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THE CEREBELLUM AND THE ADAPTIVE COORDINATION OF MOVEMENT

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INTRODUCTION

Despite continuing work on the structure and function of the cerebellum, there is still no consensus as to what it does or how it does it. Its distinguishing features are well known, but they have not been fit together into any comprehensive, coherent model of function. The question remains: What is the fundamental cerebellar operation that so depends on the stylized and stereotyped circuitry, employs such highly individualistic interactions among its neurons, gives rise to characteristic pathologic signs when damaged, and is so subtly associated with the integrated motions of the vertebrate body?

Two pieces of relatively new information encouraged this attempt at a model of cerebellar function: first, the mapping of body parts and modes of motor control within the deep nuclei (Asanuma et al 1983c, Kane et al 1988, 1989, Thach et al 1982, 1990a,b); and second, the newly assessed, much longer length of the cerebellar parallel fiber (Brand et al 1976, Mugnaini 1983). Our goal has been that the model should explain both the regional differences in cerebellar function and the one generalized function that has long been implied by the stereotype of the intrinsic circuitry. To this end, we review evidence that 1. the body is mapped separately within each of the three deep cerebellar nuclei, that 2. the nuclei operate in parallel, each nucleus controlling a different mode of bodily

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movement, and that 3. each mode is a function of the input and output connections of that nucleus. We show that 4. the beams of Purkinje cells, so linked by parallel fibers, project onto the nuclei and thus link the actions of the different body parts represented within each nucleus and the different modes of control across the nuclei into coordinated movement. We suggest that 5. the job of the cerebellum is thus to coordinate the elements of movement that reside in its downstream targets and 6. to adjust old and learn new movement synergies.

THE OUTPUT SIDE OF CEREBELLAR PROCESSING: MULTIPLE SOMATOMOTOR REPRESENTATIONS WITHIN THE DEEP NUCLEI

A series of anatomic pathway tracing studies on the macaque have helped clarify the connections and topographic organization of the deep cerebellar nuclei (Asanuma et al 1983a–d, Kalil 1982, Orioli & Strick 1989, Schell & Strick 1983, Stanton 1980), and are summarized as follows:

The output of the cerebellum, the cerebellar nuclei, project to a target area within the thalamus that is sufficiently free of other inputs as to be called "cerebellar thalamus" (Figure 1). The target area includes several architectonic subdivisions, VLc, VLps, VPLo, and X. The basal ganglia input to the thalamus arrives more anterior in VLo and VA, and the lemniscal arrives more posteriorl in VPL. This cerebello-thalamic target area projects to area 4 (VLc, VLps, VPLo, and parts of VLo) and to lateral area 6, the periarcuate area (X). In addition to this "specific" cerebellar-thalamic receiving area, there is a "nonspecific" thalamic target area, which projects more widely to the cerebral cortex: the centrum medianum.

Dentate and interposed nuclei each project in completely overlapping fashion to the whole width (coronal) of the contralateral thalamic receiving area; the fastigius projection is sparse, bilateral, and restricted and appears not to project to Xo. This itself suggests that at the level of cerebellar outflow, control of the thalamic target is multiple and is repeated across each nucleus. [The projections of the three nuclei arrive in register at a macro level only; at the cellular level, they appear to interdigitate in patches (interpositus) and rostrocaudal rods (dentate) (Asanuma et al 1983c).]

From the known somatotopic mapping in the cerebellar thalamus (Strick 1976), and from the topographic projection of each nucleus onto the common thalamic target, somatotopic mapping may be inferred within each of the cerebellar nuclei. In the cerebellar thalamus, the head is medial, tail lateral, trunk dorsal, and extremeties ventral; in the cerebellum, the head would then be caudal, tail rostral, trunk lateral, and extremities medial (Asanuma et al 1983c). This map has been supported by neural

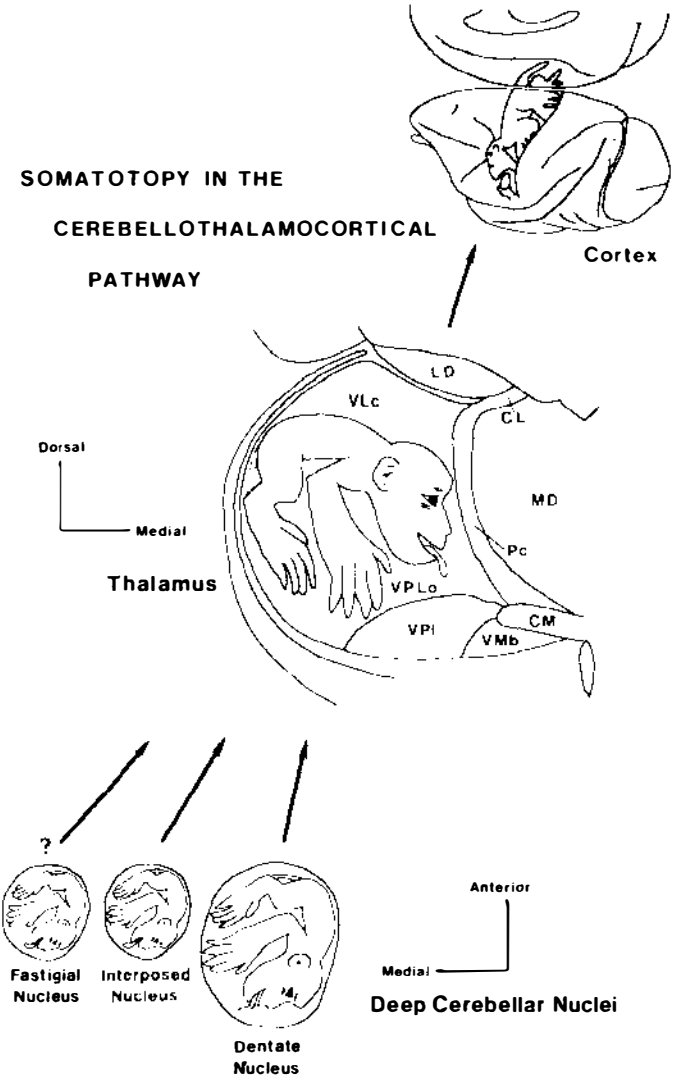

Figure 1 Diagram of the body representation with each of the deep cerebellar nuclei, thalamus, and motor cortex. VL_c, Ventral Lateral Nucleus, caudal division; VL_{ps}, Ventral Lateral Nucleus, pars postrema; VPL_o, Ventral Posterolateral Nucleus, oral division; X, Nucleus X; VA, Ventral Anterior Nucleus; VL_o, Ventral Lateral Nucleus, oral division (adapted from Asanuma et al 1983c).

recording and inactivation studies during movement (Kane et al 1988, Thach et al 1982, 1990, 1991) and is consistent with the electroanatomical *input* mapping studies in macaques of Allen and colleagues (1977, 1978).

Is the overlap complete? In the anatomical studies, the fastigius may not project to X, the medial and anterior extent of the cerebellar thalamus. This may suggest that the dentate and interpositus but not fastigius control lateral area 6, the periarcuate area. Orioli & Strick (1989) and Sasaki et al (1976) have raised the question in macaques of whether the cerebello-thalamic projection controls even further anterior cortical areas, such as area 8 and beyond.

Is there only one map per nucleus? A number of studies have raised the question of whether there is more than one body map per cerebellar nucleus (Orioli & Strick 1989, Schell & Strick 1983, Stanton 1980). If there is a separate body representation within lateral area 6 of cerebral cortex and in nucleus X of thalamus, this would seem a likely possibility.

This is not to say that the cerebellar output is exclusively or even mainly directed to the thalamus and cerebral cortex: The dentate projects to the parvocellular red nucleus, the reticular nucleus of the pontine tegmentum, and the inferior olive [principal (PO)]; the interpositus projects to the magnocellular red nucleus, the reticular nucleus of the pontine tegmentum, the inferior olive [dorsal accessory (DAO)], and the spinal cord intermediate grey; the fastigius projects to lateral and descending vestibular nuclei, the n. reticularis tegmenti pontis and prepositus hypoglossi, the reticular grey of the midbrain, the inferior olive [medical accessory (MAO)], and the contralateral motor neurons in the spinal cord (Asanuma et al 1983d).

CODING: WHAT DO THE MULTIPLE MAPS IN THE CEREBELLUM CONTROL?

If there is a separate body representation within each nucleus, it seems likely that each should control some different aspect of bodily function. Nevertheless, suggestions vary as to what that may be.

Parameters, Gain, or Something Else?

Holmes (1939), in his final analysis of cerebellar deficits, had factored the deficits into possible errors of start, stop, direction, acceleration, velocity, and force (cf. Brooks & Thach 1981). Evarts developed a technique for determining whether CNS neurons code for physical parameters of movement at single joints. The Evarts technique proved useful in testing the hypothesis of whether the causation of movement is a serial process in which each parameter is specified one after another, each in a different

part of the brain (Allen & Tsukahara 1974, Eccles 1967). The predictions were that (*a*) the movement command for initiation of movement was generated in the motor cortex–dentate loop at the motor cortex or dentate; (*b*) the ongoing movement would be servo-controlled by the interpositus, which would compare the command from the motor cortex and the feedback from spinocerebellar pathways and would execute the corrected commands through interpositus projections back to the motor cortex (via the thalamus) and rubrospinal neurons (Allen & Tsukahara 1974, Eccles 1967, Evarts & Thach 1969). The results of these experiments showed in the onset of activity of the different parts of the brain—dentate, motor cortex, interpositus—slight timing differences in the order predicted. Nevertheless, just as impressive was the near-simultaneity of onsets and the great overlap of discharge patterns (e.g. Thach 1975, 1978). Moreover, the order of the timing differences varies among the different tasks, suggesting that in some instances the dentate might be the site of the movement initiating command and in others, the interpositus (Thach 1978). This question was reviewed recently (Brooks & Thach 1981), but it is important to summarize the evidence in the light of the newer evidence and interpretation that follows.

The *dentate* and the lateral cerebellar hemisphere receive input via pons from frontal and parietal association cortex (cf. Allen et al 1978, Brodal 1978); the dentate has been thought to translate mental percepts and concepts into action plans for movement (Allen & Tsukahara 1974, Brooks & Thach 1981, Eccles 1967, Evarts & Thach 1969).

In keeping with this notion, dentate neural discharge was reported to precede movement onset performed by trained monkeys, and even to lead the discharge of motor cortex neurons (Lamarre et al 1983, Thach 1975, 1978, but see Grimm & Rushmer 1974). Correspondingly, dentate inactivation was found to delay the onset of discharge of motor cortex neurons (Meyer-Lohman et al 1975, Spidalieri et al 1983) as well as the onset of movement (Meyer-Lohman et al 1977, Thach 1975, Trouche & Beaubaton 1980). This finding was interpreted to support the idea that the dentate participates in initiating volitional movement from the motor cortex (Evarts & Thach 1969, Brooks & Thach 1981). The problem with this interpretation has been that the onset of movement is only slightly delayed by 50–150 msec. Unless the purpose of the dentate is to provide that little extra speed of reaction, the paucity of the observed deficit does not appear commensurate with the phylogenetically increasing size of the dentate nucleus.

Direction of movement has been seen in several studies to correlate with the discharge of dentate, interposed, and Purkinje neurons (Fortier et al 1989, Thach 1970a,b) and in one study with dentate but not interposed

neurons (Thach 1978). In other studies, in which different tasks were performed, little (MacKay 1988a,b) or no (Schieber & Thach 1985) direction signal was found in the dentate. Furthermore, even in studies in which dentate discharge did correlate with movement direction (Mink & Thach 1991a), the direction of the movement did not depend on a dentate direction signal: Sudden inactivation of the dentate during performance of a variety of tasks involving flexion or extension of the wrist produced no errors of these flexor and extensor directions (Mink & Thach 1991b).

Pathologic tremor (over 5 degrees amplitude, 3–6 Hz) has been attributed to dentate ablation in a number of animal studies (Botterell & Fulton 1938b, Brooks et al 1973, Cooke & Thomas 1976, Goldberger & Growden 1973, Vilis & Hore 1977, 1980). Indeed, in all of these studies, tremor appeared to be the salient deficit. The possibility remains, however, that the reason for the lack of greater deficit in task performance in these studies is that the neurons were controlling some process other than the movements in the tasks.

The *interpositus* receives fast feedback from movement and spinal motor programs via various spinocerebellar pathways and receives input also from the motor cortex via the pons (cf. Bloedel & Courville 1981). The theory held that the interpositus compared the command for movement and the feedback from the movement, sensed errors, and corrected them quickly during the course of the movement (Allen & Tsukahara 1974, Eccles 1967, Evarts & Thach 1969).

Timing studies in trained, visually triggered movements have shown that the order in which the interpositus begins to fire relative to the dentate and motor cortex is last (Thach 1978), but in movements triggered by a somatosensory perturbation of the part to be moved (wrist), the interpositus was first (Thach 1978). A crucial observation was made by Strick (1983): When the movement was made to oppose the perturbation, the interpositus led dentate; but when the movement was made in the direction of the perturbation, the dentate led interpositus. The interpositus therefore led when the reaction was hardwired, as in the stretch reflex ("hold a position despite displacement"); the dentate led when the reaction was counter-instinctive and learned ("go in the direction you are pushed").

In coding studies, Burton & Onoda (1977, 1978) and Soechting et al (1978) identified signals correlated with velocity and force during movements made by cats. Thach (1978) documented force and position correlations during positions held by monkeys; but in the latter study, coding was not absolute. Additions of load influenced the extent to which the neurons coded for position or force, as it did also with the muscle electromyogram (EMG) (cf. Schieber & Thach 1985). Schieber & Thach (1985) found no parameter correlations in interposed neurons during smooth-

pursuit wrist tracking. They noted a pattern of increased discharge at the beginning of movement, regardless of the direction (flexor or extensor) and regardless of load or muscle pattern (increasing loaded flexors or decreasing loaded extensors) used to make the movement. This "bidirectional" discharge pattern was also seen in the discharge of Ia spindle afferent neurons (Elble et al 1984, Schieber & Thach 1985), and both the Ia's and the interposed neurons carried a signal of the animal's own tremor. Repeated penetrations into the interpositus increased the amplitude and slowed the frequency of the tremor. This result appeared compatible with the suggestions of Vilis & Hore (1977, 1980) that physiological tremor and cerebellar tremor both originate from instability of the stretch reflex. It also appeared to be consistent with the theory of MacKay & Murphy (1979) that the purpose of the cerebellum is to control the gain and stability of downstream structures (Thach et al 1986).

Since the gamma loop was active in EMG-silent, shortening, or lengthening muscle, it was inferred that gamma motoneuron discharge was present in the absence of alpha motoneuron discharge (alpha-gamma dissociation). This was discussed as a possible means of reducing tremor and small movement irregularities in the "one-muscled" movement.

What perhaps is more surprising is not that interposed and dentate neurons should resemble gamma motoneuron-stretch reflex loop activities (the two have long been known to be related), but that there should be no nuclear neural activity resembling that of alpha motoneurons, despite the many prior papers that have shown the expected load, position, and direction signals in these nuclei. Was there something about this task and what the cerebellum contributes to movement that took the alphas out and left the gammas in? As discussed below, we believe that the critical factor in this task was that the animals were trained for over two years until all EMG activity occurring in the task was confined to the loaded wrist extensor or flexor muscles. The gamma loop activity was not so constrained; indeed, it was fully present in the unloaded, EMG-silent antagonist muscle, and may have been present in muscles over other joints as well.

Heretofore, the interposed nucleus (nuclei globose and emboliform in man) has had no well-identified ablation syndrome attached to it. Uno et al (1973) reported that local cooling of the interposed nucleus did not result in the prominent errors of rate, range, and force seen following dentate cooling. Interpositus ablation has since been seen to cause an accentuation of dentate tremor (Goldberger & Growden 1973).

Others have emphasized impairment by interposed ablation of certain types of task performances, such as contact placing (Amassian et al 1972a,b, 1974, Amassian & Rudell 1978) and the learned nictitating mem-

brane response (McCormick & Thompson 1984, Yeo et al 1984). These findings [with the observations above of Thach (1978) and Strick (1983) on discharge patterns compatible with long loop stretch reflex operation] would suggest the involvement of the interpositus in the control of some tasks and not others.

The *fastigius* has inputs from the vestibular complex, lateral reticular nucleus, and (indirectly) the spinocerebellar pathways (Brodal 1981, Jansen & Brodal 1940). It has been assumed to control proximal musculature, or stance and gait, or both, and has not been considered in models of voluntary control of limb movement (Allen & Tsukahara 1974, Eccles 1967, Evarts & Thach 1969).

Fastigial single-unit recordings during trained limb movement in monkeys have nevertheless been reported to correlate with force and its time derivatives (Bava et al 1983, Bava & Grimm 1978). The suggestion was made that the fastigius controlled the force of movement (and the time derivatives of force) and that the interpositus and dentate controlled progressively more abstract properties of movement, such as sequencing (Grimm & Rushmer 1974).

Other single-unit recording studies in the fastigial nuclei of decerebrate cats made to undergo walking and scratching movements have shown neural discharge correlated with the movements but have found little or none in the interpositus and dentate, respectively (Antziferova et al 1980, Arshavsky et al 1980). Fastigial ablation has been shown to impair stance and gait (Botterell & Fulton 1938a, Sprague & Chambers 1953; and see below). These observations would be more consistent with a role specialized for control of stance and gait.

MacKay (1988a), in recording from all three deep nuclei during visually triggered, single-jointed elbow movements, found little relation to distal movements or movement parameters, including direction, velocity, force, and muscle group. Yet small differences in timing served to distinguish the three nuclei (dentate fired earliest, interpositus next, and fastigius last, in agreement with other studies of Bava et al 1983, Bava & Grimm 1978, Thach 1970a, 1978a). MacKay concluded that "all three nuclei work to stabilize the same motor performance but at different levels." In studies of multijointed reaching movements (MacKay 1988b), neurons tended to discharge maximally at lift-off and minimally during returns to rest and decelerations in midtrajectory. Again, discharge appeared related exclusively to proximal movements, and with "no observable relation to kinematic parameters." The timing sequence was now changed, with fastigius firing first and interpositus last. Aside from timing, there was nothing else in the discharge that distinguished one nucleus from another.

In a recent study (Kane et al 1988, 1989, Thach et al 1990a,b, 1991), unit

activity was recorded in the cerebellar nuclei as the monkeys performed five trained movements of the wrist. The job of the animal was to flex or extend the wrist to line up the cursor within the target window on an oscilloscope (Figure 2*a*) and to maintain the alignment as the window moved. The animals performed five tasks designed to dissociate hypothetical functions of the nuclei: (*a*) Jerk, a prompt visual triggered move; (*b*) Jump, identical to that above, except required to stop within the visual target; (*c*) Pert, return to hold position after perturbation by torque step; (*d*) Ramp, tracking of visual target; (*e*) RAM, self-paced rapidly alternating movements. All tasks were performed in two directions, under two loads. The earliest changes were seen in the dentate on the Jerk and Jump tasks. The interpositus showed the earliest changes on the Pert task, and alone showed modulation in relation to tremor on the Ramp tracking. The interpositus

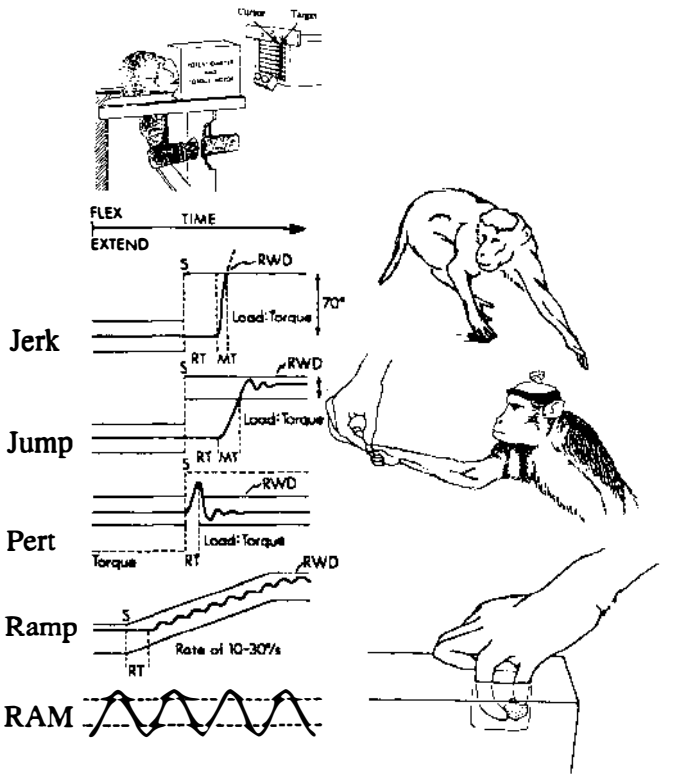

Figure 2a Two batteries of behavioral tasks. Trained wrist movements are on the *left*. RT—reaction time. MT—movement time. RWD—reward. Nontrained multijointed movements are on the *right*.

and dentate showed equal modulation on the RAM task. Fastigial neurons occasionally showed modulations, but without the trial by trial or temporal consistency seen for the other two nuclei. The results of this unit discharge-behavioral correlation study were thus somewhat similar to those of MacKay's (1988a,b). Both the dentate and interpositus seemed to contribute to some extent to all tasks, but at different times and intensities. The fastigius lacked consistent movement correlations, thus raising serious questions about whether it was taking part in these movements.

To see whether parameters of movement or movement stability depended on the neural discharge with which it was correlated, the different nuclei were inactivated with muscimol (temporary) or kainic acid (permanent) while the proficiency of performance was monitored (Kane et al 1988, 1989, Thach et al 1990, 1992). Any impairment was documented by comparing the pre- and post-injection movement traces. Several variables were examined, including onset and termination times, movement time, direction, velocity, amplitude, tremor, and EMG patterns.

For the dentate, there was a slight (47 ms) delay in reaction time on Jerks and Jumps only. There was no overshoot of final target position. There was a tremor during Ramps only; the tremor was transient, even after permanent kainate ablation. Perts and RAMs (except for superimposition of tremor) were normal. For the interpositus, a slight (10–20 msec) delay in the reaction time on Perts occurred after one muscimol injection. A tremor appeared at the end of Jumps and Perts and during Ramps; the tremor persisted. No consistent change was seen in frequency, amplitude, or regularity of rapid alternating movements, except the superimposition of tremor. The fastigius showed no detectable abnormality in the performance of any of the five trained wrist movements. Similar small delays and irregularities of velocity and force in single-joint tracking (Beppu et al 1984, 1987) and in isometric force (Mai et al 1988) and EMG (Hallett et al 1975) have been seen in studies in cerebellar-damaged patients.

To summarize: In no instance did inactivation abolish the task performance; and the inactivation was immediate, before compensation could have occurred. Inactivation of the dentate and interpositus delayed the onset of task performances with which the neural discharge appeared best to correlate, but the impairment was often so slight as to be just barely detectable. Neither was the choice of direction or velocity of movement impaired. The most conspicuous defic
several conclusions:

1. the cerebellar nuclei are not significantly reponsible for the generation of any one of the modes of movement in this study;
2. the cerebellar nuclei are not significantly responsible for control of any

of the physical movement parameters underlying these movements, excepting possibly initiation and stability;

3. the actions of the cerebellar nuclei may either be responsible for the "fine control" of any and all movement; or
4. the modes of movement that the cerebellum really controls were not included in this study.

The seemingly contradictory set of findings across the many studies of (*a*) a good correlation of discharge with some aspects of the behavior (some studies) and (*b*) little or no deficit in that behavior after ablation, again raises the perplexing question of what it is that the cerebellum does. Gain control would seem to be the logical answer. In this model, the role of the cerebellum would be through tonic discharge simply to maintain the adjustment of downstream structures—thalamus and motor cortex, red, reticular, vestibular nuclei, and spinal cord—which in turn are directly responsible for the initiation and execution of movement. Nevertheless, this idea is intuitively unsatisfying. Why should there be so elaborate an apparatus for so trivial a purpose? Engineers accomplish the same task with trimpots, tiny simple potentiometers, which very accurately bias and balance high performance amplifiers. Is there some other kind of behavior we are missing?

One idea is that the behavior is purely mental, and that we miss it in animal studies and in the routine cerebellar neurological examination because we cannot or do not look for it. Time and space do not permit review of this burgeoning body of material, however. As the quest for what-it-is-the-cerebellum-does threatens to veer away from movement and toward mind, it is useful to consider again an old question:

DOES THE CEREBELLUM PREFERENTIALLY CONTROL THE COORDINATION OF MULTIJOINTED MOVEMENTS?

The Multijoint Coordination Model Versus the Single-joint Modulator Model

It is widely held that the cerebellum coordinates movement. This idea is not a new one; its foundation dates back to 1824 when Flourens concluded, following cerebellar ablations in the pigeon, "the will, the senses, the perception remained, but the coordination of movement, the ability for controlled and determined movement, was lost" (Flourens 1824).

Babinski (1899, 1906) supported this idea in his observations and inferences from a patient who, when instructed to point his toe at a target above his supine body, first flexed the hip, and only after extended the

knee. Termed "asynergia," the deficit also implied of ability to coordinate the two joints simultaneously to the purpose of the task. The observation of decomposition of movement in patients with cerebellar deficits led Babinski to the same conclusion that one of the primary functions of the cerebellum is to link together the constituent, simpler movements that make up volitional, compound movements (Babinski 1899, 1906).

But the idea that the cerebellum plays a specific combining role in the coordination of movement has not gained universal acceptance, especially in the English-speaking nations. One of its earliest opponents was none other than the celebrated British neurologist, John Hughlings Jackson. Jackson wrote, "It will not, at all events, suffice to speak of coordination as a separate 'faculty.' Coordination is the function of the whole and every part of the nervous system" (Jackson 1870, as cited in Taylor 1932).

Luciani (1915) was even more explicit. After having described a variety of movement abnormalities produced by cerebellar ablation, he proposed that all could be explained by three primary deficits: atonia, astasia, and asthenia. The function of the cerebellum, he concluded, was to exert a supportive influence on the rest of the nervous system, which was necessary for its fine adjustments (cf. MacKay & Murphy 1979). Upon observing that a dog with half of its cerebellum removed was still capable of swimming "with perfect coordination," Luciani dismissed Fluorens' theory (of the cerebellum as being the seat of and necessary for coordination) as being "a fictitious entity, obscure, imperfect, and unintelligible." Further, that it "opens a false track to subsequent workers and has become a serious obstacle to advance in the physiology of the cerebellum."

Yet, it is interesting to note that Luciani's criticism of coordination comes but one page after the following statement: "when standing and walking, the cerebellum intervenes less as an organ for preserving equilibrium than as an organ which regulates tone and contraction of muscles to the right extent and in the proper combination."

Luciani's reductionist approach greatly influenced another British neurologist, Gordon Holmes. A tribute to Luciani concludes the final interpretation (Holmes 1939) of his own meticulous studies of acute cerebellar injury of man performed during WWI (Holmes 1917, 1922). Following cerebellar injury, Holmes had noted that simple movements, those that occur in one direction and at one joint, could be disturbed in rate, regularity, and force. In the last paragraph that he wrote on the subject, he ends: "In his classical contributions to the physiology of the cerebellum Luciani described as the three symptoms of cerebellar defect: atonia, astasia, and asthenia. These three symptoms occur in man as a result of acute cerebellar lesions and by them the irregularities of movement which constitute cerebellar ataxia can be fully explained" (Holmes 1939).

As for the irregularities observed in multijoint movements, Holmes concluded that they were the result of the errors in the constituent single joint movements, combining "as it were in geometric progresion so that the error of the whole movement is relatively greater than the sum of its parts" (Holmes 1939). He preferred to explain decomposition of movement not as a primary defect in combining movements, but rather as caused by the delay in initiation and the excessive range of movement of any one and all of the component movements relative to each other, and to defective postural fixation (Holmes 1939). Yet, Holmes provided no data on single joint-multijoint movement comparisons. Indeed, he presented some evidence against the hypothesis: "I have studied the relations of such simple synergies as extension of the wrist on flexion of the fingers, but though tracings show that when the fingers suddenly close wrist extension is less regular than normal, this does not appear to be an important element or specific factor of 'cerebellar ataxia'" (Holmes 1939). Is it possible that Holmes' elegant interpretations overcame his own evidence?

Whatever the case, the argument of Jackson, Luciani, and Holmes clearly asserts that the cerebellum exerts control primarily over the single joint has dominated physiology. And because other motor components, like the pyramidal system, even more conspicuously control single joints (Lawrence & Kuypers 1968, Schieber 1988), the role of the upstream cerebellum has inevitably been relegated to that of "modulation" of its downstream initiators and generators. Thus, Holmes (1939) stated: "The conclusions can be drawn that, in addition to regulating postural tone, the cerebellum reinforces or tunes up the cerebral motor apparatus, including subcortical structures with motor functions, so that they respond promptly to volitional stimuli and the impulses from them which excite muscular contractions are properly graded." And, Denny-Brown (1968) stated: "The cerebellum is not essential to any of these [pyramidal and] extrapyramidal mechanisms, but it exerts a modulating effect on all of them. . . . The cerebellum regulates the gamma discharge associated with all motor responses, but its modulating effect is still present in movements initiated by direct alpha drive in a deafferented limb." The statements foreshadow the important work of Gilman on the cerebellar control of gamma motor neuronal discharge in hypotonia (Gilman 1969) and of its independent control of alpha routes in ataxia (Gilman et al 1976, cf. also Granit et al 1955). The statements are compatible with the modern emphasis on primary cerebellar roles in stability control and tremor (Elble et al 1984, Glaser & Higgins 1966, Henatsch 1967, Matthews 1981, Schieber & Thach 1985, Vilis & Hore 1977). They point toward the reflex gain control (MacKay & Murphy 1979) and stability control (Thach et al 1986) theories of today.

We have previously interpreted the dramatic correlation of interpositus neural discharge with tremor and the production of tremor by interposed inactivation to support the argument for gain control (Elble et al 1984, Thach et al 1986) as have others before us (Glaser & Higgins 1966, Henatsch 1967). The argument runs that, because oscillation is a problem inherent in the mechanical-reflex design of the motor system, the cerebellum or other component of that system may have evolved as a specific solution to the problem: to actively damp the oscillation. The same problem of oscillation occurs in mechanical and electrical systems, and the solution of active damping is adopted in both: one uses dashpots, and the other uses resistors. If it is conceded that the cerebellum may damp oscillation, the question remains as to the mechanism: whether at the level of segmental stretch reflexes via gamma motor neuron modulation (Gilman 1969), or in a long loop at the level of motor cortex (Vilis & Hore 1977, 1980), or both. This mechanism still seems plausible because cerebellar units often have appeared to relate poorly or not at all to the various parameters of the task that the EMG and alpha motor neurons relate to; cerebellar units under certain conditions have related very specifically to activities of the gamma-reflex loop; cerebellar ablation has mainly given rise to instability and tremor, with little or no effect on other aspects of certain task performances; and cerebellar output is tonically active and, therefore, a priori influences the sensitivity of downstream targets to other inputs.

But does the cerebellum only control the gain and stability of downstream elements? Despite the physiologist's acceptance of the single joint hypothesis, many neurologists still infer from clinical observation that the function of the cerebellum is preferentially concerned with compound multijointed movement, and that the loss of this function is the major symptom of cerebellar damage (Rondot et al 1979). Even Dow (1987) in attempting to summarize Holmes' description of cerebellar deficits states, "when movements involve two or more joints acting synchronously or simultaneously, the disorders are more than the sum of each of its parts." This apparently amounts to a clinical intuitive feeling that the parts, that is, the deficits at single joints, do not add up to the whole, that is, the deficit in compound movements. Yet no one has really added up the parts to see whether the whole exceeds the sum or not.

Some other suggestions of a cerebellar mechanism for coordination can be found within the literature. Nashner has shown that in response to forward or backward platform translation, which produces primarily rotation of the body around the ankle joint, the normal subject compensates with a preprogrammed, fixed synergic pattern of rapid muscular contractions involving not only the muscles of the ankle, but hip and

knee as well. In a study of patients with cerebellar diseases, primarily degenerative diseases of the cerebellar cortex, Nashner & Grimm (1978) reported abnormalities in the synergic response to perturbation. There were gross delays between normally linked pairs of muscles and trials in which there was a complete absence of response in some muscles, as if the mechanism that coordinated this group of postural muscles during stance were lost.

Electrical stimulation of the baboon's dentate nucleus produced two distinct types of movement: "simple" and "complex" movements (Rispal-Padel et al 1982, 1983). Simple movements consisted of the unidirectional displacement of a limb segment around a single joint with the cocontraction of muscles around a nearby joint. Thus, for simple movements, the dentate signal appeared to carry information not only of which limb segment to move but also the postural fixation necessary for that movement to occur. Complex movements involved the displacement of two or three joints, usually noncontiguous. These movements were stereotyped and indissociable. Both types of movements could be the result of cerebellar control of muscle synergies.

At this point, the question should be stated precisely: Does the cerebellum independently control the muscles that operate each joint, or does it have a specific role and mechanism for combining the many muscles that operate many joints in a multijoint movement? Although many studies have recorded units or ablated during single-joint tasks, and many other studies have recorded or ablated during multijoint tasks, we have found no study that has both recorded and ablated during both single-joint and multijoint tasks. Indeed, only three studies either record or ablate during both single-joint and multijoint tasks. The results of these are interesting:

Van Kan et al (1986) reported in a published abstract that interpositus cells, which responded well to free-form reaching, did not correlate as well to movements about a specific joint.

Yet, Harvey et al (1979) recorded the activity of 129 related single units in the dentate and interpositus nucleus during a whole arm reaching task. They attempted to demonstrate relation of these units to a specific joint involved in reaching through "gentle manual restraint" of specific joints to reduce the task to that of a single joint. For 50 of the 129 neurons (38,76%), there was an association with movements about a particular joint (wrist, elbow, or shoulder) or whole hand finger flexion or extension.

Kane et al (1988, 1989) and Thach et al (1990, 1992) studied the effect of nuclear inactivation across nuclei on the performance of five trained single-joint tasks, and, in the same animals in the same sessions, on the performance of five untrained tasks. The untrained activities consisted of sitting, standing, walking, reaching out for bits of food, and picking small

bits of food out of deep narrow food wells with a precision pinch of the fingers. Stance, sitting, and walking were evaluated immediately after the animal was released from the primate chair in which the injection had been stereotaxically delivered. Reaching involved coordinated movement of shoulder and elbow; reaching was performed while sitting and standing on the floor, and while sitting in the primate chair. The precision pinch task required coordinated movements of the hand and fingers, including the pinch per se of thumb and forefinger and "tea-cup" posturings of the other digits to keep them out of the way of the edges of the food well. Movements were movie-filmed or video-taped and graphically reconstructed.

Each nuclear inactivation produced an incapacitating impairment of bodily movement. But for each nucleus, the type of deficit was uniquely different (Figure 2*b*). Fastigial inactivation prevented sitting, standing, and walking, with frequent falls to the side of the lesion. Interposed inactivation caused a severe action tremor of 3–5 Hz during reaching, but not during sitting, standing, or walking. Dentate inactivation caused excess angulation of shoulder and elbow in reaching, which resulted in overshoot of the target, and an increased use of single-digit strategies in attempting

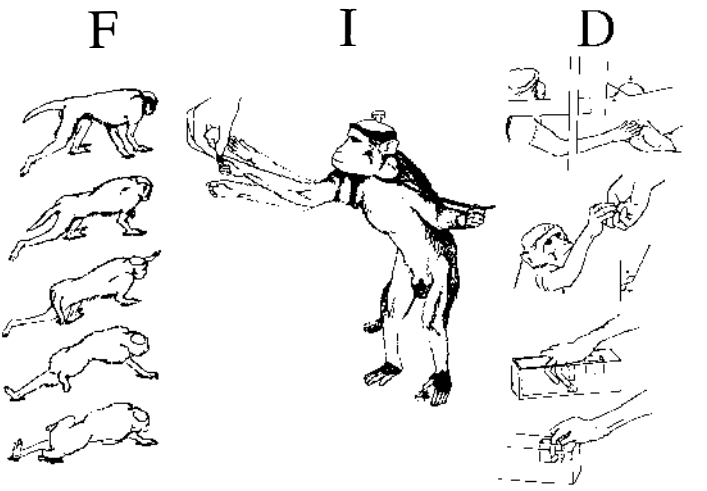

Figure 2b Major deficits produced by micro-injection of muscimol and kainic across the tasks. F represents sitting and stance after each of two fastigial muscimol injections. The figures represent sequential video frames in the course of falling that was caused by an ipsilateral muscimol injection. I represents arm position during reaching after interpositus injection of muscimol. D—deficits in reaching and pinching after dentate injection of muscimol.

to pinch and pick up food morsels, from which we inferred an incoordination of compound finger movements. The deficits were qualitatively more severe than any deficits seen in the simple, single-jointed wrist movements. Our interpretation was and is that nuclear discharge would have been primarily concerned with this last battery of tasks, and not with the first.

To summarize the studies that have specifically addressed the question of multijoint versus single-joint control, one unit recording study seemed to favor the multijoint control, whereas the second seemed to assure that single-joint control occurs. The ablation study clearly favored multijoint control over single-joint control, in addition to proposing the discrete control of different task modes for each of the nuclei.

Botterell & Fulton (1938a,b) had previously noted that midline lesions, whether the fastigial nuclei were involved or not, gave rise uniquely to difficulties in stance and gait. The animals could not stand up against gravity; if the lesions were unilateral, they fell to the side of the lesion. The essential abnormality was of much of the body musculature, but as used only in stance and gait: The midline representation was, therefore, of the whole body, but only for circumscribed functions. Lesions of the lateral hemispheres (with or without dentate involvement) and the ensuing behavioral deficits formed the corollary: Many muscles of the body were again involved, but for an entirely different set of tasks. Animals overshot the mark when reaching for an object, and showed "clumsiness" when manipulating small objects. When running headlong down the hallway, they would often bump into the wall, unable to stop in time (vision was thought to be normal).

These observations were confirmed and extended by Chambers and Sprague in cats with electrolytic lesions stereotaxically placed within the nuclei. With fastigial lesions (Sprague & Chambers 1953), the animal fell toward the side of the lesion. Anterior fastigial lesions caused the ipsilateral hindlimb to flex and the opposite to extend; posterior fastigial lesions affected the forelimb more, though the attitude (flexion or extension) was variable. Reaching and climbing were normal. In lateral hemisphere lesions (Chambers & Sprague 1955a,b), stance and gait were relatively normal, but reaching overshot and pawing movements were "clumsy."

What Is Different and What Is Common Across All Nuclei? Motor Modes and Movement Coordination

What did the rather marked changes in neural discharge relate to in all the single-joint movement studies, if it did not "generate" them? We believe that the observation that single units discharge during tasks that are not impaired by the inactivation of those neurons must mean that the neurons were indeed doing something other than controlling the monitored aspects

of the task performance. We have pointed out elsewhere (Mink & Thach 1991a,b) that unit firing may correlate with parameters of movement and yet not control them: The inactivation of those units does not impair those parameters. The lesson: Correlation does not mean causation. The monkeys were trained to perform movements of the wrist, and they did so. As we have often commented (Mink & Thach 1991a, Schieber & Thach 1985, Thach 1968, 1970a, 1978), however, monkeys usually move many muscles other than those minimally necessary to operate the wrist joint. Since after nuclear lesion the wrist joint movements were themselves so little impaired, and the multijoint movements so badly impaired, we conclude that the unit activity may have been better correlated with (and helping to cause) the covert multijoint movements.

What is the meaning, if any, of the slight ablation deficits on performance of the single-joint tasks, and how do they relate to the multijoint results? Common to the single joint tasks and the multijoint tasks is the mode in which they were made. We suggest that Jerk, Jump, and Ramp have a lot in common with Reach and Pinch: They are all visually triggered or guided hand and/or limb movements. They are "volitional" movements: They are trained and/or thought about before they are made. They probably require processing in the occipital and parietal cortices, with information sent to the dentate over cerebro-ponto-cerebellar pathways. Dentate cells fire early in relation to the single-joint performances; dentate inactivation impairs onsets of both the single- and the multijoint performances. One should point out that in the visually guided single-joint movement (Ramp), the eye and the wrist are moved coordinately. Dentate inactivation is known to impair eye-hand coordination (Vercher & Gauthier 1988), whereas single movements are only slightly delayed.

What would be the "mode" of operation of the interpositus? If, as for the dentate, we take this mode to be largely determined by the type and source of input, the spinocerebellar, visual, and auditory inputs suggest behaviors for which fast input and feeback information from the part to be controlled is used to trigger movement of the part. Examples are the long-loop reflex, contact placing, and vision and audition to control the learned blink reflex (McCormick & Thompson 1984, Yeo et al 1984) and acoustic startle responses (Leaton & Supple 1986, Mortimer 1973), respectively. The mode would be "reflexes." The question remains as to how much of these are in the cerebellum and how much in the brainstem and spinal cord (cf. Bloedel & Kelly 1988).

Previous unit-recording single-joint studies (Strick 1983, Thach 1978) show that the interpositus responds at critically short latencies to perturbation from a holding position. If the "functional stretch reflex" *per se* were fully routed through the interpositus, one might expect an impairment

of its performance by interposed inactivation. This result was obtained in one injection only (Thach et al 1990a,b); one wonders whether the function of the interpositus is best tested by the single-joint, muscle-loaded task. But the contact-placing reaction also consists of a coordinated action of a limb triggered by a somatosensory stimulus delivered to the limb. Ablation studies of Amassian (Amassian et al 1972a,b, 1974, Amassian & Rudell 1978) have suggested that this action is subserved by the interposed nuclear control of thalamic projections onto the cerebral motor cortex.

Are interpositus deficits also due to incoordination of numbers of muscle groups? Smith and colleagues (Frysinger et al 1984, Smith & Bourbonnais 1981, Wetts et al 1985) have specifically suggested from their own data that the cerebellar cortex overlying the interposed nucleus causally determines whether the flexor and extensor muscles acting at the wrist are reciprocally active (as in flexion and extension movements at the wrist) or coactive (as in the co-contraction that fixes the wrist when the fingers are used in a precision pinch). The proposed mechanism is simple: When the Purkinje cells turn off, the nuclear cells and the agonist and antagonist muscles at the wrist turn on. If this interpretation is correct, the interpositus would play a role in coordinating opposing muscles at a joint rather than synergist muscles across joints.

In the single-joint experiments of Schieber & Thach (1985), Kane et al (1988), and Thach et al (1990, 1992), loads applied alternately to extensors and to flexors always determined that mainly one of an antagonist pair of muscles was active. With overtraining in the Schieber experiment to the point that no other muscle activity was seen, not one interposed or dentate neuron fired in relation to the parameters that did engage the motor cortex and EMG. We thus conclude that the cerebellum was not concerned with alpha motoneurons in this "single muscle group" movement. Nuclear inactivation caused tremor even in the single joint movements: this may have been the result of inactivating the gamma loop system, as originally suggested. These studies therefore did not test the model of Smith and colleagues, which in essence deals with the coordination of agonist and antagonist through the range of reciprocal contraction to full cocontraction.

What about the fastigius? That fastigial inactivation impairs stance and gait is consistent with earlier observations (Botterell & Fulton 1938a, Sprague & Chambers 1953) and with the single-unit recording studies (Antziferova et al 1980) that show unit activity in the fastigial nucleus during fictive scratching and walking, with relatively little in the interpositus and none in dentatus, respectively (Arshavsky et al 1980), during these activities. They are also consistent with Andersson & Armstrong's (1987) observation of Purkinje cell activity related to walking (and its

adaptation) in the cerebellar vermis. Thus, the fastigius is concerned with a mode of activity—stance and gait—that distinguishes it from the interpositus and dentate.

Since the acts of walking (and scratching) are by their very nature coordinated multijoint tasks, what the cerebellum adds to their control is not clear from these studies. That the essential program generators for these movements and even some measure of their adaptability lie in the brainstem and spinal cord is known (Arshavsky et al 1972a,b, Bloedel & Kelly 1988). What the cerebellum adds is therefore presumably superimposed upon these fundamental motor synergies. Knowing the magnitude and range of this control may depend on experimental strategies of the type in which Armstrong & Bloedel are engaged that allow more variety of alteration of gait.

A NEURAL NETWORK MECHANISM FOR MOVEMENT COORDINATION...

Parallel Fibers, Purkinje Cell Beams, and Coordination of Linked Nuclear Cells

One of Luciani's objections to a cerebellar role in coordination was that he saw no special feature in its structure that suggested such a function. One must remember that this view somewhat preceded the discoveries of Ramon y Cajal on the architecture of the cerebellar cortex. Is the situation still the same today?

The studies reviewed here show a somatopic representation of the body within each of the three cerebellar nuclei (Figure 3). In each representation, the mapping is of the caudo-rostral dimension of the body onto the sagittal dimension of the nucleus. The hindlimbs are represented anteriorly, the head (at least for the dentate and interposed nuclei) posteriorly; distal parts are medial, proximal parts lateral. This orientation would suggest that the myotomes, running orthogonal to the long axis of the body, run primarily in the coronal dimension and thus roughly parallel to the trajectory of the parallel fibers. Since the parallel fibers are connected to the nuclear cells by Purkinje cells, a coronal "beam" of parallel fibers would control through inhibitory modulation the nuclear cells that influence the synergistic muscles in the myotome. The parallel fi
be a single neural element spanning and coordinating the activities of multiple synergic muscles and joints.

HOW LONG IS THE PARALLEL FIBER? In the above model, it is obvious that the longer a parallel fiber is, the more cells in the nuclei (via Purkinje cell control) that it can link together. The length of the parallel fiber then

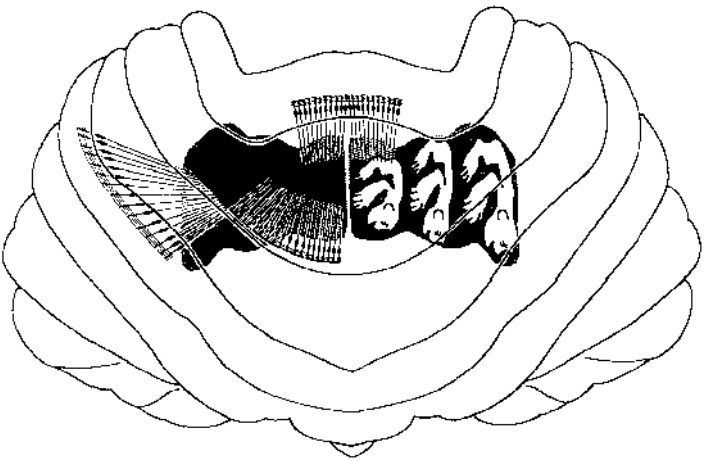

Figure 3 Diagram showing linkage into beams of Purkinje cells by parallel fibers. Beams project down onto the somatotopically organized nuclei. Purkinje cell beams thus link body parts together within each nucleus and link adjacent nuclei together. Such linkage could be the mechanism of the cerebellar role in movement coordination.

becomes a critical limit to its potential functional capacities. Ramon y Cajal believed that parallel fibers ran the full width of the cerebellum (Ramon y Cajal 1911). Since the electrophysiological studies of the Canberra group (Eccles et al 1967, Llinas 1981), the length of the parallel fibers has been assumed to be measured by the distance activity which can travel away from a local stimulus to the parallel fibers in the molecular layer. This has been about 1.5 mm. As such, this rather short parallel fiber has been modeled as a tapped delay line to generate short time intervals (Braitenberg 1967, Braitenberg & Atwood 1958).

Direct anatomical studies show parallel fibers to be much longer. In the studies of Mugnaini and colleagues (Brand et al 1976, Mugnaini 1983), cuts were made across parallel fiber beams and the fibers allowed to degenerate. Upon examination, degenerating fibers were found to extend for considerable distances: Those more superficial were longer than those deep. On the average, those for chicken were just under 10 mm, those for cat, a little over 5 mm, and those for monkey about 6 mm. The range of lengths was roughly the mean ± 2 mm. Six millimeters is roughly a third the width of the macaque's cerebellar hemisphere. A 6 mm stretch of cortex projects onto about a 3 mm beam of nucleus, which is the width of one nucleus or slightly greater (Figure 3).

Thus, a beam of Purkinje cells under the influence of a set of parallel fibers of the same origin and length affects a beam of nuclear cells across

an entire nucleus. Depending on the portion of the body map to which the *cortical* beam projects, that *nuclear* beam influences the synergic muscles across several joints in the limb (Figure 4), or the muscles of eye, head and neck, and arm, or whatever, depending on the pattern of projection and the folial orientation in the horizontal plane. We often caricature the folial pattern as being more or less strictly in the transverse or coronal plane; but a look at the cerebella of different animals shows how varied it actually is—some even sagittal, or nearly so. For example, in the vermis of the cat, there are near-sagittal and a variety of other orientations of cortical beams. Assuming that they project as such onto the nuclei, they group and regroup the cells of the fastigial nuclei in a variety of ways. As one reflects on the cat's unique and uncanny ability to move limbs and trunk while falling so as to land invariably standing, one may suspect a link between these uniquely coordinated movements and the uniquely configured cortical folia.

Beams also bridge and link nuclei, e.g. the two fastigial nuclei. This provides a means for coordination of the two nuclei and the two sides of

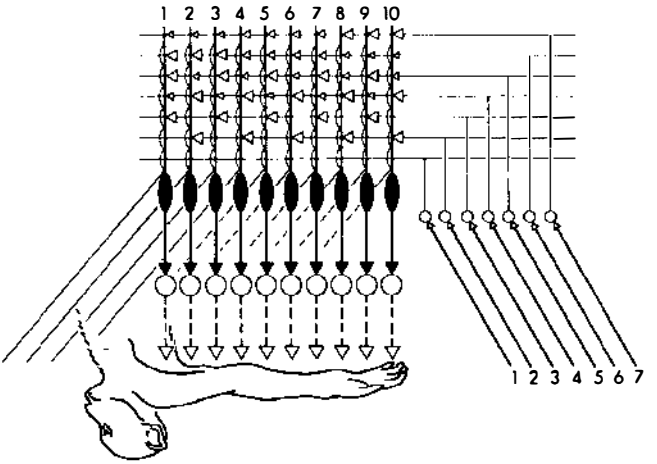

Figure 4 Model of granule cell parallel fiber control of muscular coordination: (*a*) within each nucleus, there is a use-specific (modal) representation of somatic musculature; (*b*) the orientation of the myotome is in the coronal plane; (*c*) the orientation of the parallel fibers is also in the coronal plane; (*d*) the output of the parallel fiber beam of Purkinje cells falls on the nuclear representation of the myotome; (*e*) different uses of the muscles in a limb may be coded by different subsets of parallel fibers and their differential effects on the Purkinje cells (coordination of synergist muscles); (*f*) parallel fiber beams that span the nuclei in their Purkinje cell projection may influence two or more nuclei simultaneously (coordination of modes of movement).

the body in stance and gait. Beams also link fastigius and interposed nuclei (e.g. locomotion and reflex sensitivity) and interposed and dentate nuclei (e.g. reach and reflex sensitivity), and thus coordinate their functions.

These relationships are a fact. There can be little question that parallel fibers link Purkinje cells, which inhibit nuclear cells, which in turn control the different body parts. Because of these anatomical features, linkage of body parts and modes of movement would appear to be designed into the structure. The parallel fiber is the key element of the coordination. The questions that remain are: How much does one parallel fiber control, how many parallel fibers are required to code a novel synergy, how much of coordinated behavior do parallel fibers coordinate, and what are the unique features of that type of coordination?

A Model for Controlling and Adapting Movement Synergies

1. The body is multiply represented within the deep cerebellar nuclei, with at least one body map within each nucleus.
2. Each body map controls a different mode of bodily movement, and each map and mode operate in parallel with the others.
3. Each mode has its own triggering input and its own output target (with its own inherent motor synergies), and these input-output connections determine the difference between modes.
4. The parallel fibers of the cerebellar cortex link Purkinje cells into long beams that project down onto the nuclei, which in turn link the somatotopically arranged nuclear cells into functional subgroupings.
5. These subgroupings are unique and task specific, and are the basis for the cerebellar coordination of movement.
6. The parallel fiber-Purkinje cell linkages are adjustable and are the basis of specific ad hoc learned motor synergies.
7. The learning is determined by the climbing fiber effect on the parallel fiber–Purkinje cell linkage: an error in movement activates the climbing fiber, which works to reduce the strength of connections of the parallel fiber (see below).
8. Learning occurs at synapses outside the cerebellar cortex as well, but for a different purpose: Adaptations at those closer to the motor output (or sensory input) will be generalized across all performances via those outputs (and inputs). These adaptations are useful in balancing the properties of the motor apparatus (e.g. muscles) or input (e.g. sensory organ) structures, but they are not and cannot be the mechanism for memory and control of unique task-specific synergies.
9. Memory for task-specific synergies can occur in the cerebellar cortex, where it is remote from input and output processing, and where there are adequate type and number of structures to code the many and

various synergies that make up higher vertebrate movement repertoires. The best candidate is the granule cell-parallel fiber-Purkinje cell synapse.

10. The model has predictive value.

The verification of this model will require showing the following:

1. Purkinje cells are differentially controlled in single vs. multijointed movement.
2. The parallel fiber is the agent of this control on the Purkinje cell.
3. After cerebellar cortical injury, multijointed movements are sufficiently more impaired than single-jointed movements, such that the sum of the abnormalities at the single joints cannot account for the magnitude of the abnormalities in the compound movement for all three zones and modes.
4. The climbing fibers fire along the beam when learning a synergy that involves many muscles and joints in a limb.
5. Ablation of the beam removes the learned synergy from the behavioral repertoire.

Why do climbing fibers fire in sagittal strips? Parallel fibers have been caricatured as linking together the muscles and joints in a myotomal-coronal dimension. If this is true, there remains the problem of how to coordinate the muscles and joints along the axial-sagittal dimension. One way would be to have folia slanting in a variety of ways onto the deep nuclear body map, as we have suggested may be the case in the vermis of the cat. Another way would be a time stamp across parallel fiber beams, so that learning at the elbow would reinforce contemporary and complementary patterns at the knee. Only if both are correct (or incorrect) will elbow and knee get minimum (or maximum) attention from the climbing fiber adapting both.

Relation of Output Mapping to Input Mapping

We have referred above to the common belief that the trunk is represented in the midline and the extremities laterally. This notion came from Luciani's (1811–1824) localization of abnormalities of stance and gait to midline lesions, and tremor and limb incoordination to lateral lesions (cf. also Holmes 1917, 1922). These observations have been interpreted to imply that the proximal musculature alone is used to stand and that distal musculature alone is used in reaching and manipulative movements (cf. Brown 1949). Botterell & Fulton (1938a,b), in presenting their own scheme of functional localization, commented on the lack of logic in this formulation.

Another line of work that has entrenched this belief is *input mapping* and the evoked potential studies of Adrian (1943), Snider & Stovell (1944), and Snider & Eldred (1952). These studies showed the familiar representation upside down in the anterior lobe (with vision and audition overlapping the somatosensory face) and a second representation in the paramedian lobule. The trunk was in the midline, the extremities extended out laterally into the intermediate zone cortex. Alcoholic cerebellar degeneration was found to occur first and worst in the anterior part of the anterior lobe; the chief disturbance was control of gait and the lower extremity (Victor et al 1959). This pattern fi
sentation in the anterior lobe of the evoked potential studies, and therefore the evoked potential *input mapping* has been reproduced in various clinical works as though generally representing localization of cerebellar functional *output mapping*. We agree with Botterell & Fulton (1938a) and Chambers & Sprague (1955a,b) that this idea may not be correct.

From the more recent studies of mossy fiber responses to tactile stimulation in the rat (Joseph et al 1978, Shambes et al 1978) and cat (Nelson & Bower 1990), it appears that that input mapping may generally be far more complex than originally thought. The input mapping consists of multiple representations of body parts in a pattern its discoverers have called "fractured somatotopy."

What are the physiological implications of such an input system? Nelson & Bower (1990) propose that it "may be involved in optimally controlling sensory receptor surfaces" (e.g. retina, fingers, whiskers) during sensory exploration. Quite another interpretation is suggested by the work on the associative conditioning of the nictitating membrane response (McCormick et al 1981, 1982, McCormick & Thompson 1984, Yeo et al 1984). The import of that work is that through learning, a movement pattern may be provided with a new and arbitrary sensory trigger. Any one of the many different sensory features represented in a mosaic patchwork could be selected, through learning, to drive the behavior.

...THAT LEARNS NEW MOVEMENTS

What is a new movement? One easily thinks of examples of skilled performances like riding a bicycle, skipping rope, serving in tennis, typing, or playing a Beethoven Sonata. What is new? Is it the novel combinations of the muscle and joint actions, or the application of old motions to novel conditions, or both?

An experimental paradigm that illustrates the learning of a synergy is the adaptation of eye-hand coordination in throwing a ball or a dart at a

target while wearing wedge prism spectacles (Figure 5*a*; Baizer & Glickstein 1974, Kane & Thach 1989, Thach et al 1991, Weiner et al 1983). In throwing at a target, the eyes fixate the target and serve as the reference aim for the arm in throwing. The coordination between eye position and synergy of the arm throw is a skill: It has to be developed and kept up with practice. If wedge prism spectacles are placed over the eyes with the base at the right, then the optic path will be bent to the right, and the eye will have to look to the left to see the target. The arm, calibrated to the line of sight, will throw to the left of target (Figure 5*b*). With practice, the calibration changes, and the arm throws with each try closer to and finally on-target. Proof that gaze direction and eye position in fact comprise the reference aim for the arm throw trajectory comes when the prisms are suddenly removed and the arm throws. The eyes are now on-target, but the eye-arm calibration for the previously left-bent gaze persists; the arm throws to the right of target an amount equal to the original left error (Figure 5*a*). With practice, the eye position and the arm throw trajectory are recalibrated back to the original setting: The throws move closer back to and finally on-target. A good analogy is the relation between sighting

Figure 5a Throwing darts while wearing wedge prism spectacles (base to the *right*). The subject is looking directly at the target toward which she is pointing the dart, but because the prism bends the optic path 15 degrees to the right, her gaze is deviated 15 degrees to her left in order to see the target (she is looking at you). The portion of her face behind the lenses appears to the viewer to be displaced to her left, also because of the prism's bending of the optic path. The direction of throw is normally in the direction of gaze. The gaze direction has, however, been calibrated to the throw direction, and the aim of throw is true (at you).

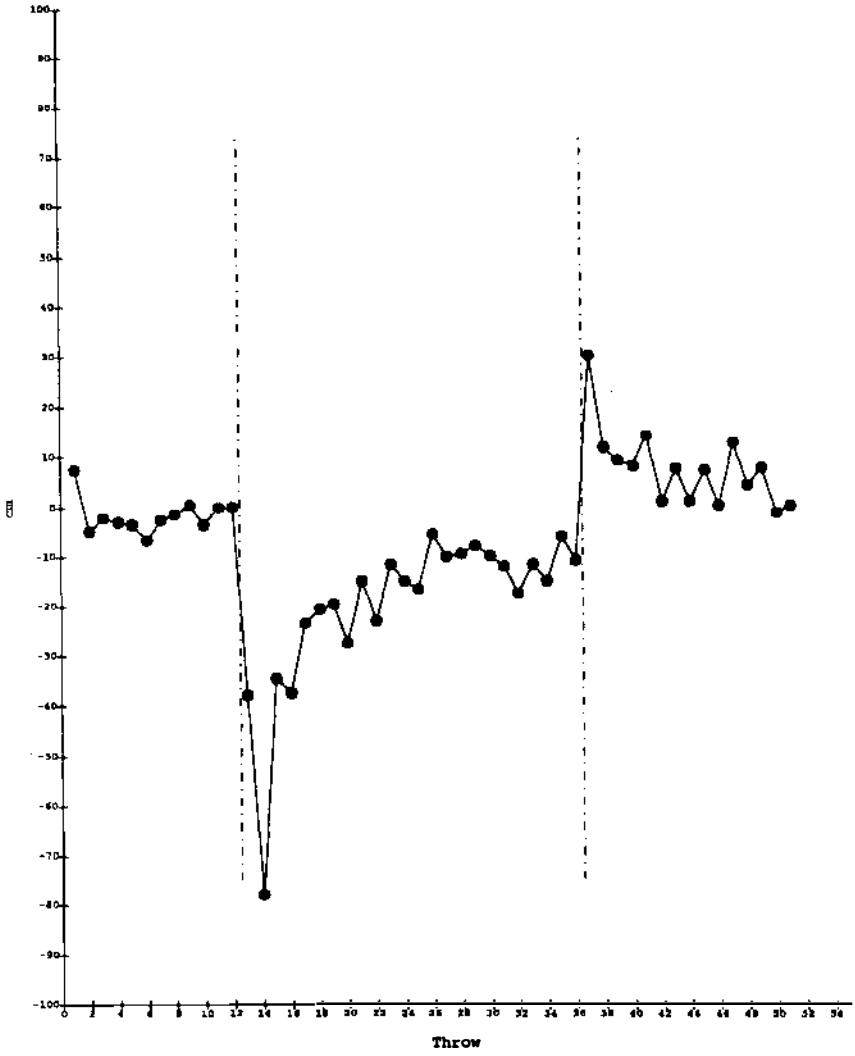

Figure 5b Normal control subject. A plot of the horizontal locations, relative to the target center, of each successive dart hit. Before introduction of the prism, the darts hit close to the center of the target. Introduction of the prism shifts the hits to the left (*down*), and with practice they normally return toward the center of the target as the recalibration of gaze direction-throw direction is made. After removal of the prism, the hits are normally shifted to the right (*up*), a result that shows that the throw direction is still calibrated 15 degrees off the gaze direction (in actuality, the error is never quite the whole 15 degrees). With practice, the gaze-throw directions readjust back to the original value.

and shooting a gun: The linkage between the sight and the bore is calibrated by adjustment and kept true through practice.

Baizer first showed in macaques that the adjustment mechanism was abolished by cerebellar lesion (Baizer & Glickstein 1974). Weiner et al (1983) confirmed the result in patients with cerebellar disease and found that adaptation was not impaired in disease of corticospinal or basal ganglia systems. We have seen that two patients with magnetic resonance imaging-documented inferior olive hypertropy (a degenerative disease of the inferior olive) could not adapt, despite otherwise normal performance (Figure 5*c*; Thach et al 1991, cf. also Gauthier et al 1979). This suggests that the adaptation mechanism could be dissociated at least in degree from those of coordination and performance. We have also seen that lesions of the mossy fibers of the middle cerebellar peduncle impair motor learning. This is not to say that the cortex, the inferior olive, and the mossy fibers are equivalent or equipotential in their control of learning, but only that they are all necessary.

Vercher & Gauthier (1988) also observed impaired coordination of eye and hand after dentate lesion; movement of both members became independently saccadic. Whereas they modeled the deficit as a lack of feedback information between independent generators for eye and hand movement (Gauthier et al 1988, Gauthier & Mussa-Ivaldi 1988), we would emphasize the lack of a common feedforward control system.

A similar task has been developed for studying the correlation of Purkinje cell discharge with, and the effect of cortical inactivation on, adaptation (Keating & Thach 1990). A monkey was trained on the Jump task (Figure 2*a*), which during the learning phase requires coordination of the eyes in observing a moving target and the hand in tracking it. An adaptation is required when, without warning, the gain of the hand coupling to the cursor is changed (e.g. increased). Thus, when the target jumps to the same familiar position and the monkey moves the wrist to its same, familiar position sufficiently to have previously brought the cursor on target, he finds that the cursor overshoots. He has to re-scale his wrist movement and make it smaller by an amount inversely proportionate to the gain increase so that the cursor lands on target. With practice, the monkey learns to move to the new target position. If, as above, the hand points to where the eye points, a calibration of the coupling of the two is needed for this kind of performance. When the gain of the handle is changed, the hand no longer points in the line of sight: The eye-hand coordination must be recalibrated for the cursor to land where the eye is looking. As in the wedge prism task, the cerebellum may control the recalibration.

For a number of Purkinje cells so far studied during the Jump endpoint

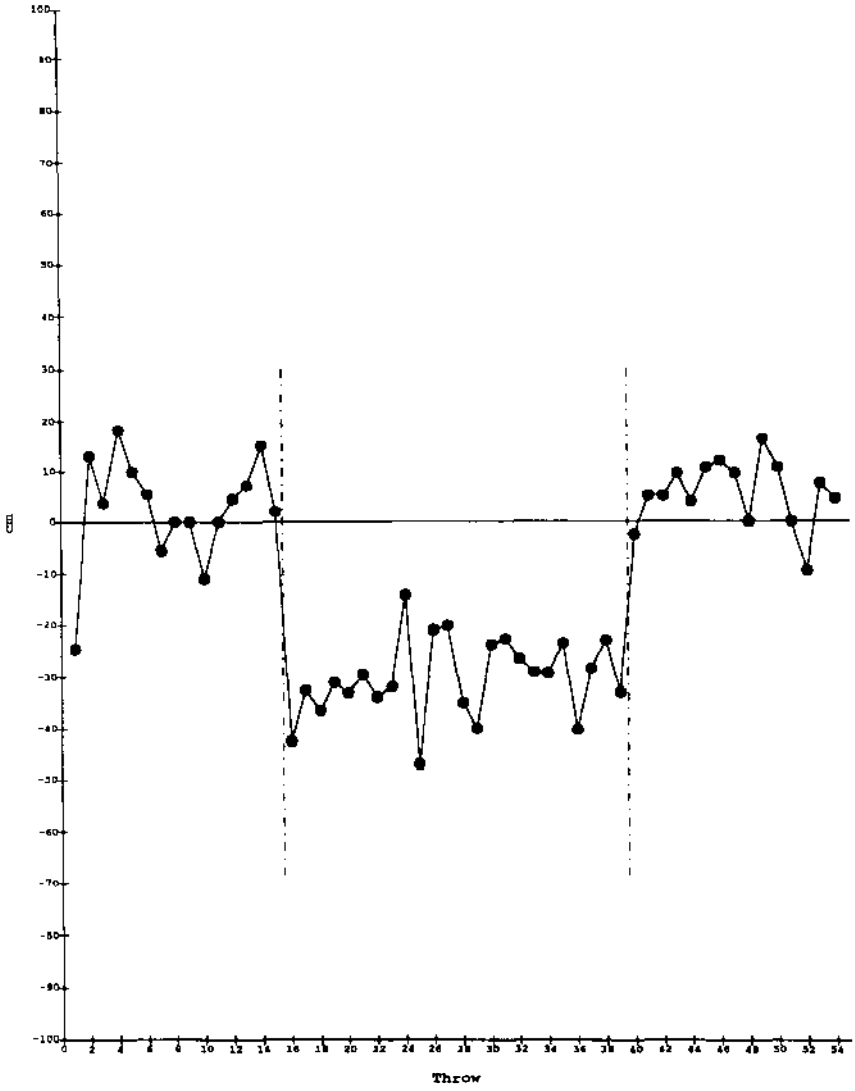

Figure 5c Patient with inferior olive hypertrophy, a degenerative disease of the inferior olive. After introduction of the prism, there is no recalibration of the gaze-throw directions, and the throws remain to the left of target center (*down*). After removal of the prisms, the hits land where they did before the introduction of the prisms, thus indicating no adaptation to the prisms in this subject.

adaptation, the behavioral adaptation appears to be related to a transient, covarying change in complex and simple spike rates, and a persistent behavioral change to a persistent change in the simple spike rate. This is a pattern consistent with the Marr (1969)-Albus (1971) theory, and one that has been seen experimentally twice previously (Gilbert & Thach 1977, Watanabe 1984).

"Learning curves" that graphically depict the adaptation are well modeled by a simple exponential decay function. The learning can easily be distinguished from the performance in the following way. The rate of change of slope of the learning curve (a time constant) is taken to reflect the learning capacity at that particular time. The scatter of data points (each representing the actual trial-by-trial position of the wrist as it jumps to target) is measured as the variance around the mean learning curve, and is taken to reflect the performance capacity at that particular time. In previous ablation studies, a lack of distinction between an impairment of learning versus an impairment of performance has been a confounding factor.

The prediction was that different experimental manipulations would affect the one or the other (learning and performance) independently. This has been confirmed by repeated injections of muscimol into the cerebellar cortex. Cortical inactivation prolongs the adaptation time by as much as five- or six-fold with low concentrations of muscimol (1 μmol). The adaptation can be impaired in the absence of any detected change in performance. At higher concentrations (5 μmol), the adaptation is abolished for several days. The effect is localized to a point in the lateral zone of the hemisphere (which we presume to project to dentate). Injections at sites more medial, anterior, and posterior do not give the deficit.

Why Is the Cerebellar Cortex Particularly Appropriate for Task-specific Learned Motor Synergies?

The site for storage of the more unique synergies should be far away from output and input sites so that the memory for one synergy does not spill over and influence another synergy. The cerebellar cortex is such a site.

The structure must be optimized for storage of multiple separate synergies. Even with multiple connections, as in the hidden layers of a connection machine, the memory and combinatorial capacity increases with the number of the hidden units. The cerebellar cortex contains the cell type that far outnumbers all other cell types within the nervous system—the granule cell, which gives rise to the parallel fiber.

The aspect of behavior that is learned or adapted must somehow be represented within the mechanism. Since the Purkinje cell projects topically onto a small portion of a deep nucleus, and similarly onto adjacent cells

without complete overlap, then a Purkinje cell "represents" its target in the nuclei. The nuclei in turn are somatotopically coded for body part and, depending on the inputs to and output targets of the nucleus, a certain "mode" of control of the body.

Purkinje cells, as representatives of the movement elements to be controlled, are linked together in large, long combinations, which then become muscle and movement pattern synergies.

Because the parallel fiber-Purkinje cell synapses are adjustable (Gilbert & Thach 1977, Ito et al 1982, Robinson 1976), the synergies can be created and eliminated. Since they are remote from input and output, creation or elimination of one synergy does not affect another synergy. There is herein the direct analogy to a look-up table with its many addresses, the addresses being fully programmable, as the memory for pre-computed commands in robotic control.

Many learnable movements are possible; the limits are set by the patterns of connection of parallel fibers, Purkinje cells, nuclear cells, downstream pattern generators (motor cortex, red nucleus, reticular and vestibular nuclei), and inter- and motoneurons. Movements are triggered in many different contexts—the limits are again set by the range of conditions represented in the mossy fibers to any given granule cell.

Some Old Puzzles Illuminated: Silent Areas, Focal Versus Diffuse Lesions

If the cerebellar cortex is viewed as the storage site that both generates old and learns new movements, some old observations are explained. One is the paradox that the cortex appears so insensitive to focal lesions and yet so vulnerable to widespread degenerative diseases. A focal lesion may wipe out one memory-movement synergy and its trigger but leave other memories and thus the means of accomplishing the same ends by similar movements. The loss or even partial damage diffusely of the whole cortex (as in cortical degenerative diseases of alcoholic thiamine deficiency, paraneoplastic degeneration, olivopontocerebellar atrophy, etc.), however, can be devastating in its effects.

Also explained is the remarkable absence of deficits after lateral hemisphere lesion in some patients, and the equally remarkable selectivity of deficits in others. Holmes (1922) commented on two musicians: the one, after removal of a left lateral hemisphere tumor, could not play left hand notes on the piano in proper sequence. The other, after a cerebellar gunshot wound, could not play the flute. We have also seen a man with a posterior inferior cerebellar artery territory infarct of the underside of the lateral cerebellum on the right who was normal (in the arm and hand) to clinical test. Yet he complained of a severe deficit. He had from youth trained

himself at the sharp dealing and shuffling of cards, at card tricks, and at other sleights of hand using coins and poker chips. After the lesion, he could no longer deal the cards evenly spaced, track card order during shuffling so as to pull from the middle or bottom of the deck, put three coins on elbow or back of hand and then flip and catch them in midair, or palm a roll of poker chips and singlehandedly and serially remove the one in the middle and place it on either end of the roll. He regarded the deficits as discrete and qualitative rather than quantitative. It was as though he had lost a number of highly trained synergies of the hand and arm, whereas others were unimpaired.

THE EXECUTIVE AND THE MODULATOR MODELS, CORTICAL AND NUCLEAR LEARNING:

Either/Or, Both, All?

Often, the two sides of a long-standing dispute that has been waged on the premise that only one side can be correct are eventually seen both to be correct: The dispute has resulted from how the question was posed or studied. We believe that this may be another such situation. The question is whether the executive mechanism that initiates and controls movement is in the cerebellum (and especially in the cortex) or in the target structures to which the cerebellum projects. The answer is likely to be "both."

It is known that the motor cortex is one of these target structures, and that its repertoire is in the domain of individuated movements rather than larger synergies (Lawrence & Kuypers 1968, Schieber 1988). We have reviewed the timing studies of cerebellum-motor cortex unit recording and ablation. These have shown that the cerebellum leads and helps initiate some movements through the motor cortex. The mechanism could be as simple as an assembly of the individuated, pauci-, or single-jointed movements into compound, multijointed movements. What about other cerebellar targets?

Within the brainstem, mechanisms control the synergies responsible for the orienting of eyes, head, and neck to visual, acoustic, and somatosensory stimuli. There are also mechanisms that control tonic neck reflexes, contact placing, righting, supporting, and the labyrinthine control of stance and locomotion. The spinal cord contains basic mechanisms for muscle synergies that mediate resistance to displacement, flexor withdrawal with contralateral extension, and quadrupedal locomotion.

Since only the fastigius projects directly to motoneurons (cf. Asanuma et al 1983d), the bulk of the cerebellar outflow must use the synergies within the thalamocortical and the brainstem nuclei on which it falls. This use is likely to lie between the alternatives of "modulatory gain control

only" and "executive coordinative control only." How might the "in between" condition be conceptualized and stated?

Ito showed that the tonically active Purkinje cells are inhibitory (Eccles et al 1967). A metaphor was created that is useful in thinking of how the cerebellar cortex can project onto and control downstream motor mechanisms that have their own resident programs: Cerebellar cortical outflow "sculpts" varied and individualistic patterns from monolithic stereotypes through disinhibition and inhibition (Eccles et al 1967). The essence of the metaphor is that the learned synergy may be achieved not by building it up, muscle by muscle and piece by piece, as in clay, but rather by chipping off, piece by piece, the unwanted parts of some undifferentiated, multijointed movement as in stone. Thus, a mossy fiber-triggered beam of parallel fibers activates basket-cell inhibition of off-beam flanking Purkinje cells, which releases the nuclear cells below from tonic Purkinje cell inhibition. This could release a primitive grasp, tonic neck, contact-placing, or labyrinthine reflex. The same mossy fiber-triggered beam of parallel fibers would give a learned and variable amount of activation to on-beam Purkinje cells, which would through thus controlled inhibition sculpt the released, undifferentiated synergy and give it the adaptive differentiated specifics.

Where then would initiation of movement occur? The quest has been for some single site, where sensory information triggers a motor response in the process we call *sensorimotor integration.* The cerebellum has been considered a good candidate, because so much of its input is so clearly sensory, whereas most if not all its output is motor. Timing studies support this view, in that motor cortex activity has consistently appeared to lag and depend on prior cerebellar activity. If the cerebellar cortex does indeed contain special apparatus dedicated both to building complex movements from simpler components and to carving out differentiated movements from undifferentiated movements, the initiation of a complex (or differentiated) movement would have to occur at the level of this mechanism. In either situation, the mossy fiber would provide the trigger. The parallel fi

inhibited Purkinje cells would provide the response. The parallel fiber would have the pivotal role in combining or carving the "pieces of movement" (Marr 1969).

Clearly, not all movement is initiated by the cerebellum. The segmental stretch reflex, the vestibulo-ocular reflex, and the blink reflex can all occur without any cerebellar input. These activities are also capable of plastic adaptation without the cerebellum (Bloedel & Kelly 1988, Lisberger 1988, Wolpaw & Carp 1990). Yet in the case of multiple context-dependent learned responses of the one reflex, as in the VOR under water, in air, with

and without trifocal spectacles (cf. Gauthier & Robinson 1975, Shelhamer & Robinson 1991), it seems likely that the cerebellar cortex participates and is necessary. It also seems likely that the initiation is distributed—that the primary vestibular afferent triggers responses both from the vestibular nuclei and from the cerebellar cortex at about the same time. In this situation, the vestibular nuclear response is "fundamental," and the cerebellar cortical response is "differential"—one of the several or many specially adapted responses. The fundamental response in the vestibular nuclei may precede (in time) the differential response in the cortex, as Lisberger has suggested (1988). Yet it would be the cortical component, which is based on the adaptation that is specific to a certain behavioral context, that provides both the individuality and the utility of the response. This is considerably more specific and important than "the fine control of the VOR." In the cortex there would be not just the one tuning but many, each and all necessary to make the fundamental VOR perform differentially and adequately across task requirements in the foveate animal. One wonders whether the cerebellum may prove also to extend the range of capability of the stretch reflex—under different conditions providing a variety of appropriate responses in relative stiffness, damping, length servo-assistance—when the system is adequately studied under varying conditions and requirements.

Clearly, coordination is not unique to the cerebellum. Each motor component that is downstream from the cerebellum obviously is built with its own type of coordination. As Denny-Brown stated, the cerebellum for the most part must work through them, but that fact does not exclude a role for the type of coordination we have proposed here, not does it condemn the cerebellum to the trivial role of a simple gain control of these structures. Indeed, for coordinated complex movements, we propose that the cerebellum is the executive; that it learns, initiates, continues, and stops complex movements through its actions on the downstream structures. As for the multiple learned-context-dependent performances of the one reflex, we agree that the initiation may be distributed, but propose that the specificity of the response is in the cerebellar cortex.

Just as clearly, motor learning is not unique to the cerebellar cortex, nor should it be. But, if cerebellar cortex does indeed contain special apparatus dedicated to combining simpler elements of movement into larger complex synergies, then the learning as well as the initiation of such a movement would have to occur at the level of the mechanism that provides for the combination. What is unique about cerebellar learning is the flexibility, ease, and speed of assigning the trigger-response (task specificity) and of building the tailor-made complex movement response. The triggering input may be changed from one sensory modality to another. The task per-

formance may be programmed and adjusted without affecting other task performances. This is not so of spinal cord, vestibular, or other low-level mechanisms.

Finally, we agree with Llinas (1981) that what had been lacking in the Marr-Albus motor learning theory is how it ties in with the rest of cerebellar function. We hope this review helps to answer that objection.

SUMMARY

Based on a review of cerebellar anatomy, neural discharge in relation to behavior, and focal ablation syndromes, we propose a model of cerebellar function that we believe is both comprehensive as to the available information (at these levels) and unique in several respects. The unique features are the inclusion of new information on (*a*) cerebellar output—its replicative representation of body maps in each of the deep nuclei, each coding a different type and context of movement, and each appearing to control movement of multiple body parts more than of single body parts; and (*b*) the newly assessed long length of the parallel fiber. The parallel fiber, by virtue of its connection through Purkinje cells to the deep nuclei, appears optimally designed to combine the actions at several joints and to link the modes of adjacent nuclei into more complex coordinated acts. We review the old question of whether the cerebellum is responsible for the coordination of body parts as opposed to the tuning of downstream executive centers, and conclude that it is both, through mechanisms that have been described in the cerebellar cortex. We argue that such a mechanism would require an adaptive capacity, and support the evidence and interpretation that it has one. We point out that many parts of the motor system may be involved in different types of motor learning for different purposes, and that the presence of the many does not exclude an existence of the one in the cerebellar cortex. The adaptive role of the cerebellar cortex would appear to be specialized for combining simpler elements of movement into more complex synergies, and also in enabling simple, stereotyped reflex apparatus to respond differently, specifically, and appropriately under different task conditions. Speed of learning and magnitude of memory for both novel synergies and task-specific performance modifications are other attributes of the cerebellar cortex.

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