) other evidence (Yeo *et al.*, 1985b,c; Moore & Berthier, 1986) and theoretical models (Albus, 1971; Marr, 1969) favor a cortical focus as the site of learning. Regardless of the outcome of this debate, the important point agreed upon by all researchers is that some aspect of cerebellar function is required for nictitating membrane conditioning.

Not all classical conditioning occurs in the cerebellum. Lavond, Lincoln, McCormick, and Thompson (1984) found no effect of cerebellar lesions on the conditioning of heart deceleration responses to a face-shock stimulus. In contrast, conditioning of the nictitating membrane to an airpuff was abolished in the same lesioned animals. The question arises why some conditioned responses involve the cerebellum while others do not. Lavond *et al.* (1984) hypothesized a critical difference in the two response types. The nictitating membrane response is discrete in character and specific in that it serves an adaptive function of protection when it precedes a noxious stimulus such as an airpuff. The heart rate change is less discrete and more nonspecific in that it does not have an explicit instrumental function particular to the aversive stimulus.

In this paper we will present one hypothesis concerning why the cerebellum is essential for certain types of classical conditioning. Specifically, we will argue that the cerebellum provides a critical computation of timing needed in discrete forms of classical conditioning and that this same timing capability is involved in the performance of a variety of tasks. To be effective, a conditioned response such as the nictitating membrane response must occur at just the right time. By our hypothesis, the reason that such responses make use of the cerebellum is because the cerebellum provides the necessary temporal computation.

We will first describe work from our laboratory that used tasks very different from classical conditioning and that have led to the view of the cerebellum as a temporal computer. Then we will remind the reader of some past research on classical conditioning regarding temporal relationships. The precise temporal character of conditioning makes it plausible that a device that computes time is, indeed, a necessary part of the conditioning task. We will then briefly raise the possibility that two other phenomena, locomotion and efference copy, also make use of the

cerebellum because this neural structure supplies a temporal computation. At the end, we will describe some provocative research suggesting that precision of timing is a key element of coordination in children.

THE CEREBELLUM AND THE COMPUTATION OF TIME

At least since the ideas of Gall in the early 19th century (cited in Changeux, 1985), suggestions have abounded that mental functions can be localized to discrete brain regions. A difficulty for such hypotheses has been to attain the right grain of analysis for what is meant by "mental functions." Modern cognitive psychology has taught us that functions that seem quite simple often are complicated and involve many elementary operations. Recently Posner, Petersen, Fox, and Raichle (1988) and Kosslyn (1988) have argued that the correct grain of analysis involves indivisible elementary operations of cognition. Posner has had notable success in parsing spatial attention into elementary components, such as engaging, disengaging, and moving attention, and he has implicated different brain structures for each operation. Likewise, Kosslyn has shown that imagery has a number of separable components, and he has demonstrated that certain components are lateralized.

Some elementary operations, or what are now more frequently called "computations," may be quite specific and designed for a particular class of tasks. Other computations, however, might be more general in purpose and at the service of many different tasks. Rozin (1976) argued some years ago that a mark of human intelligence is the liberation of computations from the task in which they originally evolved, making the computation available to other tasks. He argued, for example, that reading makes use of some of the same computations as are used in speech.

In our work we have raised the issue of whether timing is a general computation in which the same system can be called upon by a variety of tasks. That is, many tasks need precise timing—rhythmic movements of the fingers, arms, or feet, judgments of the durations of brief tones, comparisons of the velocities of moving objects, and the like. Is it possible that such different tasks use a common neural system for their temporal computation?

Our initial studies on the issue of a common computer for time made use of correlations of individual differences on different tasks. Other work by Wing and Kristofferson (1973, see also Wing, 1980) provided a theoretical case for a central timing mechanism. In our later studies using both the Wing and Kristofferson analysis and our own tasks, we were able to localize timing in either the cerebellum or the cerebellum and closely related structures.

Correlational Studies

If it is the case that a common system computes time across different motor effectors and across diverse tasks, then one might expect individual differences to correlate across the tasks. To rule out very general factors that could account for the correlations, it is important to have control tasks similar to those requiring the timing operation but without the requirement of temporal precision. The control tasks

should not correlate with those requiring timing. In a first test of these ideas (Keele, Pokorny, Corcos & Ivry, 1985), human subjects produced extensive series of timed taps. First, a pacing tone was presented that repeated every 400 msec. Subjects synchronized their responses with the tones by tapping with either a forefinger or a foot. After a few taps, the pace tone disappeared and the subjects continued to space their taps according to the internalized interval as accurately as possible. Timing accuracy was assessed by the standard deviation of the inter-tap intervals. Accuracy with the finger correlated with accuracy of the foot at about 0.60. That is, subjects who had low variability with one effector tended to be low in variability with the other and vice versa for those subjects with high variability.

The more striking result in the first study, however, concerned a second task which analyzed perceptual timing. Here, subjects compared the intervals between tone pairs. The two tones of a first pair were separated by 400 msec. The tones of a second pair were separated by a variable interval that was either shorter or longer than 400 msec. The subjects indicated which interval was longer, and based on their responses, a measure of acuity was derived for each subject. Temporal acuity on the perception task correlated about 0.50 with the standard deviation of timing on the motor production task in which subjects attempted to tap out equal time intervals.

These results suggest that finger and foot temporal production and auditory temporal perception share a common timing mechanism. Other results from the study suggested that the correlations could not be attributed to nontemporal factors, but a better study in this regard was conducted by Keele, Ivry, and Pokorny (1987). Here subjects engaged in two different tasks with each of two different effectors, either finger or forearm. One task was the same motor timing task already described: Subjects attempted to produce periodic key presses separated by 400 msec. The only notable difference from before was that the key presses were isometrically generated on a force transducer. The second task involved the same kinds of isometric movements but with an attempt to produce particular forces rather than regular time intervals. For the force task, a horizontal line appeared on a computer screen indicating a target force. Subjects made an isometric press on the key, with either finger or forearm activation. A vertical line then appeared on the screen in proportion to the amount of force. The task was to attempt to produce the target force. After a few presses with feedback, the subjects made a series of presses without feedback in which they tried to replicate the target force. On this task, accuracy was measured by the standard deviation of the produced forces on responses without feedback. The target force level was varied across trials.

For each subject, variability scores were obtained on the force control task performed with either the finger and forearm, and another two variability scores were computed on the time control task for the finger and forearm. These scores were then correlated. The results are shown in TABLE 1. What is notable is that timing acuity with the finger correlates highly with that of the forearm, extending the previous finding of a correlation between finger and foot. Likewise, force acuity of the finger correlates highly with force acuity of the forearm (and with force acuity of the foot as shown in another experiment). Timing ability does not, however, correlate appreciably with force ability, even when the same effector system is used on both tasks. Such results suggest that timing is a separable computation from force control.

All of the experiments of timing described so far involve periodic pulses. Even the perceptual task involved time intervals between two tone pulses. Thus, it might be supposed that the timing system being tapped is peculiar to intervals between pulses. With respect to perception, however, we (Keele & Ivry, 1987) have also found high correlations of about 0.75 between acuity in judging time intervals produced by tone pairs and acuity in judging durations of steady tones that last about 400 msec. Thus, it appears that the temporal ability being measured is rather general, being apparent in motor tasks and perceptual judgments of either empty intervals or steady events.

The Contribution of Wing and Kristofferson to the Concept of a Central Clock

The variability of inter-tap intervals in the motor timing task cannot be attributed solely to noise in an internal clock process. The variability must also reflect noise in the motor system that implements the actual movement. That is, the subject must not only decide when to produce a response, but must also be able to implement that decision in order for the behavior to occur. A deficit in either process will impair

TABLE 1. Correlations between Timing Ability and Ability to Control Force[a]

	Timing		Force
	Finger	Arm	Finger
Timing:			
Arm	0.90		
Force:			
Finger	0.30	0.34	
Arm	0.18	0.21	0.76

[a]From Keele, Ivry & Pokorny, 1987.

performance. Thus, when Conrad and Brooks (1974) found that cooling of the dentate nucleus of the cerebellum led to more variable movements, there was no way of knowing whether a timing mechanism separable from the motor system was the source of increased variance or whether motor implementation itself was the source. Presumably, timing in the perceptual task is also contaminated by processes specific to the auditory system. These second sources of noise are presumably one reason why the correlations reported above are not even higher.

A solution to the problem of extracting a more isolated measure of variability of the clock in the case of periodic taps was proposed by Wing and Kristofferson (1973). Their model assumes that a clock process meters out a time interval. At the end of that process, implementation of the response begins. Simultaneously with the initiation of the implementation process, the next time cycle of the clock begins. That is, it is assumed that the clock process is not dependent on receipt of feedback from each response, but operates independently of the response outcome. Given assumptions that successive clock and motor delays are independent, the variability of inter-tap intervals (σ_T^2) is given by the sum of the variability of the clock process (σ_c^2

and the inplementation process σ^2_{MD}):

$$\sigma^2_T = \sigma^2_C + 2\,\sigma^2_{MD} \quad (1)$$

The total variability is measured directly in a series of taps as the variance of the inter-tap intervals. The problem faced by Wing and Kristofferson was to get an estimate of either the clock variance or the motor variance. If one of these could be

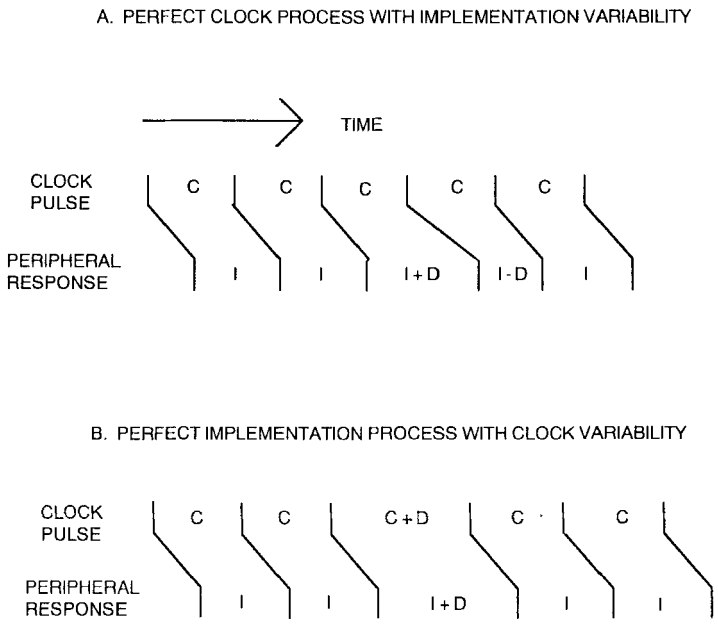

FIGURE 1. In the top panel, successive clock pulses do not vary in duration. Following a clock pulse, after some implementation time called motor delay (MD), a response appears. The fourth MD is longer than the others. This extra delay produces a longer than normal interval preceding the response and a shorter than normal interval following the response. A shortened MD will result in the opposite effect, shortening the preceding interresponse interval and lengthening the following one. The greater the variance in MD, the larger the negative covariation between adjacent intervals. The bottom panel illustrates a situation in which one clock interval varies in length but all the MDs are equal. Variation in the clock interval has no effect on covariation of adjacent intervals. Covariation of adjacent intervals estimates variation in MD.

estimated, the other could be calculated by subtraction from the total variance in accordance with Equation 1. Their solution came from observing that if on a given tap, the implementation was by random chance longer than normal, the inter-tap interval ending in that tap would tend to be longer than average and the following inter-tap interval would tend to be shorter than average.

The logic is illustrated in the top half of FIGURE 1. Here, for sake of illustration, the clock intervals are all assumed to be equal—that is, with no variance. Moreover,

all implementation durations are equal except one, which is long. Note that although one implementation is longer than normal, it has no effect on the succeeding clock interval because the clock process operates independently and, indeed, has already started timing the next interval before the preceding response appears. FIGURE 1a shows that a lengthened implementation (the fourth one in FIG. 1a) lengthens one interval and shortens the following one. If, on the other hand, the duration of a particular implementation is shortened, the reverse effect on intervals will occur. It is important to emphasize that, although this covariation of short and long intervals may appear to be a feedback process, it is actually the result of the assumption of independence of clock and implementation procedures. In other words, only variability in the implementation process produces a negative covariation between the durations of successive intervals.

FIGURE 1b depicts a series of hypothetical intervals in which there is only variability in the clock process. As can be seen, this source of variance does not produce any dependency between successive intervals. Because the successive clock intervals are assumed to be independently determined, a long clock interval (the third clock interval in FIG. 1b) can be followed by either a short, long, or accurate interval.

This dissociation between the two components in terms of their effects on the covariance function of adjacent intervals can, thus, be used to decompose the total variability of inter-tap intervals into two components (see Wing, 1980, for details). Given that the total variability can be directly obtained from the response series and that the implementation component can be estimated from the covariation of successive intervals, an estimate of the clock component can then be obtained via subtraction (see Eq. 1).

This two-process model of periodic movement has received support from a number of different experiments (see Wing, 1980, and Keele & Ivry, 1987, for reviews). Given such support for its validity, the Wing and Kristofferson model provides a tool for obtaining separate estimates of peripheral and central contributions to temporal variability, and it has allowed us to determine which source is responsible for increased timing variability in neurological patients. The pattern of results we have observed with patients provides additional validation of the model. In addition to using the Wing and Kristofferson method, we have also used our combination of motor and perceptual tasks to define a central deficit in timing. The results from these two approaches are consistent with the hypothesis that the cerebellum is critical to accurate timing. The data are reviewed in the next section.

Neural Systems Responsible for Timing

Our correlational work suggested that a unified system is responsible for timing of diverse tasks. Those results coupled with the Wing and Kristofferson model motivated us to search for the neurological structures that might be responsible for timing. Moreover, neuropsychological dissociations could provide converging evidence for the independence of putative operations (Posner *et al.*, 1988).

Among neural systems, the cerebellum has long seemed a likely candidate for timing. As early as 1962 Braitenberg and Onesto (see also Braitenberg, 1967) drew attention to the striking anatomical regularity of the cerebellum as a possible

mechanism for timing. Braitenberg (1967) noted that the Purkinje cells, which provide the only output source from the cerebellar cortex, have dendritic trees that lie in a plane. The planes of a succession of Purkinje cells lie parallel to each other, branching in the sagittal direction. These dendritic trees are intersected by parallel fibers that provide a major source of input to the cerebellar cortex from mossy fibers. A single parallel fiber, running in the laterolateral directions, will pass through a series of Purkinje cells, synapsing on each in succession. In other words, the message conveyed by a parallel fiber is relayed to successive Purkinje cells at different times following the firing of a mossy fiber source. Given the slow conduction velocities of the parallel fibers coupled with their relatively long length, Braitenberg hypothesized that these latency differences could range up to a couple of hundred milliseconds for parallel fibers spanning the extent of cerebellar cortex. Depending on which Purkinje cells transmit the message originating in the mossy fiber input, a delay line of variable length is implemented.

Despite the attractiveness of Braitenberg's idea, it has never been effectively put to test. Indeed, Fahle and Braitenberg (1984), given more recent anatomical results, have questioned whether the arrangements of parallel fibers and Purkinje cells could provide delay-line differences of more than 10 msec or so. Their revised ideas, however, still encompass the basic notion of the cerebellum utilizing its unique architecture to transform spatial signals into temporal information (see also Pellionisz & Llinas, 1980, 1982). Moreover, it is possible that the highly regular structure of the cerebellum could be used in some other way to produce precise temporal delays, for example, temporal summation at the cellular level to produce precisely timed threshold crossings.

In addition to these theoretical ideas, derived primarily from neuroanatomical observations, various empirical phenomena have also suggested that the cerebellum may play a critical role in timing. For example, Conrad and Brooks (1974) found that cooling the dentate nucleus of the cerebellum produced irregularity in the arm movements of monkeys. Moreover, analysis of the EMG patterns in rapid arm movements both of monkeys (Soechting, Ranish, Palminteri & Terzuolo, 1976; Vilis & Hore, 1980) and humans (Hallett, Shahani & Young, 1975) have suggested that cerebellar damage alters the timing of muscular activation patterns. Typically in very rapid arm movements, the agonist muscle, that muscle pulling the arm, shows a burst of activity followed by a burst in the opposing antagonist muscle that stops the movement. With cerebellar damage both the offset time of the initial agonist burst and the onset time of the antagonist become irregular, showing greater overlap than is typically seen in rapid movements.

Despite these hints that the cerebellum might be the center for a temporal computation, the idea has never gained strong force, perhaps for two reasons. One reason has been the lack of an analytic tool to identify the source of a timing problem caused by cerebellar damage. In particular, it is not clear whether cerebellar damage disrupts an explicit timing mechanism, or whether disruptions of timing occur indirectly as a result of problems in motor implementation. The second and related reason has been the lack of attempts to determine whether the cerebellum provides a temporal computation in nonmotor tasks. The conventional view has been that the cerebellum is part of the motor system, typically associated with functions such as balance and fine coordination. Some parts, specifically the more lateral regions, are

said to participate in motor planning and only indirectly affect motor control via connections to the motor cortex (e.g., Allen & Tsukahara, 1974). The more medial portions are thought to influence motor activity more directly through connections to the spinal system via the extrapyramidal pathways (see Ghez & Fahn, 1985, for a review). In either case, the cerebellum has been thought of as intimately tied to the motor system and to motor learning (e.g., Eccles, 1986), and the question has not been raised whether it might provide a specific temporal computation that is task independent.

To investigate whether the cerebellum might be involved in timing, we initiated a large study of neurological patients (Ivry & Keele, 1989; Ivry, Keele & Diener, 1988). In addition to a group of cerebellar patients, we tested Parkinson patients to assess the possible role of the basal ganglia in timing (see also Wing, Keele & Margolin, 1984), hemiparetic patients whose symptoms reflected cortical lesions anterior to the central sulcus, patients with peripheral nerve damage, and elderly control subjects with no known neurological damage (see TABLE 2).

Nineteen of the cerebellar patients presented clinical and radiographic findings consistent with cerebellar atrophy, and in some cases the diagnosis was olivo-ponto-cerebello atrophy. These patients all had bilateral damage. The remaining 11

TABLE 2. Subject Types for Neurological Studies

Group	Number of Subjects	Mean Age
Elderly controls	21	67
Parkinson patients	30	63
Cerebellar lesions	30	51
Anterior cortical lesions	12	61
Peripheral nerve damage	4	56

cerebellar patients had unilateral lesions resulting from stroke ($n = 6$) or tumor ($n = 5$).

All of the subjects were run on the three tasks already described. One task involved the production of a regular series of taps with the fingers. A pacing tone came on periodically every 550 msec. This slower pace was adapted because some patients, especially those with Parkinson's disease, have difficulty at faster paces such as the 400-msec pace used in our earlier studies. After synchronizing their responses with the pace tone, the tone was terminated. Subjects continued tapping until they had generated 30 unpaced intervals. Data were collected over many such tapping bouts per subject. The main score of interest was the variability of the inter-tap intervals.

A second task was that of perception of duration. Sets of tones were presented with two pairs of tones per set. The task was to judge which pair bounded the longest interval. The tones of the first pair were always separated by 400 msec and the tones of the second pair created an interval that was either shorter or longer. Thresholds in milliseconds were calculated for each patient and then converted to standard deviations so that they could be directly compared to the standard deviations of the inter-tap intervals of the tapping task.

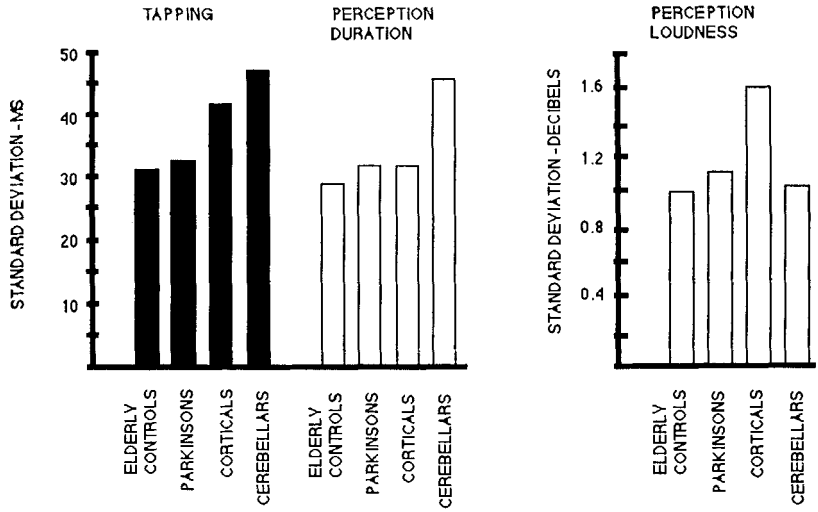

FIGURE 2. The standard deviation of inter-tap intervals and of perceptual judgments of duration and loudness for various patient types and for elderly control subjects. Note that on tapping, cerebellar and cortical patients show a deficit over the controls. On perceptual duration judgments, only the cerebellar patients show a deficit. On perceptual loudness judgments, only the cortical patients show a deficit. (Based on Ivry & Keele, 1989.)

The third task, perception of loudness, was designed as a control for the perception of duration task. Here again sets of tones were presented, but the subject's task was to judge which pair of tones was the loudest, not which interval was the longest. A threshold (in dB) was calculated for each subject. The loudness task allowed a determination of whether observed deficits on the perceptual duration task were specific to temporal judgments or whether they could be attributed to decreased auditory accuity in general.

The results on these tasks for various patient types and the controls are shown in FIGURE 2. With respect to variation in the inter-tap intervals, Parkinson patients behave the same as controls. Moreover, a subgroup of seven of the Parkinson patients was tested under two conditions, once during their normal medication cycle and once having skipped a medication period. In this latter condition, all seven patients showed a marked increase in rigidity. Nonetheless, no difference in variation of inter-tap intervals was observed despite the obvious clinical differences. Both cortical and cerebellar patients, on the other hand, show a statistically significant increase on tapping variability. It should be noted that data for any patients with lateralized damage was from trials in which they tapped with their impaired hand.

In principle, the inflated variability of cortical and cerebellar patients could be due either to difficulties with the hypothesized timer or to difficulties in implementing a movement command. This issue is addressed by the perceptual data shown in FIGURE 2. With respect to perception of duration, the only patient group that shows a statistically significant deficit is the cerebellar group. To ensure that the difficulty is with timing and not with perception per se, the data on the perception of loudness

can be assessed. There it is seen that the cerebellar group has no impairment, though the cortical group does.

The data suggest that the cerebellum (or the cerebellum together with closely related structures) is critical for accurate timing computations. Cerebellar patients show a disruption in the regular timing of motor tasks. More surprising, this deficit is not limited to motor tasks. A deficit is also observed on a distinctly nonmotor task for which precise timing is required. Cortical patients show increased variability on the tapping task, but since they show no problem on the perceptual timing task, it would appear that their difficulty is due to other aspects of motor control and not timing per se.

The tapping data were also decomposed using the Wing and Kristofferson (1973) method. Consider first the data of patients with peripheral nerve damage. These patients have inflated variability when tapping with the affected limb compared to the unaffected one. In terms of the Wing and Kristofferson model, a critical prediction is that, following decomposition of total tapping variability into clock and motor implementation components, any deficit in these patients should be attributed to the implementation component. FIGURE 3 shows such to be the case, and thus reinforces our belief that the model can be valid in neuropsychological research.

When the Wing and Kristofferson method is applied to the data from the cerebellar and cortical patients, the decomposition shows both clock and motor components to be affected in both patient groups (FIG. 4). Two issues arise here.

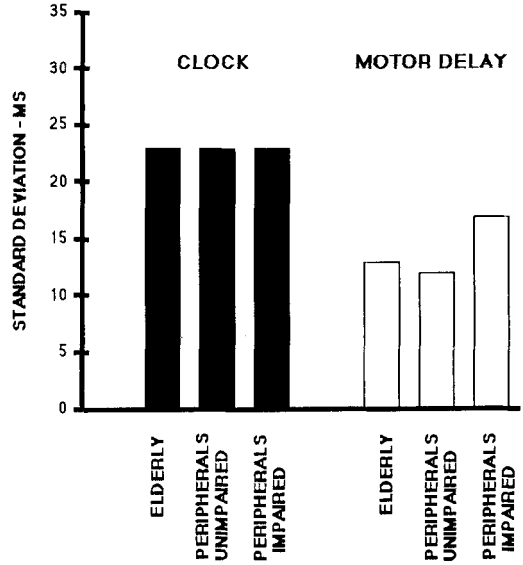

FIGURE 3. Total inter-tap variability is decomposed into clock and motor delay variability for the impaired and unimpaired effectors of patients with peripheral nerve damage. The impaired hand shows an increased motor delay variability, but the hands do not differ in clock variability. The variabilities of the preferred hand of elderly control subjects are shown for comparison. (Based on Ivry & Keele, 1989.)

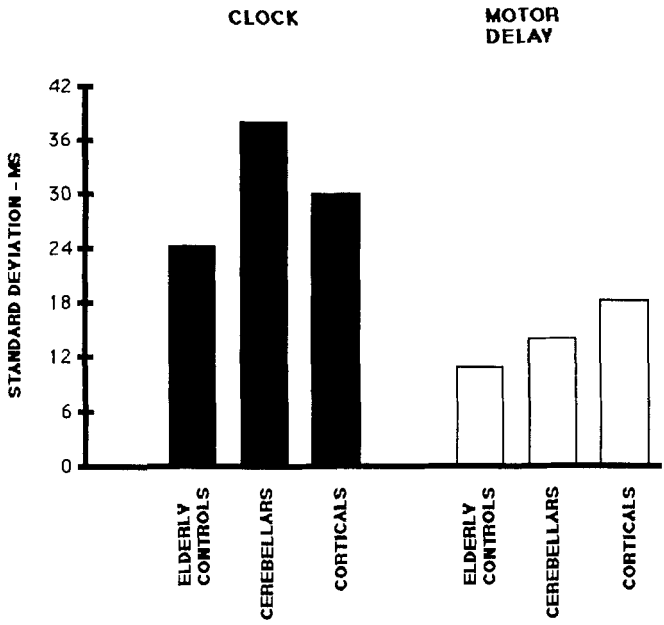

FIGURE 4. Clock and motor delay variabilities for cerebellar and cortical patients with corresponding variabilities of elderly control subjects as a comparison. (Based on Ivry & Keele, 1989.)

One concerns the discrepancy for the cortical patients between the Wing and Kristofferson analysis indicating a clock deficit and the data from the perception task which showed no deficit for these patients. A resolution of this issue will be offered, but it depends first on analysis of a second issue, namely why the cerebellar patients show impairment on both clock and implementation components.

It has long been argued that the cerebellum can be divided into two main functional parts (see Ghez & Fahn, 1985 for a general review of the cerebellum and Asanuma, Thach & Jones, 1983a,b,c for a more detailed anatomical review relevant to the current issue). The medial portion of cerebellar cortex, the vermis, has through its output nuclei relatively direct connections to descending output pathways. The lateral portion of the cerebellum has little direct linkage to descending movement signals. Instead lateral regions ultimately project to the motor and premotor cortex via the thalamus. This leads to a hypothesis that the lateral cerebellar regions are responsible for the clock component of timing whereas the medial regions are part of the implementation system. Widespread cerebellar damage may cause both clock and motor damage because both systems may be involved, at least in some of the patients.

To investigate this issue, seven cerebellar patients were examined in detail (Ivry, Keele & Diener, 1988). All patients had unilateral lesions in the cerebellum. For three patients the damage was focused in the lateral regions and for another three patients the damage was restricted to more medial regions. In addition to CT data

that indicated the lesion foci, the neurological signs were consistent with a subdivision into lateral and medial patients. The clinical data were consistent with a lateral lesion for the seventh patient, and the CT data, though less clear, were not inconsistent with a lateral lesion. FIGURE 5 shows summary data for these two patient subgroups when the Wing and Kristofferson decomposition is applied to a large set of tapping data. The comparisons of interest involve the impaired and unimpaired effectors. Unilateral cerebellar lesions primarily affect the ipsilateral side of the body, so that within-subject analyses can be made by comparing performance between the two hands. What is striking is the double dissociation between the two groups. Almost all the increased variability for the lateral patients is attributed to the clock component. In contrast, the increased variability for the medial patients is in the motor component. Thus, it appears that the critical centers for the computation of time are in the more lateral regions of the cerebellum.

Let us now return to consider why cortical patients show no deficit in the perceptual timing test but appear to show both a clock and an implementation deficit on the tapping task. We have suggested (Ivry & Keele, 1989) that this dilemma can be resolved by considering anatomical connections and the nature of the tapping and perceptual tasks. First, consider the tapping task. In our conception, before a particular tap can be realized, several computations have to be performed and

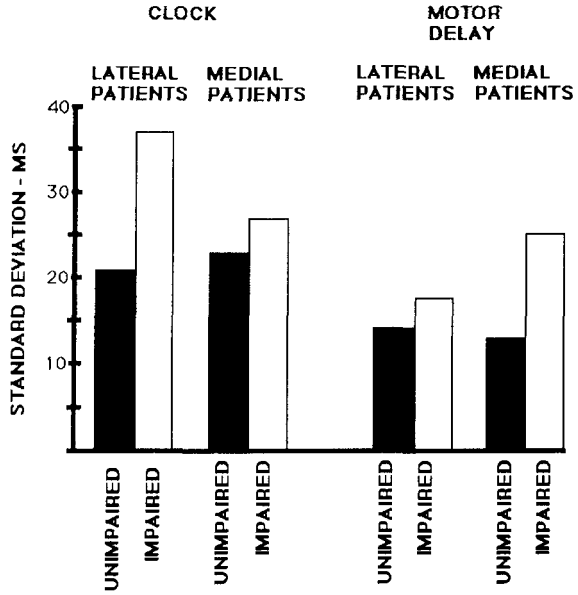

FIGURE 5. Clock and motor delay variabilities for the impaired and unimpaired hands of cerebellar patients with damage localized to one cerebellar hemisphere either in lateral or cerebellar regions. Data for lateral regions are averaged over 4 patients. Those for medial regions are averaged over 3 patients. Note that in lateral patients, the impaired hand is primarily affected in the clock component of the Wing and Kristofferson model. In medial patients the impaired hand is primarily affected in the motor delay component. (Based on Ivry, Keele & Diener, 1988.)

assembled before the response is implemented. The time of the tap must be specified, and inhibition of this response must occur until the cerebellum specifies that the time is appropriate. Other parameters of the response such as designation of the target effector and the force level of the response need to also be specified. We suggest (see Ivry & Keele, 1989; also Horak & Anderson, 1984a,b; Stelmach & Worringham, 1988; and Wing, 1988) that the basal ganglia are primarily responsible for the force computation. Selection of the appropriate effector and the goal of the action might be expected to involve cortical structures such as portions of parietal cortex (e.g., Perenin & Vighetto, 1988) and motor cortex (e.g., Georgopoulos, Schwartz & Kettner, 1986).

It is not until these various computations are assembled that a response can be released for final implementation. A likely anatomical region for final release is some area of the motor or supplementary motor cortex (Alexander, DeLong & Strick, 1986; Goldberg, 1985). When a response is released, implementation procedures take place via descending commands, some of which involve medial regions of the cerebellum. Variability in these procedures would be reflected in the implementation component of the Wing and Kristofferson model. Simultaneously with release of a response, the next cycle can begin to prepare the next response, including the circuit through the cerebellum to provide the temporal computation. Although, according to our findings, the critical temporal computation is drawn from the cerebellum, the complete cycle starts and ends in the cortex where information is assembled regarding several computations. It is for this reason that damage to a variety of neural systems may affect the clock component of the Wing and Kristofferson model even though only the cerebellar system specifically meters time. Any variability that is not in the implementation process is lumped into the clock component.

Although there are a number of open issues that result from these speculations on circuitry, we believe they are not unreasonable, and they offer a rationale for some otherwise apparently discrepant findings.

Additional Work from Our Laboratory on the Timing Hypothesis

The novel finding from our laboratory (Ivry & Keele, 1989) that cerebellar lesions impair discrimination of auditorily based intervals stresses that the cerebellum provides a particular computation rather than simply being part of the "motor system." To strengthen this argument, we have recently tested cerebellar patients on another perceptual task in which timing may be important. That task involves the perception of the velocity of moving stimuli. This work has been reported in preliminary form (Ivry, Diener & Keele, 1988) and will be reported in more detail elsewhere.

We selected visual velocity perception for a number of reasons. First, velocity, by definition, is a computation that can only be made over time. Second, the cerebellum has long been argued to play a prominent role in processes controlling eye movements (Westheimer & Blair, 1974; Ritchie, 1976; Ron & Robinson, 1973) and in oculomotor reflexs such as the vestibular-ocular reflex (e.g. Robinson, 1986; Dichgans & Diener, 1984). Specific mechanisms associated with the cerebellum such as gain modification of the vestibulo-ocular reflex (Miles, Fuller, Braitman & Dow,

1980; Lisberger & Fuchs, 1978) would appear to require high sensitivity to velocity information. Moreover, recent neurophysiological experiments conducted by Suzuki and his associates (Suzuki & Keller, 1988; Suzuki, Noda & Kase, 1981) have demonstrated that Purkinje cell activity in the vermis correlates best with a complex motion signal rather than simpler motion parameters such as eye, head, or retinal image velocity. The output of these cells may indicate target velocity and can occur independently of whether or not the animal generates an eye movement response to the stimulus (Suzuki & Keller, 1988). Given these findings, we designed a direct test of velocity perception in patients with cerebellar disorders.

The stimulus in this task was a horizontal line of evenly spaced lights. The lights moved as a single unit creating the impression of a moving line. As a light moved beyond the edge of the display, a new one appeared at the beginning, thus creating a continuous display. Perception of movement in this situation is similar to the appearance of moving messages on electronic displays. We used a line of lights rather than a single light to reduce the tendency for eye tracking. Each trial consisted of two moving stimuli. One of the stimuli moved at a standard velocity and, after an interstimulus interval of 1 sec, the other appeared to be moving at a velocity which was either faster or slower. The subjects' task was to judge which line moved faster, the first line or the second.

In the first experiment, the standard velocity was 0.75 degrees per second. As in our previous studies, we determined the ability of each subject to discriminate the standard from other stimuli moving faster or slower. The acuity score for each subject was expressed as a standard deviation of velocity. As a control, we included a second test of visual acuity in which the subjects judged which of two lines was presented at a higher location on the display monitor. The stimulus displays in the position task were identical to those used in the motion task: Both lines were composed of a series of moving lights.

Sixteen healthy, elderly people served as control subjects. The cerebellar group was composed of 21 patients in which the deficits were the result of either degenerative processes ($n = 16$) or focal lesions ($n = 5$). The results for the two tasks are given in FIGURE 6. Although on the average the patients performed worse on both tasks, the deficit was significantly more marked on the velocity perception task as revealed by a group by task interaction.

The standard and test stimuli in our initial velocity experiment were relatively slow at 0.75 deg/sec. McKee (1981) has shown that the Weber fraction, although constant over a range of higher velocities, rises rapidly (indicating less sensitivity) below 2 deg/sec. Thus, we used higher velocities in two additional experiments. In one, the standard velocity was 6.5 deg/sec and in the other velocities ranged from 2 to 5 deg/sec. A second concern with the first experiment is that we did not control for eye movements. The poor performance of the cerebellar patients may have resulted from poorly controlled eye movements generated in response to the stimulus. (Actually, our phenomenological experience as well as observations of some control and cerebellar subjects is that the stimuli did not evoke any pursuit or saccadic eye movements. Eye movement was likely obviated by the nature of the moving display.) To discourage eye movement in the two additional studies, however, a fixation point was provided and horizontal eye movements were monitored by EOG recordings.

In both experiments, cerebellar patients showed significant impairments in velocity perception relative to healthy, older control subjects. Patients (n = 3 in Experiment 2 and n = 2 in Experiment 3) with cerebellar disorders from chronic alcohol abuse were tested as an additional control group. Alcoholic patients have not shown a timing problem in our studies (Ivry *et al.*, 1988), and we believe this is because their lesions are restricted to the vermal (i.e., medial) region of the anterior lobe of the cerebellum (Adams & Victor, 1985; Allsop & Turner, 1966). The alcoholic patients had similar performance to the elderly controls.

The EOG recordings showed minimal differences between the three groups, and

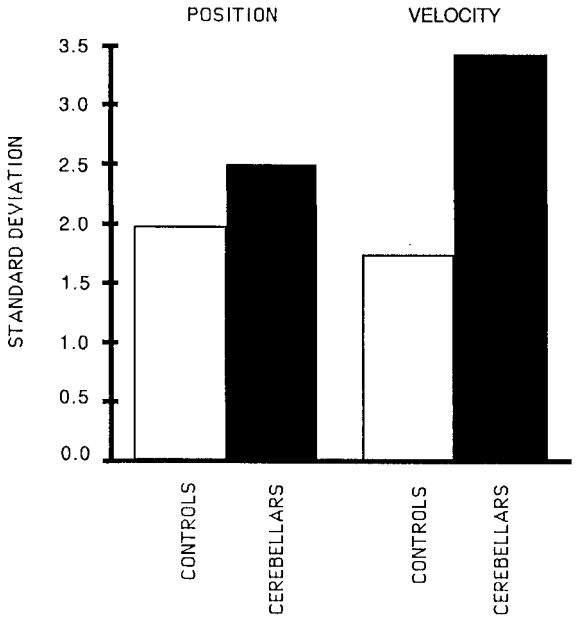

FIGURE 6. Perceptual acuity scores expressed as standard deviations of velocity and position judgments of moving lines for cerebellar patients and elderly control subjects. Cerebellar patients show impairment in velocity judgments compared to the control task of position judgment. (Based on Ivry, Diener & Keele, 1988.)

it was quite evident that the subjects were able to maintain fixation. Moreover, the output from the electrodes was similar on trials in which the responses were correct and trials in which the responses were incorrect. Thus, poor eye control cannot be the cause of poor velocity judgment in the lateral cerebellar patients.

In summary, the velocity perception experiments provide a second demonstration of how cerebellar lesions can impair performance on a purely perceptual task. The important point that needs to be emphasized is that the deficit appears to be specific and not a reflection of decreased acuity in a sensory modality. We believe that the common aspect shared by the time perception and velocity perception tasks

is that each requires the involvement of a timing mechanism. It is this shared computation that links each task to the cerebellum.

DOES THE CEREBELLUM PROVIDE A TEMPORAL COMPUTATION FOR OTHER TASKS?

We have suggested that the cerebellum provides a temporal computation and have developed some evidence for that view. Although the cerebellum may certainly perform other, unrelated computations, it is reasonable to ask whether certain tasks involve the cerebellum because they require access to a temporal computation. In particular, we consider here whether certain kinds of classical conditioning occur in the cerebellum while other kinds, not needing precise temporal specification, do not. In addition we will briefly discuss some data on locomotion and efference copy that suggests the cerebellum provides a temporal computation.

Temporal Relationships in Classical Conditioning

It has long been known that rather precise temporal relationships are obeyed for some types of classical conditioning. This would appear to be the case for situations in which the response plays a protective role for the organism by preceding the unconditioned stimulus (e.g., Ebel & Prokasy, 1963; Gormezano, Kehoe & Marshall, 1983).

Consider the features of the conditioned eyeblink response. An aversive unconditioned stimulus (US), such as an airpuff, is delivered to the eye and leads to an eye blink. Suppose that a conditioned stimulus (CS), such as a tone, is presented 500 msec before the airpuff. It would be most useful to the organism if the eyeblink would begin before the airpuff and retain closure until the puff were over to provide a protective function. If the interval between the CS and the airpuff were different, say 800 msec, it would be adaptive if the timing of the response were altered to again provide protection at the critical juncture, the point in time just preceding the US. This example makes clear that for conditioning to be adaptive, the conditioned response (CR) must be temporally set to precede the (following) US. The CR would be less adaptive if it occurred with a fixed latency with respect to the CS regardless of situation.

To provide such an adaptive function, two things are necessary. First some mechanism must be sensitive to the interval between onset of the CS and either onset of the US or onset of the unconditioned response (UR). (Gibson & Chen, 1988, have argued that it is the CS to UR linkage and not CS to US linkage that involves the cerebellum, but this issue is not critical to the current discussion.) Second, the extracted interval must be used to regulate the interval between the onset of the CS and the occurrence of the CR. Such adaptability occurs in classical conditioning, and, as recent work has shown, such conditioning requires the cerebellum (Woodruff-Pak, Logan & Thompson, this volume; Thompson, 1986; Yeo *et al.,* 1985a,b,c).

Hall (1976) has reviewed a sizeable body of older research concerned with the temporal relationships in conditioning. With respect to conditioned eyeblinks, the

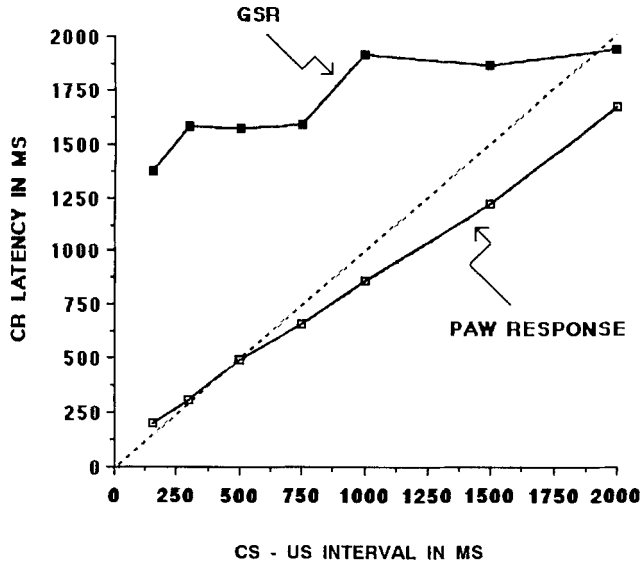

FIGURE 7. Latency of conditioned paw withdrawal and galvanic skin response following a conditioned stimulus as a function of the interval between the conditioned and unconditioned stimuli. The conditioned stimulus was a tone–light combination and the unconditioned stimulus was a shock delivered to the forepaw of cats. Responses were measured on trials on which the unconditioned stimulus was withheld. The time of the paw withdrawal shows a tight coupling with the conditioning interval, but the galvanic skin response does not. (Based on Wickens *et al.*, 1969.)

timing of the CR depends very strongly on the interval between the CS and the US. For example, Ebel and Prokasy (1963) showed that when the interval between the CS and US was changed across blocks, the interval between the CS and the CR changed, becoming longer or shorter as needed.

FIGURE 7 shows data from a study by Wickens, Nield, Tuber, and Wickens (1969) involving conditioning in the cat. The CS was a light-tone compound. The US was a shock to the forepaw. Two different URs were measured. One was retraction of the paw. The other was a galvanic skin response (GSR) in the nonshocked paw. Different CS–US intervals were employed in successive sessions, ranging from 150 msec up to 2000 msec. The CRs were recorded on trials in which the US was omitted. The data of FIGURE 7 show a very tight coupling between the conditioned paw response and the interval between the conditioned and unconditioned stimuli. Except at the shortest intervals, the conditioned paw response tended to occur slightly before the time at which the US, were it present, would occur. The GSR, in contrast, typically did not occur until sometime after the point in time at which the US, if present, would have occurred. Moreover, the GSR showed a weak coupling to the CS–US interval. The relative lack of coupling was apparent, not only in the mean time of occurrence, as shown in FIGURE 7, but also in the greater variability in onset time of the GSR as compared to the paw response.

Perhaps the paradigmatic animal experiment over the last 25 years for studying

classical conditioning has been the nictitating membrane response (eyeblink) of rabbits (Gormezano *et al.* 1983). Many of the studies have been devoted to delineating the precise temporal constraints observed in this preparation, similar to those reviewed above in studies with humans and cats. Results from a particularly complete study by Smith (1968) are shown in FIGURE 8. Four CS–US intervals were used in different conditions: 125, 250, 500, and 1000 msec. After conditioning, the time of the peak change in the nictitating membrane closely corresponded to the time at which the US would occur, providing maximal protection. Regardless of interval, the change in the membrane began about 100 msec after the CS. At the short intervals, the response quickly rose to peak value. At the long intervals the rise to peak value occurred over a longer time period. Although we have no account of the shape of the eye closure pattern, the important observation is that peak closure is very tightly coupled to CS–US interval. It might be noted that the paw response of the cat described in the Wickens *et al.* study (see FIG. 7) showed a much sharper rise to peak and then decline at all conditioning intervals than is the case for the nictitating membrane response.

It appears, therefore, that in conditioning situations involving discrete protective CRs, the temporal relationship between the CS and either the US or UR is extracted and used to adaptively time the CR. Given that the cerebellum appears crucial only for conditioning of this type, we propose that the cerebellum provides the necessary temporal computation.

Besides an examination of the relative timing of the CR, it is of interest also to examine the time interval over which effective conditioning occurs. For discrete responses like eyelid responses, nictitating membrane responses, and paw retraction, conditioning occurs roughly over intervals ranging from 100 msec to about 1500 msec (Hall, 1976; Gormezano *et al.* 1983). Indeed, in some circumstances, responses learned at one of these short intervals may undergo extinction if the interval between

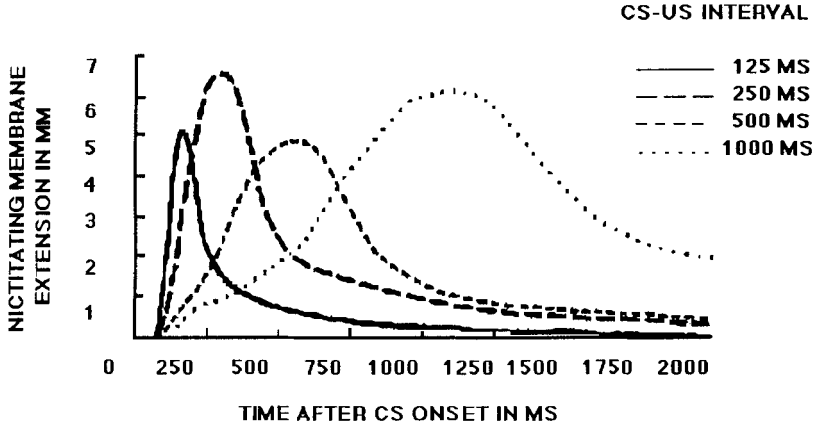

FIGURE 8. Amount of closure (measured as extension) of the nictitating membrane of rabbits conditioned to face shocks as a function of the time since the conditioned stimulus and the interstimulus interval between the conditioned and unconditioned stimuli. The response peaks at about the expected time of the unconditioned stimulus. (Based on Smith, 1968.)

the CS and the US is increased to as much as 1500 to 2500 msec (Spence, Homzie & Rutledge, 1964). Within the range at which conditioning occurs, there appears to be no precisely optimal interval, but again roughly speaking, conditioning is usually best when the CS to US interval is around 250 to 1000 msec (Hall, 1976). The best value depends on a variety of other manipulations and exactly how the response is measured.

Optimal conditioning intervals in the range of 250 to 1000 msec also fit well with the hypothesis that discrete forms of classical conditioning make use of the cerebellum because the cerebellum provides a critical temporal computation. The time intervals that we have investigated with respect to the cerebellum, intervals of 400 msec and 550 msec are at the middle of the range for effective conditioning. Moreover, psychophysical studies have raised the possibility that different timing mechanisms may be required for computing short and long temporal intervals. The shape of the psychophysical function in which variance is plotted as a function of interval duration changes somewhere between about 0.75 sec and 2–3 sec (compare Wing, 1980 with Michon, 1967). Likewise, it has been suggested that the phenomenon of beats in music cannot exceed intervals of about 1–1.5 sec (Fraisse, 1982; Povel, 1981). Thus, the time intervals that would be expected to involve the cerebellum in our tapping and perception tasks are quite similar to the effective range for classical conditioning.

Another feature of special interest is that regions of the cerebellum involved in classical conditioning are similar to those that we have localized for a timing operation. Conditioning of the nictitating membrane appears to depend on integrity of the dentate and/or interpositus nuclei. In addition, lesions of small regions of the cerebellar hemispheres, the lateral portion of the cortex, may also abolish conditioning (Yeo *et al.*, 1983b,c; but see Lavond *et al.*, 1987, for a counter view). Although localization is not nearly so precise with human cerebellar patients, it appears from our work (Ivry, Keele & Diener, 1988) that medial portions of the cerebellum are not critical for the operation of a timing mechanism. Rather, the critical regions involve the more lateral portions of the cerebellum, perhaps including underlying nuclei such as the dentate nucleus.

As stated earlier, Lavond *et al.* (1984) found no effect of cerebellar lesions on heart rate conditioning. To complete our argument, it would be necessary to show that temporal relationships for this form of learning (and for other less discrete responses) are not as precise as for discrete responses. We are not aware of studies that examine in detail the temporal relationships of heart rate conditioning, but it is the case that the optimum intervals between CS and US for heart rate conditioning are relatively long. VanDercar and Schneiderman (1967) varied the interval between a tone CS and US shock delivered near the eye of rabbits. Both heart rate and nictitating membrane responses were recorded. Optimal conditioning of the membrane response occurred with intervals between 0.25 and 0.75 sec, and no conditioning occurred with an interval as long as 6.75 sec. In contrast, the optimum interval for heart rate conditioning was 2.25 sec and conditioning also occurred at 6.75 sec. Recall also the Wickens *et al.* (1969) study showed only weak temporal coupling between the CS–US interval and the GSR in cats. Thus, generalized, reactive responses that are neither discrete nor precisely tailored to avoid an aversive stimulus do not appear to be tightly timed. Given this, it makes sense that such

conditioning would not be dependent on the integrity of the cerebellum since a temporal computation is not critical.

Locomotion and the Cerebellum

The cerebellum has frequently been implicated in locomotion. The cerebellar influence is primarily associated with medial structures (for reviews of cerebellar functions see Ito, 1984; in relationship to clinical pathology, Dichgans & Diener, 1984). Despite the fact that we have argued that the lateral cerebellum provides a general timing function and the medial cerebellum a motor function, the possibility still exists that the motor function of the medial cerebellum includes timing, though in a more constrained sense. That is, this type of timing function may be restricted to coordinating components of actual movement rather than providing timing for nonmotor functions as well. In addition, localized regions of the medial cerebellum are likely tied to particular motor effectors (Oscarsson, 1980; Robertson, 1985).

The argument that the cerebellar influence on locomotion may involve a temporal function stems from work reported by Arshavsky and colleagues (Arshavsky, Gelfand & Orlovsky, 1983). They show that rhythmic output from spinal locomotor generators is directed not only to the musculature to drive the limbs in locomotion of the cat but also upward to the cerebellum through two nerve tracts, the ventral spinal cerebellar tract and the spino-reticulo-cerebellar tract. The information reaching the cerebellum via these tracts appears to be a copy of the spinal oscillatory commands, rather than a reflection of kinesthetic feedback, because deafferentation does not abolish the transmission of information to the cerebellum.

The rhythmic signal coming into the cerebellum is then transformed into an efferent signal that imposes a rhythm on descending pathways such as the vestibulospinal tract. The influence of the cerebellum can be seen in FIGURE 9. When the cerebellum is removed, the vestibulospinal tract sends neural input down to the spinal system completely unrelated to the step cycle that the cat is in. With the cerebellum intact, however, the information sent down the vestibulospinal tract varies with the portion of the step cycle. Thus, it appears that the job of the cerebellum has been to pick up the rhythm at which the limbs are instructed to move and convey that rhythm to centers that are sending modulating information downward to the limbs. It is important to note that the rhythmic modulation is phase shifted with respect to the original locomotor cycle. Presumably the function of the cerebellum is not just to mimic the locomotor rhythm but to extrapolate forward in time to anticipate particular portions of the step cycle.

The function of the cerebellar influence can be appreciated by a hypothetical example. Suppose that an animal is walking along, and a stick in the path requires the leg to be lifted a bit higher than normal. Higher brain centers must convey the information for extra effort to be put into flexion. The problem is one of knowing the precise moment at which the extra effort should be expended. It would be counterproductive were the effort expended during extension when it was flexion that needed the boost. What appears to be happening is that the cerebellum has picked up the temporal information being sent to the periphery. That temporal information specifies the frequency and phase of the locomotor steps. The cerebellum then uses that temporal information to gate the influence of descending commands to occur at

just the proper time. This locomotion example can thus be viewed as another instance where the primary contribution of the cerebellum is in the measurement of time. The cerebellum picks up input rhythms and shifts them in time to temporally modulate the influence of other neural systems on locomotion.

Such an interpretation is consistent with the hypothesis that the cerebellum is a temporal computer. However, different portions of the cerebellum may provide a temporal computation for different systems and over different time ranges. Schwartz, Ebner, and Bloedel (1987) for example, found that EMGs in agonist and antagonist muscles of the cat during locomotion were correlated with the output of cells in the interpositus nuclei of the cerebellum. Dentate cells, in contrast, were not correlated with the phasic activity, but tended to become active at the initiation of movement

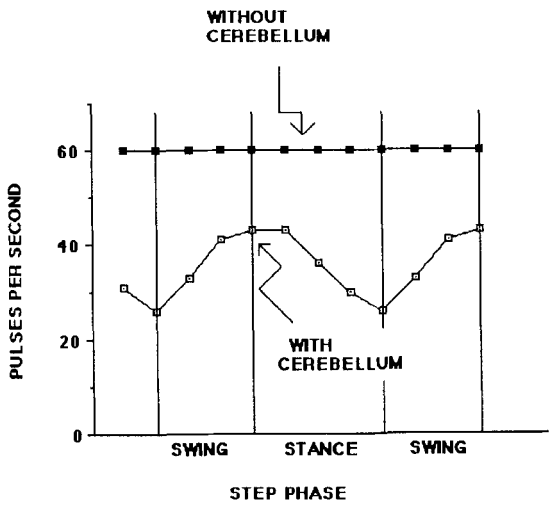

FIGURE 9. The frequency of discharge of vestibulo-spinal tract neurons, measured in pulses per second, as a function of the phase of walking in cats with intact versus lesioned cerebellum. An intact cerebellum conveys the locomotor rhythm to the descending influence of the vestibulo-spinal tract. (Based on Arshavsky, Gelfand & Orlovsky, 1983.)

after a treadmill was started. Thus, it is possible that the more medial nucleus of the two, the interpositus, is involved in the fine-grained temporal control of movement, whereas the more lateral nucleus, the dentate, is concerned with more general aspects of timing, including when movement should begin.

Efference Copy

Another suggested function of the cerebellum has been as the recipient of an efference copy signal. When a motor action is performed, particular feedback is expected from that action. The expected feedback is compared to the actually occurring feedback. If they are the same, the movement is progressing as intended. If

they differ, then something unexpected has happened, and a correction must be issued. A recent study by Gellman, Gibson, and Houk (1987) illustrates the concept of efferent copy and also raises the issue of timing and the neural structures involved.

Gellman *et al.* recorded the activity of cells in various regions of the cat inferior olive. It is important to note that the inferior olivary nucleus provides the climbing fiber input to the cerebellum. Moreover, output from the dentate nucleus of the cerebellum goes to the parvocellular region of the red nucleus, and part of that pathway returns to the inferior olive to complete a circuit (Ghez & Fahn, 1985). Gellman *et al.* observed an interesting dissociation between trials in which movement was volitional in comparison to trials in which the animal's limb was passively moved or stimulated. Many cells of the dorsal accessory olive were responsive to passive movement of the limb or to tapping or squeezing of particular portions of the paw of the cat. In contrast, when these paw areas were stimulated during the course of volitional movement, as when the paw touched the support surface, these same cells of the olivary nuclei were unresponsive. Gellman *et al.* suggest that in active movement, an efferent copy of the motor command elicits an expectation of particular feedback. If that feedback occurs, then no error signal is generated. According to Gellman *et al.*, this function may be linked to the inferior olive. In contrast, passive stimulation is analogous to an unexpected stimulus, which is signified by a neural discharge.

To further test this interpretation, one additional manipulation was tested. On some occasions when the cat was in the act of placing the paw downwards, an obstacle was placed under the paw so that contact occurred earlier than expected. In this case, neurons in the receptive area of the olive responded. Thus, it appears that efferent copy involves not just activation of expected feedback but explicit timing of the anticipated feedback. If the feedback signal comes too early or too late, an error signal occurs. Feedback that occurs at the correct time does not produce an error signal. Gellman *et al.* suggest (p. 57) that the cerebellum may be the source of the timing computation needed to adjust the efferent copy to the time of the expected feedback. This example of efferent copy emphasizes the importance of viewing input in terms of both its spatial and temporal content (Pellionisz & Llinas, 1980; 1982).

As is the case with locomotion, what the cerebellum seems to be doing is keeping track of the temporal structure of ongoing events and extrapolating forward in time in order to be in a position for rapidly modulating that action.

Strategies in Assessing Cerebellar Mechanisms

It is, of course, possible, and even likely, that the cerebellum provides functions in addition to timing. For example, Gilbert and Thach (1977) provide evidence of a cerebellar role in gain adjustment between the magnitude of sensory input and the magnitude of motor output. Nonetheless, a primary cerebellar function appears to be one of temporal computation. One hope is that by focusing on the cerebellum and associated structures as a timing computer, studies might be better directed at discovering just how that function is carried out. It is conceivable, from this perspective, that tasks of the sort we have used with human subjects (involving periodic tones, tones of differing durations, velocities of visual signals, and periodic tapping) might provide simpler and more analytic tools for studies in animals than

the tasks often used. That is, it may be better to attack the analysis of time directly rather than by studying diverse tasks for which timing is only one of the many necessary computations.

COORDINATION AND DEVELOPMENT

The idea that complex tasks are decomposable into elementary computations and that the same computation may be drawn upon by diverse tasks lends a new perspective to problems of coordination that occur in development, in individual differences, and in pathology (see Keele & Ivry, 1987, for discussion of the issue of individual differences). Consider the problem of clumsy children. What does it mean to be clumsy or coordinated, and what brain processes might be implicated?

Clumsiness typically has been defined in terms of a variety of tasks on which children of normal intelligence may perform poorly. The child may present balance problems, have difficulty in hopping, or be impaired in eye–hand coordination. An alternate approach, suggested by the current work, is to analyze coordination in terms of basic computations. Impaired performance on a variety of tasks may be due to deficiencies in one or a few computations. Moreover, if such computations can be identified with brain systems, some biological understanding of coordination and clumsiness might be gained.

Recently, this approach was explored by Williams, Woollacott, and Ivry (unpublished). They selected a sample of 25 children, 13 of whom were classified as normal in coordination and 12 as clumsy. All were intellectually normal. The children were of two age groups, 6–7 and 9–10 years of age. Coordination was defined on the basis of standardized tests that included balancing on one leg with eyes open and closed, balancing while walking on a narrow beam, body movements involving rapid changes in direction, hopping on both feet for a distance of 50 feet, and other locomotor and upper body tests.

The issue is whether, as a class, clumsy children may be deficient on a more basic computational ability, in this case timing. To assess the question, the children performed three of the tasks which we have used with our adult subjects (Ivry & Keele, 1989). The first was the motor task in which the subjects repeatedly produced a target interval of 550 msec by tapping with their finger. The other two tasks were the time perception and loudness perception tests. On different test blocks, each child compared either the intervals between tone pairs or the loudness of successive pairs.

The primary results for the tapping task are shown in TABLE 3 and those for the

TABLE 3. Variability in Standard Deviations (msec) of Clumsy and Normal Children[a]

Group	Total	Clock	Motor Delay
Normal	36	31	14
Clumsy	45	39	17

[a]Williams, Woollacott & Ivry, unpublished.

TABLE 4. Performance in Standard Deviation Units on the Perceptual Tasks for Duration (msec) and Loudness (dB)

Group	Duration	Loudness
Normal	33	1.6
Clumsy	51	1.6

perception tasks in TABLE 4. Generally speaking, performance improves with age for both clumsy and normal children (see Ivry & Keele, 1989, for a comparison of young and elderly adults). At both ages, however, clumsy children performed worse on both the tapping and perception of duration tasks than normal children. The Wing and Kristofferson analysis showed the tapping problem to be restricted to clock performance, as only that component and not the motor implementation component was significantly larger for the clumsy children. In correspondence with a clock deficit, the clumsy children were also impaired on the time perception test in comparison to the normal children. The two groups did not differ in their performance on the control task of loudness perception.

The result with the task of perception of duration is particularly interesting since it is a nonmotor task. Such a result suggests that a primary problem in clumsiness stems from a basic deficit in the timing computation rather than in motor control per se.

Given the evidence that the timing computation is linked to the cerebellum, one could also speculate that clumsy children have a subclinical impairment of the cerebellum. We are seeking replication of these results with other clumsy children and hope to investigate other assays of cerebellar dysfunction with these subjects.

Such results as these from Williams *et al.* should not be taken to suggest that difficulty with a temporal computation is the only source of clumsiness. Other computations, separable from timing, could also contribute to clumsiness or could produce distinct subtypes of clumsiness. Nonetheless, the timing results of Williams *et al.* suggest that a computational approach may hold promise not only for understanding brain mechanisms of behavior, but also for understanding development, individual differences, and pathology of motor control.

A CONCLUDING REMARK

The general thesis underlying this paper is that it may be fruitful to approach the brain in terms of computations that are demanded by different tasks. We have suggested that one such basic computation is timing, and we think evidence implicates the integrity of the cerebellum as critical for accurate timing. Other candidate basic computations required for coordinated behavior may include the control of force or a parameter associated with force (e.g., Stelmach & Worringham, 1988; Wing, 1988) and mechanisms for organizing sequential actions (Cohen, Ivry & Keele, 1990; Keele, Cohen & Ivry, 1990). The focus of our continuing work is on identifying basic cognitive computations and the neural systems upon which they depend.

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DISCUSSION

J. FAGAN III (*Case Western Reserve University*): Do you have any premorbid evidence on the intelligence of the cerebellar patients that you mentioned earlier? The reason I ask is that many of the tests you use (such as reaction time in judging relationships and so forth) are similar to tasks that various people have found to be correlated with intelligence. I was wondering how good a control you had. Were your normal controls and your patients of roughly equal intelligence?

S. W. KEELE (*University of Oregon, Eugene, OR*): We haven't given any of the patients standard tests of intelligence. From the few patients that I have observed myself, I have no reason to think they are impaired in general intelligence. Let me comment, however, that the notion of intelligence would not be able to explain the patterns of deficit we find with cerebellar patients. In general, the patients show a deficit on timing but not on perceptual judgments of loudness. Patients with localized lesions in the lateral cerebellum show deficit in the clock component of timing; those with lesions in medial regions show deficits in the motor component. These kinds of patterns cannot be explained by a deficit in intelligence.

P. SOLOMON (*Williams College, Williamstown, MA*): I'm not sure I'm understanding your point entirely. Are you suggesting that the association between the CS and

the US may be made elsewhere in the brain? The job of the cerebellum is to time? The conditioning is elegantly timed.

KEELE: Well, I am really making a kind of orthogonal point. It is an important discovery that classical conditioning requires the cerebellum. Even in timing, there is a kind of learning. The intervals could be different lengths on another occasion so it is necessary for the system to "learn" on any particular occasion the time interval. The only argument here is that in the human cerebellum, the capacity to measure time may have become especially prominent. That property is used together with a conditioning capability to provide a general temporal device. I would argue, though, that not all kinds of motor learning occur in the cerebellum, only motor learning that regulates the temporal components.

SOLOMON: So, conditioning may be a special case of this temporal ability in the cerebellum?

KEELE: They are both of comparable status. Learning in the cerebellum involves more than association. It requires a precise temporal relationship between the two stimuli.

D. WOODRUF-PAK (*Temple University, Philadelphia, PA*): I wonder if you have performed a Wing analysis on data comparing young normals and old normals, and I wonder whether you would find age differences in the clock or in the motor . . .

KEELE: Yes, you do find age differences in clock variance. We have done that and there is about a 30 or 40% increase in clock variance in the elderly controls, as compared to the college-aged subjects. But there is probably a nonmeasurable difference in the motor variances as well.

H. NEVILLE (*The Salk Institute, San Diego, CA*): The cerebellum has recently being reported to be abnormally developed in autistic kids.

R. THOMPSON (*University of Southern California, Los Angeles, CA*): It is the vermis that seems to be involved, as far as I know.

L. NADEL (*University of Arizona, Tucson, AZ*): Do you mean Courchesne's work?[b]

THOMPSON: Yes, . . . as opposed to the intermediate or lateral regions of the cerebellum.

KEELE: So, there might be a guess there that if we are on the right track then those children should show an increase in motor variance. . . ?

THOMPSON: Yes.

KEELE: . . . rather than in clock variance. That would make an interesting contrast with a study done at Oregon by a couple of my colleagues. This study was not mentioned in my presentation but is summarized in the written report. They selected children who had scores indicating clumsiness on coordination tasks and contrasted them with children who had normal scores of coordination. They asked whether there is some more basic computation that is impaired in the clumsy children other than just performing poorly on a variety of tasks like balance and upper-arm coordination. The clumsy children showed an impairment on the clock component of motor timing. On the perceptual task of duration judgment they also showed a large impairment but no impairment on the loudness-task control. So, there might be a couple different kinds of clumsiness, one involving an aspect of the motor system and

[b]COURCHESNE, E., J. R. HESSELINK, T. L. JERNIGAN & R. YEUNG-COURCHESNE. 1987. Abnormal neuroanatomy in a nonretarded person with autism: Unusual findings with magnetic resonance imaging. Archives of Neurology **44:** 335–341.

another in the temporal computation. The children mentioned by Neville and Thompson might have a motor impairment.

M. NOETZEL (*Washington University School of Medicine, St. Louis, MO*): Have you done any studies on adults who had cerebellar hypoplasia, or some of the patients that you have studied who had the cerebellar atrophies? Have you studied them over time to indicate whether there is a further deterioration in their clock?

KEELE: I don't know what cerebellar hypoplasia is.

NOETZEL: It is a congenital malformation of the cerebellum in which the cerebellum never develops. Could the clock then appear somewhere else?

KEELE: We have never tested any patients like that. The patients who had unilateral lesions, though, were sometimes studied shortly after the lesion and sometimes after substantial recovery, and there does seem to be a bit of a difference there. Within about 8 months of a unilateral lesion there may be a perceptual deficit. Then with further recovery, the perceptual deficit may disappear, perhaps reflecting the possibility that cerebellum in either hemisphere could be used for perception of time. Even after substantial recovery, however, the ipsilateral hand remains impaired compared to the contralateral hand.

N. FOX: You said that there were unilateral prefrontal lesions. What was the distribution of side, and did that have any influence in terms of use of both the dominant and nondominant hand on your tests?

KEELE: Of those 12 cortical patients, all were run on the perception task, only eight of them on the tapping task. Of those 12 patients, I believe six were right and six were left patients. I don't know that those were broken down by side of lesion as far as the perception task, but on the average, the cortical patients had no particular deficit on the perceptual task. With respect to the tapping task, I have even a more evasive answer because of the 8 patients there I don't know for sure how many of those were right and how many were left.

FOX: My vague understanding, though, would be that the left prefrontal areas may be involved in sequential fine motor action and that damage there might have a more profound effect in terms of your tapping task than would an infarct involving right prefrontal cortex.

KEELE: I like that question for another reason, which is that in our conception one needs to distinguish between sequential representation and timing. That is, the sequential representation specifies what follows what. That representation would specify what force follows what force, what spatial target follows what spatial target, and what time follows what time. The latter is not timing per se but an aspect of sequence specification. I suspect that prefrontal regions (at least this is a hypothesis we are investigating) are responsible for sequential representation. Damage to that area, by this hypothesis, could impair knowledge of what times to produce but would not interfere with the timer per se.

The perceptual task is also not really a sequencing task; it is just comparing two intervals. I suppose in some sense you have to remember which interval was the first one but that doesn't make any particular demand on the sequencing mechanism. So, if I were to ask what kind of cortical area would act in concert with the timer to complete the computations necessary for that task, I would judge that it would be a temporal region and not a prefrontal region.

FUSTER: I would like to second that. Timing behavior is vastly different from the timing of behavior. Frontal cortex has something to do with the second, the timing of behavior, not with timing behavior. There is a difference.

KEELE: A difference exists, and one can get into a lot of arguments about this, but let's say that behavior, of course, takes place over time. That doesn't mean that it is all timed.

We must also distinguish between a representation of a sequence of different times and a clock that actually has the circuitry for producing the times. Consider a melody in music. One might speculate that the sequence of intervals that constitute the melody resides in the temporal lobe. That sequence representation is also responsible for directing motor systems to the correct keys in production, say, on the piano. In fact, we believe that we have some evidence that sequence representation is not in the motor system but in a more modality-specific system. (That is a problem in which we are currently investing quite a bit of effort.) Now, in such a conception the sequence of times may be cortically represented, but the neurological system that implements a requested time is in the cerebellum. This would be much like the setup in a computer. A clock in the computer knows nothing about what interval follows what interval. When the program requests an interval, however, such as an interval of 400 msec, then the clock can meter out that interval. We believe the cerebellum is the clock, but we suspect that it is not the place that stores the pattern of successive intervals.

The upshot of this is that a cerebellar patient probably should have no difficulty matching auditory temporal patterns to visual temporal patterns. In other words, as long as the cerebellum was intact enough to be able to say that the first interval is long, the next two are short, and so forth, then a cortical mechanism that stores the patterns could make the decision. There are probably several computations involved in something like appreciating a temporal pattern. Only one of those computations would involve the actual timing of an interval. It looks as though some good studies could be done here.

J. RANCK, JR. (*SUNY Health Sciences Center, Brooklyn, NY*): One of the most exquisitely timed of all behaviors is swallowing, in which 24 or so sets of muscles have to act in order. If they don't do it in the right order, food goes backward. There is a lot of sequencing, but at least there is some timing. And, of course, the swallowing has to work perfectly at birth, yet the cerebellum isn't quite put together at birth.

KEELE: Again, all I can say is that sequencing and timing are not the same thing, so you have to make sure that you are dealing with precise temporal control rather than just keeping things in the proper order. So one would need to examine whether there is a temporal deficit.

R. CLIFTON (*University of Massachusetts, Amherts, MA*): But swallowing doesn't work perfectly at birth; they spit up all the time. Things come back up a lot in the newborn. As the infant gets older, you don't have that problem anymore. It isn't very well timed at birth.

RANCK: All right.

R. NAKAMURA (*National Institute of Mental Health, Rockville, MD*): Is that timing or sequence?

CLIFTON: Perhaps sequence, but I'm not sure.

KEELE: I should make another comment with respect to that, and, again, these kinds of things are speculation on my part. But, when we say that the analysis shows that there is a motor deficit following the medial cerebellar lesions, does that mean temporal computation does not occur there as well? My intuition is that probably even those regions provide a kind of temporal component, but those temporal components are on a much faster time scale, and they are for particular kinds of motor acts. For example, locomotion is disturbed by only medial damage, as I understand it, say, from the work of Arshavsky.[c] Among the analyses that I have looked at, if you analyze what contribution the cerebellum is making to locomotion, I claim that it is a kind of temporal contribution. It is not timing the legs, but it is measuring the temporal output that goes from spinal generators to the legs. It is measuring that, and then using the result to control the time at which descending motor commands are modulated. So, one could probably pursue the case that even the medial portions of the cerebellum are to a very large degree involved in controlling the timing of more molecular aspects of particular movements.

E. KNUDSEN (*Stanford University School of Medicine, Stanford, CA*): How is that consistent with the role of the cerebellum in the adjustment of saccadic eye movements, saccadic dysmetria? Can you get some sort of a timing aspect to that control?

KEELE: This raises another issue. One would never want to get put in the position of saying that there are not other computations that occur in a structure as large as the cerebellum. The one example that I am familiar with, that I can't think of any kind of timing explanation for, is the work by Gilbert and Thach (1977) that suggests that there is a kind of gain (or magnitude adjustment). I don't know how gain can be translated into time. (Maybe somebody else has an idea on that.) So, also in a case like dysmetric eye movements, maybe there is a gain problem there. But there is another aspect to consider, and I would need to know a little bit more about how eye movements function. If you make rapid flexion movements, cerebellar damage will also affect that. But the way in which it appears to happen is this: You have an agonist EMG burst. In normals that terminates rather abruptly and is replaced by an antagonist EMG burst, and then sometimes there is a third EMG burst in the agonist again. You have a so-called triphasic pattern. If you look at cerebellar patients, what seems to be impaired are the temporal relationships between those components, so that the initial agonist burst sometimes lasts longer than it should, and the antagonist burst sometimes overlaps with the other one at variable degrees. That kind of deficit will produce a kind of dysmetria. I also speculate that the timing of that pattern is perhaps a medial function, but I'm not sure. Maybe eye movement dysmetria can be explained in a similar way.

KNUDSEN: Part of it can and part of it can't. There are two parts: The initial part that you're talking about is similar to controlling an arm movement, but there is also the step, the holding force. That also needs to be adjusted, and that also is dependent upon the cerebellum, a different part of cerebellum.

KEELE: Well, that could be a kind of gain.

KNUDSEN: That is more like a gain, right.

[c] See Arshavsky *et al.*, 1983.