A THEORY OF CEREBELLAR FUNCTION WITH APPLICATIONS TO LOCOMOTION. II. THE RELATION OF ANTERIOR LOBE CLIMBING FIBER FUNCTION TO LOCOMOTOR BEHAVIOR IN THE CAT†

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Abstract

A previous theoretical study has demonstrated that the spino-olivocerebellar, climbing fiber apparatus of the cat cerebellar anterior lobe is a mechanism for exerting prolonged, "tonic" biases upon muscle usage during locomotion. This report specifies the nature of such biasing and predicts both the sources and distribution of climbing fiber activity to be expected in various locomotor performances. Operation of the spino-olivary system is found to have an intimate relationship with propriospinal networks coupling homolateral limbs.

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Work commences with a survey of the spinal production of locomotion in mesencephalic cats, and of its modulation by both peripheral and central influences. Early on it is observed that locomotor movements are neurally programmed in terms of muscle "linkages" governing several joints--muscles whose contractions covary as a result of shared afferent and/or efferent signals. Contraction of a linkage appears to be modulated in three basic ways: (a). By adjusting the relative amounts, or ratios, of activity in the component muscles; (b). By altering the overall activity level of all muscles; or (c). By changing the contraction timings of the muscles. Experimental evidence indicates that (c) is exclusively the purview of spinal circuitry (in mesencephalic animals), while the cerebellar anterior lobe can perform both (a) and (b). Type (a) (termed "structural") adjustments ensue from the redistribution of relative amounts of activity among different anterior lobe corticonuclear compartments, and type (b) ("metrical") from changes in the absolute activity in those compartments. Since volleys in Oscarsson climbing fiber strips have been shown theoretically to alter, for an extended period, the distribution of relative compartmental excitation, it is concluded that the spino-olivary system effects prolonged, "structural" tuning of locomotor muscle linkages. Specifically, it adjusts the proximal-distal, abductor-adductor, rostral-caudal, and ipsilateral-contralateral balance of muscle usage for periods of several step cycles.

The extended time course of climbing fiber effects implies that the spino-olivary system cannot function on a movement-by-movement

basis in "real time," but rather that it must establish its "structural" biases for all locomotor movements at once, even though the movements themselves are sequential. This fact, together with data on the muscle linkage specificities of corticonuclear compartments and other considerations, implies the existence of only two qualitatively different patterns of Oscarsson strip activity in each anterior lobe half during locomotion. The demonstrated existence of only two different patterns of homolateral limb coupling, "rack" and "trot," in cats suggests a connection between different propriospinal circuits and particular Oscarsson strip distributions. It is a fairly simple matter to make this connection concrete, and to predict the Oscarsson strips and corresponding "structural" muscle biases that should be associated with different locomotor gaits. Experimental tests of these conclusions are proposed.

The compartmental organization of the anterior lobe and its matching Oscarsson strips of climbing fibers allow the anterior lobe to telescope temporal sequences of movement into a compact spatial representation. Consequently, either peripheral or central information is permitted to manipulate the locomotor act as an holistic structure, rather than as a collection of disjoint motor events dispersed in time. The resulting cohesiveness which develops between successive elements of an action may well lie at the heart of the cerebellar strategy for motor coordination.

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1. Introduction

This report is the second in a series of theoretical investigations focussing on the contribution the cerebellar anterior lobe complex makes to the locomotion of the mesencephalic cat described by Shik and Orlovskii[168,196,198]. The rationale for choosing locomotor behavior as a working example of cerebellar operation has been outlined in the first paper of the series[22]. So also were the reasons for singling out anterior lobe climbing fiber afferents for special consideration. What the present study attempts, in part, is the fusion of the physiological theory for climbing fibers developed earlier[22] with the various spinal and supraspinal locomotor control mechanisms as they are now understood. The fusion has been made sufficiently complete so as to allow detailed predictions both of the climbing fiber activity to be expected in connection with particular locomotor gaits (section 3.2 below), and of the peripheral and central signals activating certain climbing fiber populations (section 3.3). One should be able to test these predictions experimentally without resorting to new techniques (section 4.2).

The theoretical correlation of climbing fiber activity with certain attributes of locomotion depends upon the prior adoption of

several general principles of motor control organization (developed in a review of locomotor mechanisms; section 2). The most basic of those principles states that movement is centrally programmed not in terms of individual muscle contractions, but rather in accordance with linkages of many muscles. A "linkage," simply enough, is a group of muscles whose activities covary as a result of shared afferent and/or efferent signals. For example, judging from studies of muscle usage in normal stepping, in the recovery from external perturbations, and in the classical spinal reflexes, it seems quite clear that locomotor movements are organized in terms of basic flexor and extensor linkages involving both proximal and distal joints (see section 2.3.1; also ref. 157). More abstractly, linkages are examples of mechanisms which reduce the controllable degrees of freedom in the skeletomuscular system, thereby diminishing the complexity of the control problem. This powerful conception, which will recur throughout the present work, was first set forth by Bernstein[15,16] and later developed by Gel'fand and Tsetlin[73] and Greene[83,208].

The linkage principle is important to the interpretation of climbing fiber activity in the following way: The cerebellar anterior lobe seems to be subdivided into a series of sagittal cortico-nuclear "compartments," each of which governs one or several descending tracts facilitating, as a rule, only one generic type of locomotor muscle linkage (flexor or extensor, in either hind- or forelimb; section 2.3.3). The author's earlier investigation[22] (also reviewed in section 3.1 below) employed a mathematical model of the anterior lobe

cortex, cerebellar nuclei, and pre-cerebellar reticular nuclei to demonstrate that activation of climbing fibers restricted to the sagittal strip zones of Oscarsson was well suited to altering activity distributed among those compartments. It was found that activity in an Oscarsson strip leaves relatively unchanged the level of cerebellar nuclear excitation within its own compartment, but results in the suppression of activity in compartments mediolaterally adjacent. Therefore, it follows that Oscarsson climbing fiber strips have the capacity to potentiate certain types of locomotor muscle linkage at the expense of others. But why? Might climbing fibers be used to generate stepping? This clearly is false, since stepping is present in spinal animals (section 2.1). Indeed, it has been shown (section 2.3.4) that cerebellar outflow has the capacity to influence muscle linkages only when they are contracting actively under spinal direction. The cerebellum is not the cause of contraction; and it has no impact (at least directly) upon contraction timing. There appears in fact to be some sort of spinal "gating" to which cerebellar information is subject. Consequently, climbing fiber function must be bound up in the "tuning" of locomotor muscle linkages. In some way it adjusts only the forces developed within episodes of muscle activity that are programmed spinally (section 2.4).

By introducing a parameterization for muscle linkages and then relating it to the compartmental organization of the anterior lobe (sections 2.3.1, 2.3.2), it is possible to develop a rather concise hypothesis on the type of tuning climbing fibers actually provide

(section 3.1): In simplified terms, it is concluded that they adjust the relative amounts of contraction distributed among muscles, according to different gaits. For instance, they help shift activity into distal muscles during gallops (section 2.1.4).

Now the previous theoretical study[22] also indicated that reciprocal connections between the anterior lobe and the pre-cerebellar reticular nuclei could mediate the temporary "storage" of excitation distributions created by climbing fiber inputs. The duration of storage is largely a function of the strength of recurrent excitation between the cerebellar and reticular nuclei; but in principle, it might be several seconds or longer. This finding once more casts doubt upon the association of climbing fiber activity with the immediate performance of individual movements in either locomotion or other types of action. Instead, it seems that the anterior lobe could possess a dynamic (as distinct from plastic) short-term memory faculty that would allow it to extend the consequences of climbing fiber inputs occurring during, say, one step cycle to several subsequent cycles. The conjecture meshes with the intermittent use of descending cerebellar influences by spinal networks (above). The cerebellum is permitted to store information in its ongoing activity since muscles are unaffected by it unless ordered spinally to contract. Obviously, if the cerebellum were always "on-line" with respect to the musculature, such storage would be impossible.

Along with the linkage notion, the hypothesis of cerebellar short-term memory coupled with its spinal "readout" forms another

general motor control principle by which cerebellar transactions may be understood. How? To sample a few ideas, it can be shown that this scheme may underlie the phenomenon of so-called "next-cycle modulation" (section 2.4), whereby events (e.g., perturbations) encountered in a current movement influence the course of a later act. That is, the cerebellum automatically develops from present doings the feed-forward context for future action (allowing, for instance, open-loop movement preprogramming). It can also be easily demonstrated (sections 3.2, 3.3) that the anterior lobe, as a consequence of its memory and spinal gating, is able to "see" the separate motions of an act simultaneously--as a set of co-active Oscarsson strips, each dealing with a subset of all muscle linkages required for the act. In other words, movements which take place serially in time can be represented in space (the compartments of the anterior lobe) as though they were coincident. As a result, the entire act is manipulable as a cohesive, coordinated whole by common information distributed over this cerebellar space. Such information is characteristic of mossy fibers, and the discussion of cooperative actions of the climbing and mossy fiber systems comprises much of the conclusion of this report (section 5).

In a certain sense, the predictions relating climbing fiber activity to locomotor phenomena (see earlier) are the culmination of the present work. But general motor control principles have been stressed in this introduction because it is hoped the paper offers an adequate example of a paradigmatic approach to the analysis of a

difficult motor control problem. It seems doubtful that cerebellar function can be completely understood in a behavioral context through sheer empiricism. There are already more data available on the organ than can be conveniently kept track of; and there is no accepted means, other than intuition, for assessing which of these data are worth remembering. The time clearly has come to "know less, and to understand more" (Greene, personal communication). The predictions made here, therefore, are of secondary significance. No one would be more surprised than the author if they proved correct. It is the process of arriving at predictions, of bridging the gulf between the physiology of the cell and the physics of movement, that demands emphasis. The process to be presented below is no doubt wrong; but that is of no real consequence. It succeeds if it is wrong in the right way--in the way that inspires, however slightly, both the experimentation and the speculation that together will asymptotically lead to the truth.

2. The Locomotor System: A Review

The locomotion of vertebrates and invertebrates has been the subject of many biophysical and physiological studies over the past century (e.g., refs. 82, 102, 140, 188). Very recently, Grillner [91] has produced a superb survey of locomotor mechanisms in both the cat and lower vertebrates. Grillner's review primarily covers the spinal mechanisms important to the locomotor performance. While some of these circuits are briefly described below (section 2.1), the major concern here will be the specification of descending influences upon

spinal locomotor centers, particularly those stemming from the cerebellum. The reader is thus referred to Grillner[91] for more of the spinal details.

2.1 The Spinal Generation of Locomotion

2.1.1 Definitions

Each limb of a locomoting mammal performs a repetitive step cycle divided into two epochs: The stance (or support) phase refers to the interval of paw contact with the support and the transfer (or swing) phase to the period of limb retrieval for the next step. With a few exceptions[149], the durations of the step cycles in all limbs are approximately equal during constant-speed locomotion[12]. Yet the stance (and transfer) phases within the cycle can have different durations in different limbs. For example, forelimbs tend to remain in stance longer than hindlimbs, perhaps because forelimbs have the primary tasks of balancing and steering an animal, while the hindlimbs are principally thrusters. Step cycle asymmetries also occur among the laterally paired limbs in the gallops[157,161]; these will be of special interest when locomotor muscle usage and its cerebellar correlates are considered (sections 2.1.3, 2.1.4, 3.2).

The relative phasing of step cycles among the limbs determines the gait of locomotion. For this discussion gaits will be broadly divided into alternate-step and bilateral-step classes, referring to the operation of the laterally paired limbs. In the alternate-step category for cats are the walk, trot, and rack (see ref.

188 for definitions). The bounds and gallops are principal representatives of bilateral-step gaits[82]. Various authors, seeking a single central mechanism to explain the programming of the gaits, have attempted to show that all gaits can be "derived" from each other by continuous phase advances or retardations of interlimb stepping depending upon speed[46,188]. However, interlimb coordination changes discontinuously in the transitions between the alternate- and bilateral-step gaits (section 2.1.2), and even between the alternate-step trot and rack (section 2.1.3). Several programming mechanisms are thereby implied, to which discussion now turns.

2.1.2 Step Cycles of Paired Limbs

a. External attributes. In the locomoting cat or dog both the transfer and stance phases of the step consists of episodes of flexion or extension in each limb joint (for details, see refs. 12, 78, 91, 195). EMG studies[59,93,160,214] demonstrate that activity in limb extensors dominates all the stance phase and the latter portion of transfer (limb approaching the support), while flexor contractions are seen in the initial portion of transfer. This gross EMG picture is subject, however, to much "tuning" by peripheral and central influences, particularly in distal joints (treated in sections 2.1.4, 2.3, 3.2, 3.3).

Although the transfer and support phases of the step cycle may appear to mirror each other, their properties are actually quite different. For example, regardless of locomotor speed or gait the duration of the transfer phase is found to be nearly constant in

treadmill dogs[12] and cats[224] or free-moving cats[78], while all changes in speed stem either from alterations in stance phase duration (or total step cycle time) or length of stride. In fact, the flexion phase of transfer appears designed to retrieve the limb from the variety of extended positions achieved during stance in various gaits and to return it to a "standard position" before re-extension to the support[179]. Careful measurements by Goslow, et al.[78], of hindlimb excursions during free cat locomotion show that the hip is restored after transfer-flexion to within $\pm 1.5^{o}$, and the ankle to within $\pm 2^{o}$, of the same standard position prior to re-extension, irrespective of gait (walk, trot, gallop). Conversely, the ankle is retrieved by transfer flexion from a sizable range of extended positions (130^{o} in walk vs. 154^{o} in gallop).

From the theoretical viewpoint of Bernstein[15,16] and others[73,83,208], the standardizing of transfer-flexion relative to stance-extension may be a mechanism for reducing the number of controllable parameters governing locomotion, thereby "simplifying" in some sense the coordination problem confronting the brain (see Introduction). Many other such simplication strategies are inherent in locomotor circuits, as will be apparent (cf., the executive control of locomotion by a descending noradrenergic system, described in section 2.2). Transfer-flexion standardization is itself due mostly to powerful segmental reflex activity (section 2.3.1), although the standard final limb positions can probably be altered centrally to some extent as a function of horizontal limb loading[180].

In the alternate-step gaits the alternation of the paired limbs is generally quite rigid, regardless of whether one refers to the midpoints of transfer and stance on opposite sides (these coincide) or to periods of EMG silence and activity in homologous muscles[91]. There appear to be central mechanisms actively enforcing, to some degree, that alternation: Kulagin and Shik[122] demonstrated (in mesencephalic cats) that if paired limbs were constrained to step at different speeds through the use of a split treadmill belt, then the stance and swing phases of stepping in each limb would be altered to preserve both alternation and equal step cycle durations (i.e., one limb would acquire a short stance and a long transfer relative to the other). In a similar split-treadmill experiment with toads, Gray[82] found that the phasing of alternating limbs could be changed, but only up to the point where in-phase stepping would occur; then one limb would be delayed until the other could achieve alternation with it again.

The above findings should be contrasted with those in the bilateral-step gaits. The conversion from alternate- to bilateral stepping in cats[203] and other animals[82] is marked by sudden quasi-synchrony of the paired limbs, particularly the hindlimbs. That is, there appears to be an abrupt breakdown of the prohibition against simultaneous paired limb movements seen in alternate stepping (and, conceivably, an actual proscription of alternation). As mentioned in section 2.1.1, certain authors[46,188] treat the bilateral-step gaits as the end-product of a continuous "transformation" of

alternate-stepping, so that a single central mechanism can be held responsible. Yet even the dramatic differences between footfall patterns in trotting and galloping cats[203] suggest the presence of two qualitatively different limb-pair interactions. The notion of continuous gait transformations probably arose from the association of gait changes with continuous changes in speed. Gray[82], however, presents one nice illustration of how slow, bilateral-"step" swimming in toads converts abruptly to slow, alternate-step walking upon first contact with land. It will be assumed in this report, therefore, that two different neural mechanisms are responsible for alternate and bilateral stepping, respectively. More will be said below about the nature of those mechanisms and about the usage of the musculature during stepping (section 2.1.4).

b. Spinal mechanisms. Stepping in paired limbs can be produced by spinal circuitry isolated from the rest of the brain in many lower forms: Székely[116,207] demonstrated that isolated spinal segments of the salamander could generate rhythmical limb movements upon receiving non-rhythmical afferent stimulation. In fact, exchange of forelimb and hindlimb buds by embryonic grafting, with subsequent limb innervation by the "wrong" spinal segments, had no effect upon these segments' capabilities for producing rhythmic movement. Constant electrical stimulation of turtle thoracic spinal cord (lateral columns) will induce swimming movements[125]. The spinal dogfish (transection 5-9 segments below cranium) swims spontaneously[87,90].

"Spinal stepping" of the hindquarters in spinal dogs (cervical transection) was described by Sherrington[194]. This usually appeared when the hips were elevated such that the legs were passively extended by gravity, whereupon alternating hindlimb stepping began. On occasion, synchronous "galloping" was seen instead. It was observed that muscle usage during the "transfer" and "stance" phases of the alternating spinal step corresponded almost exactly with that of the ipsilateral flexion/contralateral crossed-extension reflex that can be obtained in paired limbs by a variety of peripheral stimuli given to the ipsilateral limb (also noted by Miller and van der Meché [157]). In this case, hip extension appeared to be the stimulus triggering flexion in one hindlimb and crossed-extension in its contralateral partner. The resultant contralateral hip extension then reversed the sequence, leading to alternating stepping. Interestingly enough, hip extension increases by only 4° between the walk and gallop in free-moving cats[78], suggesting that it also serves as a transfer-flexion trigger in normal locomotion.

Sherrington[194] was able to produce bilateral stepping in both hindlimbs of spinal animals when pressure was applied to the footpad of either. Thus, bilateral stepping likely has a relationship to another spinal reflex, the "positive support reaction"[188], elicited by splay of the digits. One may conclude immediately, therefore, that an association exists between each of the two types of paired limb stepping and a classical spinal reflex mechanism.

Notwithstanding the early observations of locomotor-like reactions in spinal mammals, only recently was actual spinal locomotion demonstrated: In spinal cats, Jankowska, et al.[107,108], saw that the noradrenergic precursor, L-DOPA, when injected intravenously, dramatically prolonged motoneuron and spinal interneuron discharges got by stimulating flexor reflex afferent (FRA) components of limb nerves (Note: The FRA are those myelinated afferents whose stimulation will evoke a flexion/crossed-extension reflex in the spinal cat--in particular, low- and high-threshold cutaneous, G II and G III muscle, and high-threshold joint afferents[62,133]). Reciprocal influences between flexors and extensors were also heightened (see also ref. 69,) leading those authors to suggest that DOPA might "release" spinal stepping circuitry. Grillner[66,89] was finally able to demonstrate true treadmill locomotion of the isolated hindquarters in acute spinal cats (thoracic transection) under DOPA or chlonidine (a noradrenergic receptor activator). He later found that chronic, thoracic-spinal kittens could locomote without drugs[89]. The chronic animals also revealed hindlimb sway and tactile-placing reactions[67,68,89], formerly considered to require supraspinal intervention[13,188].

To the eye the hindlimb locomotion of acute or chronic spinal cats is essentially "normal," as are the limb EMG patterns[66,89]. At low treadmill speeds the hindlimbs step alternately. An abrupt transition to a bilateral gallop appears at higher velocities. The deficits that do exist largely pertain to limb extension (as Sherrington[194] also anticipated). Extension of distal joints is sometimes hypometric;

and the stride length never increases with increasing speed as it usually does in intact animals, remaining instead virtually constant at all speeds. Lateral stability is also lacking. The general competence of spinal segments to carry out locomotion, however, is truly striking.

The parallels between spinal reflex patterns and the stepping of limb pairs might suggest that the peripheral inputs triggering reflexes are also necessary for stepping, but this almost certainly is untrue. Fel'dman and Orlovskii[176] (see also ref. 64) have demonstrated that very slow (1/sec) cyclic modulation of hindlimb motoneurons can be obtained in mesencephalic cats following the immobilization (and loss of γ-activation) caused by ventral root section. Grillner[91] reports other examples of autonomous generation of stepping patterns by spinal mechanisms (see also refs. 93, 223). Recordings have been obtained from cat spinal interneurons whose periodic discharges in the absence of equally periodic afferent inputs indicates that they may be part of an intrinsic spinal locomotor generator[64,177]. Theoretical studies have demonstrated how "interneurons," either in reciprocal inhibition[97] or wired into a ring-like structure around which clumps of excitation could travel[116], could readily form a locomotor oscillator (Note: The ring-structure may be closest to physiological reality[177]). The justifiable excitement surrounding the triumph of the central pattern generation concept over that of "reflex" control of movement (in this limited case!) has, however, resulted in an equally dramatic downplaying of the influences peripheral inputs <u>do</u> have upon locomotion. As it happens, there are striking parallels in the ways

cerebellar and peripheral inputs are conducted to the musculature. Thus, more time will be spent on the peripheral-influence topic in section 2.3. For now, let it be said that the autonomy of stepping generators in no way jeopardizes the conclusion that their <u>circuitry</u> is associated with, or identical to, that of the "locomotor" spinal reflexes (flexion/crossed-extension and positive support).

To summarize:

1. Regardless of locomotor speed or gait, the transfer phase of the limb step cycle is highly standardized. On the other hand, the stance phase is quite mutable.

2. Alternate-step gaits are characterized by internal constraints which prevent any tendencies toward synchronous stepping in the paired limbs. Those constraints appear to be abruptly broken upon the conversion to bilateral stepping. For these (and other) reasons, it is probable that at least two different central mechanisms are responsible for the two gait categories.

3. The spinal cord, either chronically or under the influence of noradrenergic potentiators, can support both alternate- and bilateral-step locomotion in single limb pairs. The two types of stepping may thus have their origins in two distinct spinal reflex mechanisms--the flexion/crossed-extension reflex (alternate stepping) and the positive support reaction (bilateral stepping). However, peripheral inputs appear unnecessary for the sheer production of stepping.

2.1.3 Gait Relationships Among Fore- and Hindlimbs

a. External attributes. The footfall and limb movement patterns of alternate-step gaits most often employed by free-moving dogs, cats, and horses[12,82,188,203] usually reveal more or less in-phase motion of diagonally opposed limbs; homolateral limbs move more antiphasically. However, "pacing" gaits (rack, amble[188]) involving in-phase stepping of homolateral limbs are also found. In fact, cats appear to prefer the rack when walking on treadmills at low speeds [160,224]. Miller and colleagues[160] measured relative EMG onset times in homolateral fore- and hindlimbs of intact treadmill cats and discovered saltatory timing changes accompanying the transition from low-speed rack to higher speed trot (or vice-versa). That suggested the presence of two discrete neural "programs" for the trot and rack. When Miller[160] went on to examine the gallops, he found that one set of homolateral limbs was coordinated according to the "trot" regimen, the other according to the "rack" (see below). It was thus concluded that two different coupling mechanisms, the "rack" and the "trot," govern the homolateral limbs much as do the alternate- and bilateral-step mechanisms coordinate the paired limbs. The Miller group has hypothesized that all gaits are essentially synthesized out of "competition" between the various limb coordination programs[161]. A similar idea will be introduced in another guise in sections 3 and 4 of this work.

The alternate-step gaits, whether in trot or rack form, are characterized by symmetric step cycles in the laterally paired

limbs; limb movements differ from each other only in their phasings. On the other hand, the simultaneous presence of rack and trot homolateral limb couplings in the gallops results in bilaterally asymmetric step cycles: Each of the two limb pairs, while attempting to move synchronously, is biased such that one limb leads the other slightly. In the leading limb, transfer-flexion is shortened relative to the trailing limb, and the forces developed in each limb are said to differ[161]. Such observations of symmetry and asymmetry in the various gaits will be of considerable interest in understanding cerebellar influences upon the muscles of locomotion (sections 2.1.4, 3.2).

b. Spinal mechanisms. Sherrington[194] noted that eliciting the flexion/crossed-extension reflex in one limb pair of a spinal dog often resulted in a weak, reverse effect in the other pair. That is, the interlimb "coordination" of certain alternate-step gaits (trot, walk) was revealed. Miller and coworkers[156,159] have shown that electrical stimulation of hindlimb extensor nerves (hip and knee) polysynaptically facilitates flexion reflexes of ipsilateral forelimb flexors and antagonizes those of extensors via ascending propriospinal pathways, accounting in part for Sherrington's effect. The homolateral hind-fore influence is prolonged and is potentiated by DOPA[156] (which also releases spinal stepping; section 2.1.2). Matsushita[145,147] has anatomically identified an analogous propriospinal tract arising partly from lumbosacral interneuronal areas and impinging upon certain ipsilateral cervical motoneurons (see also ref. 119). One must conclude, therefore, that the spinal cord has circuitry by which to

orchestrate the movements of homolateral hind- and forelimbs (ref. 160 discusses the point further).

Spinal circuits notwithstanding, it has not yet been possible to produce coordinated stepping of all limbs in high spinal cats using drugs of any sort[91,160], although it can be seen in amphibians[91]; and some semblance of it apparently will appear in spinal cats infected with Newcastle virus (discussed in ref. 160). But according to Shik and Orlovskii[195], if a treadmill is abruptly set in motion beneath an intact dog, paired limb stepping is established more quickly than are proper hind-fore phasings. It thus seems that spinal homolateral coordination mechanisms do not have the potency of those generating stepping in paired limbs. One might look accordingly toward supraspinal centers for additional inputs facilitating homolateral limb couplings. Miller[161] describes certain medullary regions possibly involved in hindlimb-forelimb coordination. Cerebellar contributions to the process will be hypothesized in section 3.3.

In summary:

1. Two types of constraint on the movements of homolateral limbs--one yielding roughly antiphasic movements ("trot") and the other in-phase ("rack")--appear to be responsible for the hind-fore coordination of most gaits. In alternate-step gaits only one or the other constraint is present at a time, and step cycles are symmetric across the midline. In bilateral-step gaits, limbs on one side of the midline are governed by one constraint, and contralateral limbs

by the other. Step cycles are thus asymmetric on each side of the body.

2. Certain long propriospinal pathways may be responsible for the homolateral hindlimb-forelimb couplings seen in spinal animals. It is doubtful, however, that spinal circuitry alone can coordinate homolateral limbs nearly as well as it can opposed limb pairs. Supraspinal contributions may be required.

2.1.4 Use of the Musculature in Locomotion as a Function of Gait

What are the parameters of muscle activity which account for the properties of various gaits? Those which first come to mind are the timings of EMG bursts and the absolute levels of EMG activity. In a given muscle the product of the two is related to the "impulse" (or momentum change) imparted to the limb by the muscle. Engberg and Lundberg[59] examined EMG timing and, to a lesser extent, activity levels in limbs of freely locomoting cats in different gaits. Surprisingly enough, the timings of limb extensor EMG's were found to be nearly invariant with respect to the step cycle, irrespective of gait. Higher speeds were accompanied by higher EMG levels, but the activity periods of muscles relative to each other were unchanged. Thus, the programming of extensor activity could be thought to involve a single sequencing mechanism which creates "slots" of EMG activity at appropriate times in the step cycle, and an intensity control which governs the levels of EMG to be seen within the slots. Much more will be said about such a conception at the conclusion of this review (section 2.4).

Engberg and Lundberg[59] did not find quite so simple a picture when flexor behavior was examined. Both activity levels and timings were very much a function of gait. This may seem peculiar in light of the standardization of transfer-flexion (section 2.1.2). Yet the stereotyped flexion retrieval of a limb from any number of extended initial conditions (positions, velocities) may well demand a wide spectrum of flexor activity. It is likely that some portions of the flexor EMG constellation, particularly timings, are computed "on-line" by fast-acting segmental reflex mechanisms which measure limb extension (section 2.3.1); that fact, however, in no way implies the absence of supraspinal flexor modulation (see sections 2.3.2, 2.3.3).

Alterations of EMG timing and activity level in individual muscles do not seem to capture quite all the muscular events that are correlates of gait changes. There also appear to be certain gait-dependent differences in the large-scale deployment of muscle groups. One example of this may be drawn from locomotor movements of the trunk. Flexions and extensions of the trunk become quite important in the gallops[82], for they are the sole means of increasing speed[98] and also function to conserve elastic energy[78,98]. But trunkal motion is not nearly so important to the alternate-step gaits, since step-cycle duration as well as stride length are manipulated to establish speed[98]. Another example lies in the degree of proximal vs. distal limb joint movement as a function of gait. Compared with alternate-step gaits, gallops produce much more movement of distal joints than proximal.

High-speed locomotion in some animals (e.g., humans) produces a complete shift from plantar- to digigrade stepping, presumably because of increased distal extensor action[91]. Still a third example is inherent in the shift from symmetrical to asymmetrical step cycles in paired limbs when an animal switches from trot to gallop (section 2.1.3). "Leading" limbs ostensibly feel a flexor bias, and "trailing" an extensor.

Each of the above examples has in common a gait-related change in the relative utilization of specific muscle groups within the entire ensemble of all muscles involved in locomotion. That is, trunk muscles may become more or less involved in a given gait, relative to limb muscles. Or proximal muscles may be more or less active than distals, or flexors on one side of the body more or less active than homologous contralateral flexors. In this report, the relative amounts of muscle activity distributed among the muscle groups used to execute a gait, and which change with gait, will be termed the muscle structure[165] for the gait. Roughly speaking, structure may be thought of as a set of ratios of EMG activity among different muscles averaged over the step cycles of all limbs--i.e., it is a parameterization independent both of absolute EMG levels and of contraction timing.

The notion of structure must remain more or less a formalism at this point in the discussion. It will be shown later to be a concept useful for the decomposition of cerebellar locomotor modulation (sections 2.3.2, 3.1), since one component of that modulation may both tune many muscle groups simultaneously and also be "invariant" with

respect to the step cycle. Unfortunately, outside of what can be deduced from the examples above, the muscle structures associated with different gaits are unknown. Even the examples admittedly have little EMG data to support or refute them (but some EMG evidence for the proximal-to-distal conversion at high speeds is available for humans 91). Sherrington[194] evinced an interest in the structure of certain spinal reflexes--the degrees to which different muscles were involved therein--but few have considered the problem since (cf. refs. 24, 121). Hopefully, that will be remedied soon.

In the absence of more detailed information, it will simply be assumed here (as in a previous report[22]) that the structure of muscle activity, along with its amplitude and timing, is a quantity altered with certain types of gait change. Nothing has been said about what mechanisms should account for changes in structure, but it may be hypothesized that supraspinal centers are at least capable of exerting a bias on structure. Witness, for instance, the incompleteness of distal extension in spinal locomotion (section 2.1.2). Section 2.3.2 will present further information on the structural changes got by stimulating certain of the brainstem "output" nuclei (red nucleus, Deiters nucleus, etc.) through which cerebellar anterior lobe outflow affects the musculature. Other sections (2.2, 2.3.4, 2.4) will deal with supraspinal control of EMG timing and absolute activity levels.

To summarize:

1. Muscle usage changes with gait along three gross lines: EMG timing in some muscles (primarily flexors) is altered with respect

to the step cycle. Absolute EMG levels change in essentially all muscles. And the relative amounts of activity distributed among different muscle groups--the muscle structure--may also be shifted.

2. Supraspinal centers can influence structure (along with performing other functions, of course).

2.2 The Executive Control of Locomotion

In his investigation of the relationships between spinal reflexes and stepping in spinal dogs, Sherrington[194] noted that continuous, non-periodic faradization at or near the cut end of the spinal cord would elicit stepping in one or both hindlimbs, even after attempted deafferentation. He concluded that some type of continuous supraspinal influence might be capable of awakening those "reflex" circuits generating periodic stepping. It is now known that he was entirely correct and that those descending influences probably emanate from certain regions of the reticular formation which in turn are under the control of mesencephalic and hypothalamic centers. It appears that this locomotor "executive" system operates, at least in part, through the infusion of the neurotransmitter noradrenalin into the spinal circuitry. But that is not all: The noradrenergic executive also appears to "power up" that portion of the cerebellar complex required for locomotor modulation, but not vice-versa (see below). One need go no higher in the locomotor control hierarchy, therefore, in order to place reasonable bounds on the cerebellar station within that hierarchy.

Below, the properties of mesencephalic locomotion, wherein the noradrenergic executive operates, will be examined, followed by a brief survey on the structure of that executive system. The stage will thus be set to "trap" the cerebellum between the executive and spinal-generator levels of the locomotor hierarchy.

2.2.1 Production and Properties of Mesencephalic Locomotion

Graham Brown (described by Lundberg and Phillips[134]) demonstrated that chronic, precollicular decerebrate cats could be made to locomote on a treadmill if the treadmill were set in motion under them (see ref. 92 for others' findings). Once locomotion began, the animals required no external support of the trunk. As the treadmill's speed was increased, the gait adapted appropriately, finally becoming a gallop at high speeds. All in all, the preparation was said to walk "beautifully." No electrical stimulus was employed. Yet as mentioned above, such stimuli applied to certain points of the cut spinal cord will induce alternate stepping in dog hindlimbs[194], suggesting that a brainstem electrical stimulus might also cause a decerebrate cat to step or locomote. This in fact was the discovery of Shik, et al.[198] in acute, pre-collicular, post-mammilar ("mesencephalic") cats: Here the plane of brainstem section[92] runs from the rostral margin of the superior colliculus to a point between the mammillary bodies (rostrally) and the exit of nerve III (caudally). It leaves intact brainstem nuclei at and below the level of the red nucleus (the latter sectioned roughly between its magno- and parvicellular portions, leaving unaffected the origin of the rubrospinal

tract). The electrical stimulus, a fairly weak (10-90 μa) 25-60 hz, continuous pulse train, is applied to the region of the cuneiform nucleus, just ventral to the caudal margin of the inferior colliculus but dorsal to the brachium conjunctivum[92,199].

According to the original description of Shik et al.[198], the preparation is inert prior to cuneiform stimulation; there is no decerebrate rigidity[188,199]. After initiation of the electrical stimulus, a latent period of as much as several seconds passes before the cat suddenly "comes to life" and stands upon the treadmill. If the treadmill is set into motion, the cat then walks. Only at rather high currents does the cuneiform stimulation itself produce locomotory movements[92,160], and only at very low stimulus frequencies (10 hz or less) is there any synchrony of muscle activity with the stimulus. The hindlimbs have a lower locomotor "threshold" than the forelimbs in this preparation, but with sufficient stimulus strength well coordinated locomotion of all four limbs is possible. The cat ceases locomoting very shortly after stimulus cessation. A "mesencephalic fish" has also been described recently[113,114].

Aside from apparently activating locomotory circuits, midbrain stimulation in mesencephalic cats appears mainly to specify limb extensor forces during each step cycle (recall that extensor deficits are seen in spinal locomotion). Thus, with a fixed stimulus current, cats will change gait appropriately with increasing treadmill speed, but will do so with nearly constant stride length. The stance duration shortens as a result, while the transfer phase, as in intact

animals, is fixed[198]. At fixed speeds, however, increase of the stimulus increases stride length (and somewhat shortens the transfer phase duration), but stance duration stays nearly constant. These findings imply that augmenting the stimulus augments extensor force, which governs length of stride. It is even possible to induce galloping with sufficiently large stimuli[198].

Cuneiform stimulation apparently controls extensor activity by regulating only the number of recruited motoneurons. Motoneuron firing rates are essentially constant regardless of speed or degree of brainstem stimulation; and timing of motoneuron bursts is a function of treadmill speed[192]. It would seem, then, that stimulation of the cuneiform nucleus has no direct effect upon the stepping frequency created by spinal generators, but again, only upon muscular forces (extensor) produced during the step cycle. Should these forces happen to propel the animal to a higher velocity, then the step cycle frequency may change, presumably in response to peripheral inputs (e.g., faster hip extension; section 2.1.2).

What has been described above is behavior of the "basic" mesencephalic cat. It also has some variations of interest. For example, the cuneiform nucleus is not the only region capable of potentiating locomotion. If the pyramidal tract is sectioned at the level of the rostral inferior olive in a mesencephalic cat, and the tract then stimulated rostral to this cut, locomotion will be possible[169,197]. Without pyramidal section, cuneiform-stimulus locomotion is inhibited by pyramidal stimulation. Coagulation of the

cuneiform area and regions ventral to it, extending into the vicinity of the nucleus reticularis pontis caudalis (NRPC), abolishes pyramidally elicited locomotion[197]. The NRPC originates a reticulospinal projection to be considered in section 2.2.2. It appears, therefore, that the pyramidal system is a locomotor facilitator only in that it has collaterals distributing to bulbar areas more directly concerned with locomotion; certain spinally-projecting reticular neurons do receive monosynaptic excitation from the pyramidal tract[169].

Another variation is the so-called "thalamic cat"[168,169,205], produced by transecting the brainstem above the mammillary bodies, leaving intact (in particular) the posterior hypothalamus. This preparation can walk spontaneously on a treadmill (and is probably equivalent to Graham Brown's cat above). It does so in bouts lasting 10-20 sec, with a few minutes of "rest" interposed. During rest the animal maintains extensor tone (unlike the mesencephalic cat, which collapses unless locomoting). Spontaneous thalamic locomotion is often none too good, though, with the forelimbs showing either disturbed coordination or no movement at all. Administration of caffeine improves the performance[205]. If the treadmill is stopped during spontaneous walking, the cat "protests" with convulsive limb movements, scratching, etc. If the treadmill is started during a rest, locomotion is often instituted. Weak electrical stimulation of the posterior hypothalamic region inevitably induces locomotion[168,169]. Simultaneous cuneiform stimulation has a summative effect on locomotor vigor[168], but a cuneiform stimulus during a "rest" will usually not potentiate

locomotion. Coagulation of the cuneiform has no effect upon spontaneous locomotion, but hypothalamic destruction reduces or abolishes it, along with its "emotionality"[168]. It thus appears that the posterior hypothalamus is executive to the cuneiform nucleus in locomotor control. The subject will not be further explored here, save to note one interesting observation (Orlovskii[169]): Areas of the pontine reticular formation projecting to the cord (probably the NRPC) appear to receive some monosynaptic excitatory connections from the posterior hypothalamus and send return projections to it. It is tempting to speculate that a "positive feedback" circuit could be involved in the bistable spontaneity of the thalamic cat--or at least in the prolongation of its tonic-locomotor-tonic episodes.

How good a model of locomotion in intact cats is locomotion in the mesencephalic preparation? To the eye, it can be quite good (refs. 92, 196, and author's observation of film by S. Miller). The EMG patterns of limb muscles also appear to be similar to those of the intact cat[93]. Shik, et al.[196,198] found that interlimb influences and gait were also essentially as in intact animals, one of the few differences being that, at the transition from trot to gallop, hindlimbs could step bilaterally while forelimbs retained alternate stepping, an unusual situation in the intact cat. The reactions of locomoting animals to perturbations of the limbs and the like will be considered in section 2.3.

It can be argued that the mesencephalic cat lacks the visual, vestibular, and neck proprioceptor information which could possibly

modulate the locomotion of normals. Even the treadmill locomotion of the latter can be peculiar[214,224] perhaps because of the unnatural visual and vestibular consequences of movement. But while the mesencephalic cat is blind, it does at least have some tonic inflow from the vestibular apparatus[178] and probably from the neck[134]. And it may also be that certain vestibular postural reflexes are actually blocked during locomotion and are accordingly irrelevant: Phasic discharges evoked in Deiters neurons by lateral tilt are greatly reduced by stimulation of the cuneiform nucleus[178] (even without actual production of locomotion). These reflexes, which appear to adjust the limbs to stabilize the head[188] might conceivably impede locomotor action were they allowed to act. Melvill Jones, however, insists that they may aid it[150,152] (see also ref. 203).

Whether the mesencephalic cat is also a good model for <u>cerebellar</u> locomotor modulation can, at present, only be deduced from the presence of similar symptoms in normals and mesencephalics following cerebellectomy[45,170,226], and the presence of cerebellar cortical[174] and nuclear[175] neuronal activity correlated with locomotion. The latter phenomena are described in sections 2.3.2, 2.3.3, and 4.

In summary:

1. The mesencephalic cat is a precollicular, post-mammillar decerebrate preparation capable of treadmill locomotion upon continuous stimulation of the cuneiform nucleus. This stimulus appears mainly to regulate extensor force during the step cycle; gait is determined by treadmill speed.

2. Transection of the brainstem above the mammillary bodies yields a "thalamic" cat which can locomote spontaneously. The key to this spontaneity appears to be the posterior hypothalamic region.

3. Mesencephalic locomotion appears to be fairly representative of straight-line travel in intact animals including, at least in part, the cerebellar role therein.

2.2.2 The Noradrenergic Locomotor "Executive"

As was pointed out in section 2.1, spinal circuitry controlling both stepping in the paired limbs and interactions between homolateral hind- and forelimbs can be potentiated by drugs which facilitate the build-up of noradrenalin in the cord. Recently, Grillner and Shik[92] reported that, in the mesencephalic cat, the effects of cuneiform nucleus stimulation upon motoneuron pool excitability and upon short- and long-latency reflexes to FRA stimuli were essentially identical to those produced by DOPA in the spinal cat. At the same time, drugs antagonizing noradrenergic receptor sites prevent mesencephalic locomotion[89]. Such findings suggest that the cuneiform nuclear stimulus somehow results in release of noradrenalin at cord levels. The question is, exactly how does that come about? And does cerebellar outflow influence it?

Carlsson, et al.[32] found (in mice and rats) that noradrenergic and 5-HT (serotonin) axons in the cord are concentrated in the lateral and ventral funiculi, and in the superficial posterior horn. The fibers are exceedingly thin (diameter 0.3-1.0 μ; about that of parallel fibers of the cerebellar cortex[50]). Ventral horn cells--

including motoneurons--receive numerous contacts from terminals of both chemical types[40]. Engberg and colleagues[60,61] showed in cats that a large region of the reticular formation could produce some DOPA-like effects in the cord via the dorsolateral funiculus; however, long-latency muscle responses to FRA stimulation, which seem to characterize the locomotor state[92], were actually suppressed through this pathway[60]. Thus, presuming the monoaminergic terminals in the dorsal horn (substantia gelatinosa[40]) are not critical to locomotion, only ventral funiculus fibers remain candidates.

Classical anatomy dictates that reticulospinal fibers in the cat ventral funiculus stem from the pontine reticular formation, chiefly the NRPC (see ref. 166 for review). Because their terminal regions overlap those of known extensor-facilitating tracts (e.g., lateral vestibulospinal tract), the pontine reticular formation was thought likewise to excite extensors[166]. Since extensor force appears to be dictated by cuneiform nucleus stimulation, and since lesions encroaching upon the NRPC abolish locomotor facilitation by pyramidal tract stimulation[197] (section 2.2.1), the pontine reticular region seems a likely facilitator of locomotion.

Edwards[56] has recently published an autoradiographic study of the descending projections from the cuneiform nucleus in the cat. He traces fibers to the NRPC, which agrees both with the conclusion above and with physiological data[169]. However, he also finds a cuneiform projection to the medullary nucleus reticularis gigantocellularis (NRG), thought to be a flexor center according to the anatomy[166].

Still, both the NRPC and NRG can be antidromically driven from the ventral funiculus[169].

Unfortunately there are several unresolved difficulties preventing the immediate acceptance of the NRPC-NRG complex as a principal component of the noradrenergic locomotor executive: The high conduction velocities of axons leaving these areas[55,169,227] are difficult to reconcile with a thin-fiber noradrenergic system (see above). Furthermore, both the NRG and NRPC are part of the so-called "inhibitory region" of the classical reticular formation and as such will induce IPSP's in both flexor and extensor motoneurons in acute precollicular cats[109] (but see section 2.3.3). And lastly, noradrenalin-containing cells are said to be scarce in the NRPC and NRG in rats[39]. New observations in monkeys, however, indicate catecholamine-containing cells (which would include 5-HT) in the NRPC region[72].

If one performs a complete spinal section in the rat, only two brainstem noradrenergic sites are said to show marked degenerative changes (accumulation of noradrenergic fluoresence)[40]. One is a nondescript sector of the caudolateral medullary reticular formation lying between the pyramidal decussation and the caudal inferior olive; little is known about its relationship (if any) with the cuneiform nucleus. The other area is a portion of the substantia nigra, which also cannot be immediately associated with the cuneiform locomotor region, according to Edwards' study[56]. However, a possible nigral role in locomotion is worth considering for the following reasons: It is affected, as was stated, by spinal transections, even

though its principal exchanges are well known to be with the basal ganglia (which play no part in mesencephalic locomotion). Stimulation of the substantia in cats[228] apparently facilitates monosynaptic reflexes in both hindlimb flexors and extensors--an effect abolished both by ventral funiculus lesions and by noradrenergic antagonists. And a precollicular brainstem transection which passes caudal to the red nucleus, dividing the substantia nigra, extinguishes mesencephalic locomotion, although lesions of the red nucleus alone will not[199]. In the last case, of course, it is possible that connections from the cuneiform area to the NRPC-NRG are interrupted. Nevertheless, it is interesting to note that human parkinsonism is usually accompanied by degenerative changes in the substantia nigra, and that a classic feature of the disease is "hypokinesia"--a difficulty in breaking free of a given posture, particularly to initiate locomotion. Similarly, bilateral lesions of the substantia nigra in monkeys and rats produce hypokinesis[201,216]. Could it thus be that parkinsonian hypokinesia partly results from a loss of noradrenergic facilitation, by the substantia nigra, of particular spinal circuits--e.g., those used in locomotion?

While the details remain elusive of how the noradrenergic locomotor executive is constructed, one principle important to this report can be established with some confidence: The cerebellum is not part of the executive system. That locomotion can be initiated and maintained in normal[181,226] or mesencephalic (or thalamic)[170] animals following cerebellectomy makes this obvious on its face. It

is also evident anatomically in the apparent absence of direct cerebellar inputs into either the cuneiform or hypothalamic locomotor centers, although substantial cerebellar influences are felt in the NRPC-NRG complex (see section 2.3.3) which, as described above, may have some noradrenergic effect upon spinal locomotor circuits. On the other hand, it is most clear that the noradrenergic executive system holds considerable sway over the cerebellum, particularly the vermal and paravermal "locomotor" cerebellar zones: Edwards[56] has shown that descending fibers from the cuneiform nucleus contact essentially all pre-spinocerebellar centers--the nucleus reticularis tegmenti pontis (NRTP; in which the projection is heaviest), lateral reticular nucleus, locus coeruleus, and inferior olive. Olivary terminations are restricted to the medial accessory olive, which originates the majority of climbing fibers to the vermal and paravermal cerebellar cortex[8,217,221]. Interestingly enough, noradrenergic terminals exist in abundance within this olivary region, but rarely elsewhere in the olive[70]. In decerebrate cats, administration of the monoamine oxidase inhibitor, harmaline (which causes a buildup of noradrenalin), causes synchronous, periodic climbing fiber responses (cfr's) in Purkinje cells restricted to the vermal and paravermal cortex[130], in agreement with anatomical findings.

The above evidence justifies the assumption that the noradrenergic system activated by either the cuneiform nucleus or hypothalamus is the supreme locomotor executive of the mesencephalic cat. It creates the chemical milieu for the awakening of spinal locomotor

circuits, potentiates both the (reticular) mossy and climbing fiber pathways to the "locomotor," midline cerebellum, and performs these functions in a top-down manner, without reciprocal connections from the centers it controls.

To summarize:

1. The highest levels of the noradrenergic locomotor executive in cats lie in the cuneiform nucleus (or the posterior hypothalamus, if present). Activity in that region makes its way, most probably via the NRPC-NRG complex, to thin noradrenergic fibers descending in the ventral funiculus of the cord. The subsequent release of noradrenalin into spinal networks potentiates locomotor stepping generators and interlimb interaction pathways. It is conceivable that the substantia nigra may also have a remote role in this process.

2. The cerebellum appears to be subservient to the noradrenergic executive, in that its outflow does not directly influence the cuneiform (or hypothalamic) region, while the latter projects strongly to all pre-cerebellar nuclei originating mossy and climbing fiber projections to the vermal and paravermal, "locomotor" cerebellum.

2.3 The Modulation of Locomotor Performance

The adjustment of spinally-generated locomotor stepping patterns by either peripheral or central signals may, at first glance, seem to involve merely altering the timing, and possibly the intensity, of individual muscle contractions. As will be seen below, however, locomotion appears to be programmed according to the behavior of groups of muscles, not individuals, adjustments thus being applied to all

members of the group. Moreover, except in certain special circumstances, those adjustments have no effect on the timing of contractions within the groups, but only upon amounts of activity seen at certain fixed times. In fact, both peripheral and central inputs are usually prevented from influencing muscle groups at the "wrong" times. Outflow from the brainstem output nuclei of the cerebellar anterior lobe also obeys these principles, raising several conjectures about the nature of cerebellar processing which will be important to discussion in later sections.

2.3.1 Muscle Linkages, Synergies, and Their Description

a. Muscles linked by shared afference and efference. The known effects of proprioceptive (particularly muscular) and cutaneous afferent influences upon single muscles or simple agonist-antagonist pairs are widely documented[80,81,99,100,101,148,200]. What is not so well known is that most such afferent inputs influence muscles at more than one joint. Thus, Loufbourrow and Gellhorn[131] found that stretching individual muscles of fixed limbs in anesthetized cats and monkeys led to activity changes in muscles of remote limb joints. It was found that interjoint muscle groups sharing such stretch facilitation were generally identical to those groups cooperatively contracting during the evocation of classical spinal reflexes following nerve stimulation[132]. Insofar as spinal reflex mechanisms are also responsible for the programming of locomotor stepping (section 2.1), it follows that spinal locomotor circuits deploy limb muscles which are linked together by afferent information. Generalizing from this, a

muscle linkage will be defined here to be any set of muscles whose activity qualitatively covaries as the result of shared peripheral afferent, or central efferent, influx (coupling of muscles by efferent signals will be taken up momentarily).

The operation of afferentially coupled muscle linkages in locomotion is most evident among limb flexors, as illustrated in several experiments of Orlovskii and colleagues: In one study[179], dogs were fitted with a force brake at the elbow joint and then were allowed freely to locomote on a treadmill. Very brief application of the brake during transfer-flexion of the forelimb not only resulted in slowing of the movement at the elbow, but also at the shoulder and wrist. Yet within 30 msec a return to the original velocities in the various joints was achieved, suggesting the intervention of spinal mechanisms. A similar linkage phenomenon is seen in thalamic treadmill cats if hip motion is retarded during flexion[173].

The spinally-mediated afferential coupling between flexors is probably responsible for the extreme standardization of transfer-flexion that has been seen in the step cycle (see section 2.1.2). That stereotypy in turn permits the noradrenergic locomotor executive to concentrate primarily on the extensor forces during stepping (section 2.2.1). The linkage also, in theory, permits limb flexion to be controlled by many fewer parameters than would be required if the muscles were dealt with independently. In cats, hip information appears to be singled out for percolation throughout the linkage[173]. Thus, as was pointed out in the past by Bernstein[15,16], the existence of

linkages among muscles effects simplication of the motor control problem.

Unlike the situation with flexors, there appears to be no afferent linkage between extensors during locomotion. That conclusion is based upon braking experiments[179] which showed no influence of knee extension perturbation upon other limb joints (but see ref. 91). The "open-loop" nature of extension with respect to afferent inputs has also been described by other authors in non-locomotor contexts[58,59 150,151]. But surprisingly enough, locomotor extensor activity over the limb joints is far from anarchic. EMG's in simple limb extensors retain a rigid relationship to the step cycle regardless of speed (described in section 2.1.4). Moreover, activity appears to grade similarly over all extensors when speed increases or decreases[59]. In other words, it seems that a linkage is wrought among extensors through the sharing of common efferent commands. One source of such common extensor efferent signals is, of course, the noradrenergic executive system (section 2.2.1). Another is certain of the brainstem output nuclei transmitting cerebellar anterior lobe outflow to the spinal cord. The latter also provide efferent signals to flexor linkages, as will be discussed in sections 2.3.2 and 2.3.3.

In view of the capacity of the isolated spinal cord to orchestrate multijoint flexor and extensor activity, there can be little doubt that spinal circuits supply at least some of the linkage "wiring" among flexors and extensors. The differences in accessibility of flexor and extensor linkages to afferent information can probably also

be ascribed in part to spinal architecture: G II muscle afferent excitation from both flexors and extensors is led to flexors alone, for example[135]. However, the blocking or switching of certain peripheral signals depending upon the spinal state (section 2.3.4) may also play a part.

b. The structural and the metrical prescriptions of a muscle linkage. It will be of considerable help in subsequent sections to have some means to parameterize the deployment of a muscle linkage. For this reason the following terminology is introduced:

1. The structural prescription of a linkage is defined as the set of qualitative ratios of activities in the linked muscles, independent of their absolute activity levels.

2. The metrical prescription of a linkage specifies the absolute level of activity.

The notion of muscular structure was introduced in section 2.1.4. A structural prescription for a linkage merely indicates the relative amounts of activity present in its muscles. On the other hand, the metrical prescription resembles a "scalar" quantity multiplying the activities in all muscles of the linkage. To use the example of a spinal reflex linkage[194], the structural prescription is akin to the "local sign" of the reflex and the metrical prescription to the intensity of the stimulus evoking the reflex.

c. Synergies. To describe in later discussion the utilization of muscle linkages in the context of a motor act, the concept

of synergy will be adapted from Russian authors[73,96]:

> A "synergy" is a collection of muscle linkages, all sharing a common pool of afferent information and/or apparently common efferent commands, which is deployed as a unit in a motor task. Those linkages showing activation increases in a synergy are called its "agonists;" those showing decreases are its "antagonists."

It should be understood that the above use of "synergy" is not that of most Western authors, for whom "synergists" are muscles having similar actions at a joint (a subgroup of "agonists" in the above formulation). "Synergy" here will always connote the use of muscle linkages in some behavioral situation (e.g., stepping). The step cycle thus consists of a flexion synergy and an extension synergy, whose agonists and antagonists are obvious. On the other hand, the synergies of voluntary movement may have "agonists" which are actually morphological antagonists (i.e., where agonist-antagonist co-contractions are involved), an important generalization treated elsewhere[23].

The muscle linkage and the synergy are both concepts emphasizing the spatial use of muscles as distinct from the temporal. The timing question has been deliberately left vague in both the linkage and synergy definitions. Do the muscle contractions of a linkage have to be simultaneous? That problem is considered in section 2.3.4.

To summarize:

1. Spinal locomotor circuitry appears to effect linkages among limb flexors and extensors, respectively. The linkages allow the modulation of multijoint movement with a paucity of central (or peripheral) signals.

2. The deployment of a muscle linkage can be parameterized through its structural and metrical prescriptions.

3. Agonistic and antagonistic muscle linkages are used, under some form of common central and/or peripheral control, to construct synergies for the execution of motor acts.

2.3.2 Relationship of Cerebellar Modulation to Linkages and Synergies

The locomotor act appears to be programmed in terms of flexion and extension synergies, and not in terms of the behaviors of individual muscles. Thus, one should attempt to understand the cerebellar modulation of locomotion on a synergic basis. Now the musculature to be used to construct locomotor synergies appears to be specified spinally. Therefore, one should not look to the cerebellum for the construction of synergies, but rather for the tuning of synergic parameters--the structural and metrical prescriptions of the agonist and antagonist linkages within the synergies. With respect to the cerebellar anterior lobe, it will be argued below that:

> Structural prescriptions are tuned by adjusting the relative amounts of activity distributed among descending spinal tracts influenced by the cerebellum, while metrical prescriptions are governed by the absolute activity levels in those tracts.

In section 2.3.4 it will be shown that, by and large, only the agonist linkages of synergies are subject to such cerebellar manipulations.

Descending spinal pathways coming under direct anterior lobe control are the vestibulospinal, rubrospinal, and reticulospinal tracts. Each of these is well known to facilitate only one of the two primary functional groups of muscles, the flexors or the extensors (see ref. 22 and sections 2.2.2 and 2.3.4 for further details). Thus, the rubrospinal tract and lateral funiculus reticulospinal tract (from the NRG) are associated with flexors, and the lateral vestibulospinal and ventral funiculus reticulospinal (NRPC) tracts with extensors[166]. The flexor and extensor linkages of the step cycle should therefore be selectively addressable from one or another of these tracts, and that has in fact been shown[171]. The amount of linkage facilitation appears to grade with the activity levels in the facilitating tracts, from which the association of activity level with the metrical prescription of a linkage follows immediately.

Why does more than one descending pathway from cerebellar levels facilitate the same muscle linkages? Might it be because each exerts a differing structural bias on a given linkage? Orlovskii[171], for instance, found that simulation of the NRG region during mesencephalic locomotion primarily affected distal flexors (ankle), while red nucleus stimulation influenced both those muscles and, to some extent, hip flexors. That is, there does appear to be a structural component inherent in the descending flexor facilitation mediated by these two centers. They are not "redundant." Unfortunately, the

literature is rather contradictory regarding the anatomical substrate for such structural biasing. It will simply be assumed here, therefore, that different descending tracts, although facilitating the same muscle linkages, do exert differing structural biases on those linkages. Consequently, the relative distributions of activity among those pathways will govern the structure of locomotor synergies. Any external agency titrating excitation levels in the descending tracts concomitantly alters structural tuning. Such an agency, as will be argued in section 3.1, is the spino-olivocerebellar, climbing fiber system.

In summary:

The flexor and extensor linkages of locomotor synergies are each facilitated by several descending tracts carrying cerebellar anterior lobe outflow. Metrical prescriptions of the linkages are adjusted by the absolute magnitude of activity in those tracts. Structural prescriptions (e.g., emphasis upon proximal or distal groups) are assumed to be established by the relative amounts of activity distributed among the different tracts.

2.3.3 Detailed Topography of Anterior Lobe Linkage Influences and of Climbing Fiber Inputs

The purpose of this section is to provide a "glossary" of anterior lobe outputs to spinal levels and also of the peripheral sources of Oscarsson climbing fiber strip inputs. This information will be especially important to subsequent discussion. Figure 1, whose features are described below, summarizes the data. Only the

vermal and immediately paravermal sectors of the cortex are treated in this report since they coincide with the anterior lobe "locomotor area" of Chambers and Sprague[33,34]. Lesions of this cortex (and of its associated cerebellar nuclei) reportedly have a somewhat selective disrupting effect on postural and locomotor skills in cats, deficits not seen following damage to more lateral cerebellar regions (hemispheres, dentate nucleus).

In the course of their cerebellar lesion studies, Chambers and Sprague[33] noted that vermal cerebellar regions and the fastigial nucleus seemed to influence only the use of extensor musculature, while paravermal zones and the interpositus nucleus favored flexors. They thus provided early evidence for a longitudinal (sagittal) subdivision of anterior lobe corticonuclear regions into compartments having particular affinities for certain functional muscle groups--i.e., muscles having the same generic actions irrespective of body location. In a series of anatomical investigations in cat and ferret, Voogd[219,220,221] has more recently confirmed the existence of corticonuclear compartments, finding them to have a surprisingly fine grain; their relationships to functional muscle groups will be considered in a moment.

Classical studies (reviewed in refs. 28, 45) have also revealed the existence of a gross somatotopic organization of cerebellar outflow. With reference to the anterior lobe, more rostral lobules tend to affect hindlimbs and posterior lobules, forelimbs. Consequently, anterior lobe muscle influences can be said to be decomposed according to an "orthogonal" coordinate system, with muscle function indexed

mediolaterally and muscle location sagittally. In section 5 the significance of that decomposition for the interpretation of climbing fiber effects will be explored.

Figure 1 illustrates both the statements above and the further details given below. The central portion of the figure shows a schematic top view of two principal lobules (IV and V) of the anterior lobe (vermal and paravermal regions), separated by a dotted line. Symmetric regions on both sides of the midline are presented. At the bottom of the figure the gross functional muscle influences of sagittal anterior lobe zones are indicated as they have been classically established by Chambers and Sprague[33], Pompeiano[187], and others[45]. The vermal area is seen to be associated with extensors (EXT) and the paravermal with flexors (FL). Along the sides of the figure one sees the rostrocaudal somatotopy (hindlimb, forelimb) of the anterior lobe. Subsequent paragraphs deal with the remainder of the figure.

The termination of climbing fibers in sagittal strips is a subject that has been already discussed in detail in another report[22]. There it was pointed out that fibers branch to terminate in narrow "microstrips," which are in turn gathered into broader Oscarsson strips. Fibers excited through pathways carried in different funiculi of the spinal cord terminate in a characteristic set of strips; on occasion, fibers associated with more than one funiculus share a strip (and origin in the inferior olive[155,158]. The known strips (pertinent to the "locomotor" anterior lobe) associated with all funiculi are indicated on the left of the schematic anterior lobe in figure 1. Each

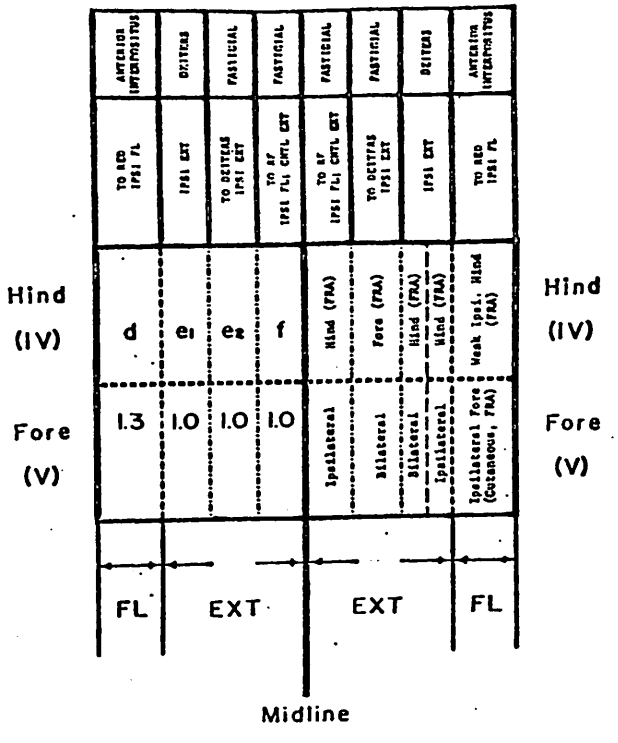

FIGURE 1

Vermal and paravermal, "locomotor" portion of anterior lobe cortex, indicating muscular influences and Oscarsson climbing fiber strip associated with each sagittal corticonuclear compartment. Central portion of figure is top view of lobules IV and V of anterior lobe. Oscarsson strips and widths indicated on left; somatotopy and modality of strip inputs given at right. Lower portion of figure gives gross muscular influence of vermal and paravermal zones (FL = flexion; EXT = extension). Upper portion gives immediate cerebellar or vestibular nuclear region within each compartment. Immediately beneath, the brainstem output nucleus (if any) and functional muscular group affected are both indicated. See text for details.

strip is designated by letter (d, e_1, e_2, f), according to the plan of Oscarsson[182]. The width of each strip (mm) is indicated beneath its label[182].

Oscarsson strips were originally identified by means of peripheral afferent stimulation. It will be of interest in later sections (3.2, 3.3) to know something of each strip's receptive field and of the modalities of afferents exciting it. These data have been culled from reviews by Oscarsson[182,183] and are printed within the strips on the right hemi-anterior lobe, as appropriate. Where climbing fibers influenced from two different spinal funiculi are merged into a single strip, so also have their receptive fields and modalities been merged. It will be noted in figure 1 that all strips have in common the activation from the FRA--that is, those afferents potentiating spinal reflex networks which may be homologous with certain spinal stepping generators (section 2.1.2). One (d) has added cutaneous (footpad) facilitation (see ref. 189). This information will be employed later to connect different strips with different locomotor performances. Also, it is significant that vermal strips (e_1, e_2, f), while receiving information specific to only hind- or forelimb(s), exert their influence across <u>both</u> lobules IV and V of the anterior lobe, thereby affecting cerebellar output to both hind- and forelimbs. That finding suggests a hierarchy of control between locomotor generators (e.g., hindlimb dominates forelimb) which shifts depending upon which strip is active. Section 3.3 will explore this idea and will also predict additional sources of strip input not shown in figure 1.

As was mentioned above, Voogd[219,220,221] and other workers (reviewed in ref. 22) have obtained evidence that the anterior lobe cortex is divided into sagittal zones, each projecting to a unique cerebellar or vestibular nuclear region (hence the corticonuclear "compartmentalization" spoken of earlier). Voogd[221] describes three compartments for each half of the locomotor anterior lobe: Referring to figure 1, these appear to approximate Oscarsson strips d, e_1: and e_2-f, respectively (an important point; see below). The e_2-f zone may itself be divisible into two parts to be described momentarily. Across the uppermost part of figure 1 are shown the cerebellar or vestibular nuclear targets of each anterior lobe zone[219,221]. Thus zone d projects to (inhibits) the anterior interpositus nucleus, e_1 to the Deiters, and e_2-f to the fastigial.

For anterior lobe zones d and e_1 it is possible to continue immediately to deduce their muscular influences, which are indicated in figure 1 immediately below the designations of related cerebellar and vestibular nuclei. The brainstem output nucleus involved (if any) is also stated. Facilitation of flexors by the red nucleus (and its excitation, in turn, by the anterior interpositus nucleus), and of extensors by Deiters, have been amply treated in another report[22]. Activity peaks in the red and Deiters nuclei coincide with contractions of the muscles they supposedly influence (section 2.3.3) during locomotion; interpositus activity is well correlated with that in the red nucleus[175]. Cerebellectomy abolishes both red[173] and Deiters[172] locomotor modulation, proving that they are under cerebellar control.

Note that the muscular influences of zones d and e_1 accord with the classical zonation of cerebellar outflow to functional muscle groups (bottom of figure 1).

It is unfortunate that so simple a picture of the muscular affinity of Voogd's zone e_2-f, the "fastigial" zone, cannot be painted. Classically, this is an extensor region. The fastigial nucleus is to project to Deiters, thereby potentiating extension directly (see ref. 22), and it seems to have been assumed that fastigial connections with the ipsi- and contralateral reticular formation (NRG, NRPC) would also serve the same purpose. However, according to Orlovskii[175] locomotor activity fluctuations in the Deiters and fastigial nuclei are considerably out of phase. Instead, fastigial units behave much more like certain reticular neurons (which also cease modulation following cerebellectomy[170]) in the vicinity of the NRG; and the fastigio-reticular system is most excited just prior to, and during, the transfer-flexion phase of the step cycle in the ipsilateral hindlimb, which completely contradicts the classical interpretation of fastigial function. Of course, part of the discrepancy between fastigial and Deiters activity episodes may stem from the added direct cerebellar cortical control over the latter (from zone e_1, figure 1). But that still does not explain the fastigial correlation with flexion, nor why the Deiters nucleus should receive "flexor" excitation from it, only to have the excitation apparently canceled (and converted into an extension signal) by cortical inhibition. Although the present report is not intended to be an anatomical treatise, the author would like to advance

an alternative hypothesis--namely, that the rostral fastigial nucleus (that portion related to the anterior lobe) is divided into two parts: a medial portion potentiating ipsilateral flexion and contralateral extension via reticular centers, and a lateral area potentiating extension primarily through Deiters nucleus. As figure 1 illustrates, it is also proposed that sagittal cortical zones (equivalent to Oscarsson strips e_2 and f; see below) can be associated with the two fastigial regions. Evidence can be mustered to support at least some parts of this conjecture as follows:

Pompeiano and colleagues (reviewed in ref. 187) found that, following a unilateral lesion of the rostrolateral fastigial nucleus in a decerebrate cat, decerebrate rigidity was intensified by stimulation of the vermis overlying the remaining, rostromedial fastigial nucleus (controls for fibers of passage, etc., were done). Presumably, then, cortical inhibition of the rostromedial fastigial nucleus facilitates ipsilateral extension; conversely, excitation of this region should "inhibit" extension. Now the ipsilateral fastigio-reticular pathway largely originates from the rostral fastigial nucleus and consists principally of large-diameter axons[219], likely implying large cells of origin. Such cells are concentrated rostromedially in the fastigial nucleus[146]. By comparing peripherally evoked responses in the medial and lateral portions of the rostral fastigial nucleus with those in the "medial reticular nucleus" (NRG, NRPC), Eccles and colleagues[55] have recently reached the same conclusion. Therefore, by Pompeiano's result above, the rostromedial fastigial nucleus must

"inhibit" cells of the reticular formation which facilitate ipsilateral extension. However, the fastigio-reticular projection has been shown to be excitatory[51,55,106]. Thus, the "inhibition" of ipsilateral extension may actually come about by facilitation of ipsilateral flexion, fitting with Orlovskii's data presented earlier. Indeed, stimulation during locomotion of the reticular region receiving ipsilateral fastigial inflow[175] facilitates ipsilateral transfer-flexion and inhibits ipsilateral extension[171]. It is likely that this region corresponds to the NRG, which, according to the anatomy, should facilitate ipsilateral flexors[166].

The fastigial nucleus also originates, via the so-called "hook bundle," a contralateral fastigio-reticular projection. While some believe that almost all fastigial excitation of reticular cells arrives by this route[222], others feel there is a mixture of both crossed and uncrossed fibers[146,219]; the latter accords with physiological results[51,106]. The muscular effects of the contralateral projection are unknown. It would seem, however, that if ipsilateral fastigio-reticular outflow facilitates ipsilateral flexion, then in the alternate-step gaits studied by Orlovskii, the contralateral projection should likely excite contralateral extension (perhaps via the NRPC[166]), lest such gaits be disrupted by bilateral flexor facilitation (but spinal "switching," treated in section 2.3.4, may obviate that concern). This hypothesis, open to test, has been entered in figure 1 (strip f, the proposed medial fastigial area). It is possible, therefore, that a rostromedial fastigial neuron behaves like a spinal interneuron mediating an ipsilateral flexion/crossed-extension

spinal reflex. As it happens, the nucleus does receive a large contingent of ascending fibers from the contralateral ventral spinocerebellar tract[144] which transmit excitatory volleys during contralateral hindlimb extension in locomoting cats[10] (to be dealt with elsewhere; Boylls, in preparation). The rostromedial fastigial nucleus can still be connected with the classical notion of exciting antigravity muscles, but perhaps only by considering its contralateral influences.

It is known that Purkinje cell axons from strip e_1 (figure 1) traverse the rostrolateral fastigial nucleus on their way to Deiters nucleus[187]. Fastigial neurons in this region can be seen to send axons to join this bundle[146], and the fastigial nucleus does indeed excite Deiters neurons[103]. It seems reasonable, then, to conclude that the rostrolateral fastigial nucleus, and the roughly corresponding strip e_2 of figure 1, are involved with setting excitation levels of Deiters nucleus and, consequently, of ipsilateral extensors (as shown in figure 1). Naturally, since no evidence seems available on whether strips e_2 and f can be associated with segregated regions of the fastigial nucleus, the division indicated in figure 1 must remain conjectural.

Inherent in figure 1 is an hypothesis which will be crucial to all later discussion--namely, that Oscarsson climbing fiber strips and Voogd corticonuclear compartments coincide; or alternatively, that activation of individual Oscarsson strips influences unique functional groups of muscles. This conjecture would appear to be experimentally addressable either anatomically or electrophysiologically, but thus

far, no one has undertaken the project. Perhaps the material to follow, coupled with the allusions made by other authors (cf. refs. 5, 22) to strip/compartment similarities, will inspire such an investigation.

In summary:

The cerebellar anterior lobe is divided into a series of sagittal corticonuclear compartments, each influencing a specific functional group of muscles over the entire body. The compartments are overlaid by Oscarsson strips of climbing fibers, and it is proposed here that each compartment is coextensive with one such strip. The strips themselves are activated by, especially, FRA inputs originating in particular limbs. Anterior lobe muscular influences are indexed functionally along the mediolateral axis (by the strip/compartments) and somatotopically along the rostrocaudal. Figure 1 documents this organization, the muscle groups so controlled, and the peripheral sources of climbing fiber inputs for use in subsequent sections.

2.3.4 Dependence of Peripheral and Cerebellar Synergic Modulation Upon the Spinal State: Spinal "Switching"

Natural or electrical stimulation of peripheral afferents often results in reflex contractions of muscles; and muscle contractions likewise can be produced by stimulating descending spinal pathways. The question is, is there always a rigid connection between such peripheral or central activity and the muscular behavior seemingly associated with it? In short, the answer is no. For example, using

conditioning techniques in monkeys it is quite possible to dissociate in large measure the activity in motor cortical neurons (some of which project directly to spinal levels) from the muscle contractions with which their activity is usually associated[63,65,190]. However, it is not necessary to retreat to the complexities of the cerebral cortex to find such phenomena. Both classical and recent studies have demonstrated that peripheral and cerebellar muscular influences are subject to gating (and sometimes actual rerouting) at spinal levels as a function of the state of spinal circuitry--of the locomotor stepping generators in particular. The mechanisms and effects of such spinal "switching" (as it will be called here) will be explored below.

a. Spinal switching of peripheral and central inputs into the musculature. In a report by Lisin and coworkers[127], the sural nerve (a cutaneous nerve of the lower leg) was electrically stimulated at the ankles of decorticated cats capable of spontaneous locomotion. It was found that during periods of inactivity (standing) the somewhat noxious stimulus evoked a standard flexion-withdrawal response of the hindlimb; however, delivery of the identical stimulus during locomotion yielded extension instead, a complete response reversal apparently associated with the locomotory state. Reversals of reflex responses in limbs of spinal dogs and cats have also been described by Magnus[138], Sherrington[194], and very recently, Grillner[67,89]. In most such work, electrical stimulation of a limb nerve or certain types of cutaneous stimuli applied either to the limb or to a variety of other places (e.g., tail) produces a flexion reflex of an already-extended limb or extension of a flexed one. Presumably, what happens in such

reversal phenomena is that spinal circuitry, by means of other afferent inputs, is able to assess the attitude of the limb and so route the stimulus energy into one or the other of antagonistic muscle linkages.

Actual reversal of the effects of central activity upon the musculature does not seem to have been demonstrated. However, spinal switching in the form of simple gating of central influences is quite prevalent. For example, Gellhorn[74] studied muscular contractions which could be elicited by electrical stimulation of motor cortex in monkeys and found that changing the position of an affected joint could either enhance or extinguish evoked muscular activity. If initial joint position were such as to stretch a responsive muscle, its discharge increased; similarly, fully shortening the muscle reduced or extinguished the response. Reversal was never seen. In a later study Gellhorn[75] showed that such state-dependent cortical effects were actually functions of the "aggregate stretch" (or associated joint angles) in the linked agonists of particular limb muscle synergies: It was possible to facilitate a cortically-evoked response in one muscle by placing fellow agonists under stretch. Inhibition of synergic antagonists could likewise be intensified. It happens that cerebellar influences from various nuclei may be "switched" into synergic musculature in much the same way, and this will be taken up after the mechanisms of switching are explored.

b. Mechanisms of spinal switching. The simplest mechanism explaining either the reversal or gating type of spinal switching would involve changes of the excitability of the motoneuron pools

receiving "switchable" inputs (either central or peripheral). Spindle afferent influx from stretched muscles could provide the necessary excitability alterations, accounting for the routing of switchable inputs into such muscles (cf. Gellhorn's experiments above and ref. 138). However, Forssberg, et al.[67], found that reversible reflex responses elicited during hindlimb stepping in chronic spinal cats did not have amplitudes well correlated to the stepping EMG's of responding muscles. As they point out, the result is incompatible with a motoneuron excitability explanation for switching (but see below).

If switching does not take place at motoneurons, then one could assign the phenomenon to presynaptic influences upon peripheral afferent or descending terminals. Primary afferent depolarization (presynaptic inhibition) by descending pathways is well known[17]; less well known are observations showing similar blocking of descending signals by peripheral inputs[206,218]. Spinal switching could also involve interneurons. Fel'dman and Orlovskii[64] have observed what appears to be active step-cycle related inhibition and excitation of spinal interneurons mediating reciprocal Ia inhibition between antagonists. That is, the muscle stretch information carried by these interneurons could easily be transmitted or blocked depending upon the spinal state.

There obviously is not enough evidence available to decipher which of many possible spinal switching mechanisms operate in specific gating situations. Yet it does seem clear that not all

switchable spinal inputs enter the same mechanisms: Only certain types of peripheral inputs are subject to actual rerouting in reversible reflexes. All others, including central influences, experience only gating. Until more is known, the most economical hypothesis accounting for the discriminatory treatment seems to be that:

1. Certain peripheral inputs participate in reversible reflexes because they directly trigger spinal stepping generators.
2. Central (and other peripheral) inputs subject only to gating have no direct access to the generators; indeed the generators control the gating by controlling linkage fabrication and activation.

The first portion of this hypothesis derives principally from the assumption that what one sees in a reversible reflex are merely different halves of the step cycle, depending upon the initial position of the limb. Reflex reversal appears to be obtainable only in preparations capable of stepping, and it is well established that stimuli akin to those involved in reversal (cutaneous[66,194]; dorsal root shock 29) will, if presented continuously, facilitate spinal stepping. The reason the stimulus class which promotes stepping (i.e., simuli involved in reflex reversal) is of interest is because it may comprise part of the input class causing climbing fiber responses in Oscarsson strips of the anterior lobe cerebellum (see section 3.3).

The second portion of the above hypothesis follows more or less directly from the evidence presented earlier (see also discussion

immediately below). It is worth mentioning that the demonstration of Forssberg, et al.[67], described above has nothing to say about the role of motoneuron excitability in the gating of descending central influences into the musculature. In fact, it is quite conceivable that spinal locomotor generators consist of an "inner circle" of interneurons into which reversal-subject peripheral inputs enter, and an outer circle of interneurons and motoneurons driven by the inner circle and also receiving only gatable descending and peripheral inputs.

c. Spinal switching and cerebellar locomotor modulation. Orlovskii has found that firing frequencies of neurons in the brainstem output nuclei (red[173], Deiters[172], reticular (NRG)[170]) are modulated with the step cycle. As might be expected, activity peaks correspond to peak EMG in the muscle linkages facilitated by the various nuclei (section 2.3.2). The modulation, however, is superimposed on substantial levels of background discharge (averages: 33 hz in red nucleus[41,173], 35 hz in Deiters[172], and 49 hz in reticular[175]). The depth of modulation of background discharge averages about 22% in reticular neurons, 23% in Deiters, and 45% in red (author's calculations from averages presented by Orlovskii[172,173,175]). This indicates that even when a given muscle linkage is undergoing passive stretch (EMG silence) during a portion of the step cycle, its associated brainstem nuclei remain quite active, showing only a 22-45% reduction from "background" (on the average). Such a reduction might in itself be sufficient to disfacilitate motoneuron pools when EMG silence is required. Then again, it is also conceivable that, like the peripheral and other central influences described above, cerebellar

outflow through the output nuclei could be subject to a state-dependent, spinal-switching operation which alternately blocks and releases cerebellar influences into the muscles. This in fact does occur:

In a most remarkable experiment with the locomoting mesencephalic cat, Orlovskii[171] stimulated the "hindlimb" areas of the red and Deiters nuclei with current levels sufficient to activate many cells therein (50-150 μa). When the cat was inert, stimulation of Deiters nucleus caused contraction of an ipsilateral hindlimb extensor linkage, as in Pompeiano's classic work in decerebrates[45,187] (presumably, stimulation of contralateral red nucleus would facilitate flexor linkages as Pompeiano also found, but Orlovskii gives no data on this). When locomotion was induced, however, stimulation of red or Deiters still augmented flexor and extensor contraction, respectively--but only when those linkages were contracting actively during the step cycle. That is, stimulation of the red nucleus during stance did not trigger transfer-flexion, nor did Deiters stimulation cause premature extension during the latter. Yet at the proper times in the step cycle, such stimulation facilitated muscle contraction considerably.

Stimulation of reticulospinal neurons (receiving from the fastigial nucleus in the NRG and NRPC) during locomotion revealed a reciprocal effect[171]. Ipsilateral flexion was facilitated, but only when flexion was being carried out. Ipsilateral extension was reduced during the extensor (stance) phase, yet never was there

"breakthrough" flexor activation at this time. It seems that reticulospinal information, too, is subject to spinal switching.

On the basis of experiments conducted with human cerebellar patients (outlined in section 2.4), Terzuolo and Viviani[209] have argued that the cerebellum must play an integral role in the orchestration of agonist-antagonist interactions in particular synergies. However, Orlovskii's work[171] indicates that at least during locomotion, cerebellar influences are directed primarily at agonist linkages alone. Only when muscles are spinally ordered to contract do they feel a cerebellar influence--that is, only when they are participating in an agonist linkage. The principle holds regardless of whether the linkage is facilitated or inhibited by increased activity in a descending tract controlled by the cerebellum. The notion that descending movement control systems generally concentrate upon agonists was advanced and tested (in human ankle movements) by Kots[120] (see also ref. 79). He argued that the disfacilitation of antagonist linkages in synergies is accomplished primarily at segmental levels (thanks to crossed inhibition between antagonists[30]). This, of course, represents still another neural ploy for simplifying the control task.

The switching or gating of brainstem output nuclear (consequently, cerebellar) influences into the musculature can only be "proved" to occur at spinal levels in the case of the red nucleus. Between the nucleus and cord are no known waystations; and the nucleus itself can only be actively inhibited (so far as is known) by pyramidal tract collaterals[215] (presumably inactive in mesencephalic

locomotion). "Inhibition" by disfacilitation is possible, but unlikely in view of the high background discharge level in the nucleus. It will be assumed here that outflow from the Deiters and reticular nuclei are also gated spinally.

More likely than not, spinal interneuronal process or presynaptic inhibition are involved in the gating of cerebellar influences, as distinct from changes in motoneuron excitability (see above). This can be deduced from the times at which two-joint muscles acting as flexors of one joint and extensors of another can be facilitated by descending pathways. Orlovskii[171] observed that even when EMG activity was present in such a muscle for much of the step cycle (i.e., the motoneuron pool was always above firing theshold), it could be accessed by a supraspinal pathway for only a portion of the activity period--the portion in which the muscle acted according to the functional specificity of the tract. Thus, tract signals must be gated prior to reaching motoneurons.

Traditional concepts of the cerebellar contribution to movement control have always tacitly considered that contribution to be continuously present. The assumption occurs both in "feedback" theories of cerebellar function, such as Eccles' dynamic loop hypothesis [47,48,49,53,54], or in ideas about cerebellar "feed-forward" governance of open-loop motor subsystems, as arise in Ito's notions of model-references control[104,105]. Murphy[163] has entertained the possibility of intermittency in cerebellar inputs (none ever having been demonstrated), but Orlovskii's results indicate that the "intermittency"

is on the output side. Of course, the spinal switching of cerebellar outflow can be easily incorporated into either the feed-forward or feedback viewpoints with no change in the philosophical foundations of either. However, the discontinuous use of cerebellar and other central influences during locomotion suggests a somewhat different approach to the understanding of motor control dynamics--namely, that there exist two independent processes out of which control functions are synthesized. One selects and times motor events (e.g., muscle contractions), the other tunes those events (establishes, say, contraction amplitudes). The significant point about this scheme vis à vis the cerebellum is that the time frames in which the two processes are neurally computed are not necessarily identical. Certain tuning prescriptions may extend over many motor events and thus may change but slowly relative to the timing of ongoing movement. This leads to the contemplation of possible extended time-course phenomena in the cerebellar anterior lobe complex with regard to locomotion, a topic addressed in the next and final section (2.4) of this review.

To summarize:

1. Both peripheral and central inputs into the spinal cord are subject to spinal "switching" prior to being permitted to influence muscle linkages. Switching can take the form of actual rerouting, as in the case of reflex reversal to certain peripheral stimuli; or it can merely involve gating, as seems to apply to central (including cerebellar) influences.

2. Peripheral inputs involved in reversible reflexes are

probably actually triggering spinal stepping generators. On the other hand, the gating of central inputs may result from excitability changes wrought by locomotor circuits in interneurons or motoneurons transmitting these inputs. Other factors (e.g., presynaptic inhibition) may also play a role.

3. Descending signals from the brainstem output nuclei of the cerebellar anterior lobe are subject to spinal switching. Muscle linkages facilitated by each nucleus can only be accessed by the cerebellum when spinal circuits order their contraction. Consequently, the anterior lobe influences only the agonists of locomotor synergies.

2.4 Conclusion of Review: A Two-Process Hypothesis for Locomotor Control and Its Implications for Cerebellar Locomotor Modulation

The preceding review has outlined (a) the computation of locomotor stepping algorithms by intrinsic spinal circuitry; and (b) the potentiation and modulation of those algorithms by the noradrenergic executive system and the cerebellar complex. This apparent division of labor with respect to locomotor control can be formalized as a definitive functional hypothesis:

The locomotor act is synthesized from the contributions of two identifiable control processes computed at anatomically distinct sites. The processes are:

1. The gait execution process, resident at spinal levels. Based upon peripheral and central signals, it decides upon the appropriate gait, selects and constructs (by linkage-formation) muscle synergies for the gait, times the

contractions of muscles within the synergies, and gates or switches descending and peripheral inputs into the musculature as appropriate.

2. The synergic tuning process, associated with the noradrenergic executive and cerebellum. It is responsible for establishing the energy output of locomotion and adjusting the structural and metrical prescriptions of synergic linkages.

The observations most immediately justifying the above hypothesis are, firstly, the ability of isolated spinal segments to compute properly timed contractions of linked muscles during stepping (section 2.1); and secondly, the inability of noradrenergic and cerebellar influences directly to alter the timing of those contractions, while still adjusting the structure of linkages and their activity levels (sections 2.2, 2.3). It is not entirely clear, of course, that spinal circuits can coordinate the movements of homolateral hind- and forelimbs as effectively as they can the laterally paired limbs (section 2.1.3), but it will be assumed here that propriospinal pathways do at least provide critical timing markers for the turning points of homolateral step cycles[91,160]. It may also not be accepted in some quarters, that the cerebellum has no immediate connection with movement timing, at least in locomotion. This last assertion is rather controversial and deserves some additional discussion:

There has been long-standing debate over the question, does the cerebellum primarily govern the timing of muscle contractions or

merely the magnitude of contraction present at times dictated by other neural centers? Arguments favoring the timing conjecture have been built around observations such as those of Terzuolo and Viviani[209], who recently found that the normal timings of biceps-triceps muscle bursts which arrest forearm movement following sudden release from a condition of isometric tension (the Holmes rebound test) were disrupted in human cerebellar patients. The timing of eye muscle activity during saccades has also been attributed to the cerebellum[117,118,128]. Several theories of cerebellar cortex have indeed indicated how it could function as a "stopwatch" for muscle contractions[25,26,27,117,118]. For the timing element, the theories rely primarily upon parallel fiber conduction delays.

On the other hand, some of the experimental and theoretical demonstrations which seem to support cerebellar movement timing are certainly debatable. Thus, Terzuolo's observations on cerebellar patients, in that they are akin to his results in deafferented monkeys with cerebellum intact[210], might conceivably stem from the well known loss of spindle sensitivity which accompany particular types of cerebellar damage[76,77,126,142]. Spinal circuits clearly make use of such information (e.g., arising from hip extension) in computing the timing of step cycle epochs (section 2.1.2). The evidence from saccadic eye movement studies is beyond the scope of this report; but Dev[44] has advanced a saccade control theory in which timing is the product of a number of neural centers' operations. The cerebellum is involved, but is certainly no "clock." At one time the delay-line hypothesis

for cortical parallel fibers was an elegant explanation for their properties. However, the author has recently shown[22] that those properties could arise as a consequence--an epiphenomenon--of close-packed granule cells evolved for the computation of certain non-linearities by means of threshold recruitment.

As far as locomotion is concerned, any sort of cerebellar timing conjecture is difficult to justify when confronted with Orlovskii's evidence[171] that stimulation of descending pathways from the cerebellar complex during locomotion affects only the magnitude of muscle contraction within fixed activity periods, leaving unchanged both the period duration and the timing of periods relative to the step cycle (section 2.3.4). Orlovskii's finding also accords with other data showing that cerebellectomized mammals, though ataxic when locomoting, have little difficulty producing the movement sequences of swimming (i.e., wherein limbs do not have to generate force to support the body[188,226]). It is said, too, that locomotor interlimb phasing in cerebellar-damaged dogs is grossly normal[181]. Of course, like the noradrenergic system (section 2.2), the cerebellum can have an indirect effect upon movement timing by altering muscle force; spinal circuits will then detect the consequences (using peripheral and, perhaps, "internal" cues) and adjust the timing of subsequent movement epochs. Yet it seems safe to conclude that the anterior lobe cerebellum, in the limited behavior of locomotion, does not "think" in terms of muscle timing, but rather in terms of muscle contraction magnitudes--the structural and metrical prescriptions of

agonist linkages (section 2.3.2).

The most significant corollary of the two-process hypothesis for locomotor control relates to the time frame in which each process may be computed. It seems clear that spinal circuits must formulate the gait-execution process (see above) in a time frame homologous to that of the movements it produces--that is, in "real time." On the other hand, it appears equally clear that at least some of the centers dealing in the synergic tuning process may not operate in real time at all, but in a time frame slower than that of ongoing movement. This corollary arises as a straightforward consequence of the gating of supraspinal, synergic tuning signals by the spinal gait-execution process: Is it necessary to extinguish and then re-create, during the course of each step cycle, those synergic tunings which do not vary from one cycle to the next? No--activity representing such a tuning could continue throughout the cycle, blocked spinally during portions of the step where it is not needed. As a result, the time frame in which the tuning exists will become prolonged with respect to real movement-time. To a first approximation, then, spinal circuits could be considered to supply a timed constellation of "slots" of muscle activity for a locomotor action. "Shining through" the slots, figuratively speaking, will be more temporally extended supraspinal (and some peripheral) influences tuning the muscular contractions according to their synergic organization.

The above principle is no bald assertion. It is well illustrated in the behavior of the noradrenergic executive system, whose

activity (in the cuneiform nucleus, etc.) can remain constant over many step cycles and gaits; the activity changes only when an increase in overall extensor force is demanded. Engberg and Lundberg[59] (see section 2.1.4) perceived that speed increases in freely locomoting cats were not accompanied by changes in the timing of extensor EMG "slots" relative to the step cycle, but rather by increases in the EMG levels within the slots--that is, by commands for greater force reminiscent of those originating in the noradrenergic system and subject to spinal slot-gating. While studying human handwriting movements, Denier van der Gon and Thuring[43] likewise noted that in a given subject, the force used to move the pen was almost always the same amplitude. The character of different strokes was imparted through nuances of timing and directionality of that force. Force amplitude only differed when an alteration in the overall size of the script was requested.

It should now become evident why the specification of the timing of muscle contractions in linkages and synergies was left vague when those terms were defined (section 2.3.1)--and also why the definition of muscle structure in a gait required averaging over step cycles (section 2.1.4): The two-process hypothesis indicates that EMG timings of muscles in linkages or synergies may be widely scattered even though the muscles themselves are truly linked. In EMG patterns one primarily sees the operation of the gait execution process, the "slots" of muscle activity; but it is more difficult to detect the temporally extended, synergic tuning process which lies "behind" the slots unless one is

able to ignore slots by blurring (or averaging over) them.

Is the metaphor of slowly changing synergic tunings sampled by real-time spinal slots also applicable to the adjustment of agonist linkage prescriptions by the cerebellar anterior lobe? Anterior lobe outflow is clearly subject to spinal switching (section 2.3.4). In theory, therefore, nothing would prevent the establishment of "resident" cerebellar activity patterns corresponding to aspects of agonist linkage tuning which are invariant over step cycles. Section 3.1 spells out such "invariant tunings" for locomotion. But the present, and more fundamental, problem is to decide whether any aspect of cerebellar operation is in fact characterized by an extended time frame--i.e., by the carrying over of cerebellar modulation for one movement of an act either into subsequent movements or into repetitions of the same movement. There is some evidence that such a phenomenon can and does occur:

Beginning with the early investigations of Clark[35,36], physiological data have been accumulating which implicate the cerebellum in a variety of long time-course motor modulation processes. Briefly stated (see ref. 22 for details), Clark observed postural biases lasting minutes in awake, freely moving cats following momentary, direct surface shocks of the cerebellar cortex. More recent work by Passouant, et al.[185] has confirmed Clark's findings. Clark attributed his results to "reverberatory loops" existing in the cerebellar complex[36]. This was--and is--sheer conjecture. However, recent anatomical and physiological evidence (ref. 22) has demonstrated the existence of

powerful recurrent excitation mediated by connections between the cerebellar nuclei and certain pre-cerebellar reticular nuclei. Allen and Tsukahara* suggested that this excitation could act to retain cerebellar activity patterns in the manner of a short-term memory. The author[4,208] proposed a similar idea and demonstrated its implications for climbing fiber operation using computer simulation of anterior lobe networks[22,24] (see section 3.1). It was shown that one consequence of repeated climbing fiber volleys in an Oscarsson strip (section 2.3.3) should be a short-term alteration in the distribution of neural activity among various regions of the cerebellar nuclei, depending upon the location of the strip. Interestingly enough, following repeated unilateral stimulation of the caudate nucleus in acute cats under barbiturates, Gresty and Paul[85] have recently documented progressive changes in the responses of both fastigial nuclei; the contralateral response is facilitated, the ipsilateral inhibited. This "adaptation" appears to be a short-term, repeatable phenomenon (i.e., not involving plasticity), and the authors cite other results indicating that it is connected with climbing fiber volleys. They give no further explanation of their findings. In any event, the scattered physiological and anatomical observations from Clark's studies down through Gresty and Paul's surely hint at the presence

*Allen, G.I., Tsukahara, N., "Cerebrocerebellar communication systems," Physiol. Rev. 54, 957-1006 (1974).

of temporally-extended (but non-plastic) activity connected with cerebellar operation. Unfortunately, the all-pervasive and semantically empty assumption that the cerebellum is "obviously" a high-speed computer regulating movement has perhaps stifled the sorts of experiment which could determine where the gunpowder ends and the molasses begins (see ref. 22 for some examples of such experiments). One can leave this state of affairs behind, however, and turn to a more behavioral line of evidence indicating that some portion of cerebellar modulation is intended to apply to a series of movements stretched out over time. The data stem from studies of so-called "next-cycle adaptation":

Next-cycle adaptation refers in general to the modification of subsequent movements in an act based upon events (usually perturbations) occurring during an antecedent movement. In the case of repetitive movements such as step cycles, the modification is thus seen in the "next cycle" following perturbation. Orlovskii and Shik[179] appear to have been among the first to call attention to next-cycle adaptation, which they observed following the momentary application of a brake during transfer-flexion at the knee of intact, trotting dogs (cf. section 2.3.1):

Braking temporarily retarded flexion, but by the beginning of the next cycle, the normal trajectory had been restored. However, in the next step cycle (800-900 msec following braking) it was found that transfer-flexion again was first delayed, then shortened, almost as though the brake had been reapplied and the reflex response again

elicited. This "phantom braking response" disappeared after one further cycle. But if the brake actually had been applied at the same time in each step cycle, such a response would have effected an adaptation to it--a short-term recollection of both the perturbation and the recipe for its correction. Shik and Orlovskii also found in another study[195] that slightly negative correlations exist between joint angle excursions of successive step cycles in dogs, again suggesting that a record of previous performance (presumably including perturbations) is used to tune the present step cycle.

Next-cycle adaptation is one of the few mechanisms performing the environmental adjustment of locomotion. Several authors have pointed out[86,88,92] that conduction delays even in fast-acting segmental reflexes are sometimes too long to allow the correction of perturbations within the step cycle epoch in which they occur. Moreover, the extension phase of the cycle, which would probably require the most environmental tuning, seems to lack any significant (in terms of force development) segmental supervision whatever (see section 2.3.1). The absence of immediate segmental reflex control of human movement[3,95,150,151] (Nashner, in press) is also striking. A long-neglected factor, the mechanical stiffness of muscles, is now being found to contribute a great deal of whatever rapid perturbation corrections do take place in these situations[18,86,88,95].

What central mechanisms account for next-cycle adaptation? Melvill Jones[150,151,152] and others[202] have proposed an origin from long latency reflexes conveniently timed so as to influence the programming

of future movement episodes, a modern variation on the old theme of "reflex chaining"[84]. The primary difficulty with the explanation lies in reconciling nominally fixed reflex timings with movements executed at different speeds. Alternatively, might it not also be that next-cycle adaptation is a manifestation of a long time-course synergic tuning process which receives information about present movement, "remembers" it for some period, and employs this memory in tuning subsequent movement epochs? That is, could next-cycle adaptation actually be another manifestation of the two-process hypothesis and its two time-frame corollary presented in earlier paragraphs? An affirmative answer to this question, and some strong evidence that the cerebellar complex aids (or, perhaps, is the site of) the memory faculty of next-cycle adaptation, has been obtained by Nashner and Grimm (Nashner, in press) in human subjects:

By way of background, earlier experimental work by Nashner (in press) had established that a "stretch reflex" can be elicited from the ankle muscle of normal human subjects when the ankles are abruptly rotated by a platform upon which they are standing. This reflex has a latency of about 110 msec (see ref. 150 for a description of a similar phenomenon), suggesting that it is not segmental; however, the latency is too short to represent voluntary intervention. The reflex muscle contraction causes the subject to fall in the direction of ankle (i.e., platform) rotation. Consequently, on subsequent rotations reflex EMG amplitudes diminish until the reflex disappears altogether. Other strategies of platform manipulation (Nashner, in

press) can cause similar adaptive augmentation of reflex amplitude.

It is clear that Nashner's long-latency stretch reflex is subject to next-cycle adaptation, since one ankle rotation determines the reflex response level to the next rotation. In addition, in quietly standing subjects the adaptation appears to have a decay "time constant" of about 2 or 3 minutes--it is a short-term memory process. Tests of motoneuron pool excitability (using the H-reflex; Boylls and Nashner, unpublished) show no adaptation-correlated changes, indicating that adaptation may originate supraspinally. Yet informing subjects of incipient platform maneuvers does not cause pre-adaptation, implying that the memory mechanism is not consciously accessible.

Given the above findings in normal subjects, Nashner and Grimm (in press and in preparation) have examined reflex adaptation in patients with cerebellar extirpations. What they have found, quite simply, is that the long-latency stretch reflex remains present, but the capacity for its next-cycle adaptation disappears. This remarkable demonstration reveals another instance of the separation of the production and timing of a movement (the reflex) from its tuning. It further shows that the tuning process is associated with a short-term memory facility capable of extending tunings over a succession of movement episodes. And it implicates the cerebellum in the tuning-memory computation, although one cannot ascertain the details of its involvement. But judging from the evidence presented earlier for long time-course physiological processes in the cerebellar complex, it certainly is conceivable that next-cycle adaptation could owe itself

to intrinsic cerebellar properties.

In conclusion, it would appear that to synthesize locomotion (and, perhaps, other classes of action) the motor system has not adopted the jaded engineering strategy of presenting a desired pattern for movement to a set of on-line servomechanisms--the cerebellum among them--which use continuous feedback to secure the faithful execution of the pattern. There is a "desired pattern" certainly enough, a constellation of timed muscle activity slots created spinally and a distribution of excitation in descending pathways, representing synergic tuning, to be gated through the slots. However, this pattern is executed in very nearly an open-loop fashion (see ref. 71 for a similar idea developed in another context). Errors are noted, but rarely acted upon when they occur. Instead, the errors are "remembered"; they and other elements of past performance are retained in a short-term memory by the synergic tuning process--by, quite possibly, the cerebellum--and are used as an anticipatory or feed-forward context for future movement. Ito[104,105] has perhaps been the most ardent exponent of cerebellar participation in supplying such feed-forward information. He has proposed that the cerebellum functions as an internal model of the environment, that the motor system uses the techniques of model-referenced control developed by engineers. The idea being proposed here, though, is that the cerebellum simply continues to update its agonist linkage tunings (structural and metrical prescriptions) based upon, in part, the unfulfilled demands of past performance. Insufficient flexion on a previous step calls for

increased flexion now, for example. This cannot really be construed as an "internal model" in Ito's sense since the causal chains in the environment which lead to a demand for some change in movement are not modeled. Only the demands themselves are, regardless of why they arise. In other words, there is only "one unit" of memory. This may seem crude, but Greene[83,208] has pointed out that a mere modicum of feed-forward data can be remarkably beneficial in simplifying the complexity of a control problem.

The two-process hypothesis, separating the synergic construction and timing functions from those of synergic tuning, thus suggests a somewhat natural connection of tuning with short-term memory and feed-forward, anticipatory fabrication of motor commands. The cerebellar association with such operations cannot be so satisfactorally established owing to large holes in the literature. However, if one assumes the two-process hypothesis and its consequences correct, it is possible to produce some rather detailed, experimentally addressable predictions about cerebellar behavior during locomotion. These predictions are the subject of the next four sections.

In summary:

1. Locomotor control appears to be achieved through the synthesis of two distinct processes: The gait execution process, computed spinally, constructs locomotor synergies and times the contractions of their muscles. The synergic tuning process, computed by the cerebellum and noradrenergic executive, adjusts synergic parameters.

2. The spinal gait execution process essentially creates a constellation of timed EMG slots in locomotor muscles. Synergic tuning is applied "through" the slots by the action of spinal switching.

3. The gait-execution computation is carried out in real time. However, the calculation of synergic tunings can, at least in part, be accomplished within a time frame slower than that of ongoing movement.

4. The extension of synergic tuning over several step cycles is best illustrated in the phenomenon of next-cycle adaptation. In this situation, some part of short-term memory is employed to construct feed-forward contexts for future movement based upon information gathered in the present. It is quite possible that the tuning of locomotor agonist linkages by the cerebellar anterior lobe is characterized by such a short-term memory faculty.

3. The Theoretical Analysis of Climbing Fiber Operation During Locomotion

What contribution does the cerebellar anterior lobe complex make to the control of locomotion in cats? According to the review just concluded, it tunes the properties of locomotor muscle synergies--or more precisely, it adjusts the structural and metrical prescriptions of the agonist linkages in those synergies. Furthermore, the anterior lobe computes its agonist tunings so that they extend over a sequence of actions in time. There is a continuous updating of tunings, but events of the recent past distinctly color present

cerebellar transactions.

In an earlier report[22] a theory of the physiological function of climbing fibers was developed by using computer simulation and mathematical analysis to interpret existing data on the fibers within an anterior lobe setting. By now placing that theory in the above context, it is possible to devise a set of conjectures relating climbing fiber physiology to behavioral events in locomotion. This task is initiated below (section 3.1) by recapitulating the major results of the earlier work[22] and then understanding them in a muscle linkage context using information given earlier here. The outcome--a relationship between linkage tuning and climbing fiber activity--next leads to predictions of activity to be expected in different locomotor gaits (section 3.2). Thereafter, it is possible to say a few things about the peripheral and central sources of climbing fiber inputs, subsuming what is already known about the subject and adding several new hypotheses (section 3.3).

Any discussion of the cerebellar influence on locomotion would be incomplete without some mention of midline posterior lobe regions. Thus, a few utter speculations on the topic are offered at the close of this analysis (section 3.4); however, those statements are not meant to be taken particularly seriously because so little information is available on the posterior lobe.

3.1 Climbing Fiber Activity and the Tuning of Agonist Structure for Locomotor Synergies

3.1.1 Physiological Consequences of Climbing Fiber Activation

As was described in section 2.3.3 above, the cerebellar anterior lobe is composed of a series of sagittal, corticonuclear compartments, each of which appears to be under the influence of a single Oscarsson strip of climbing fibers. An Oscarsson strip can in turn be resolved into a number of microstrips (perhaps a continuum thereof). The impact of both single and repeated, synchronous microstrip volleys upon ongoing neural activity in the anterior lobe complex has been assessed elsewhere[22] using a mathematical model. It was shown that such volleys redistribute the excitation among cerebellar nuclear regions in the manner schematically illustrated in figure 2 (from Boylls[22]): Here the cerebellar nuclei and two of their brainstem projection targets are shown as two-dimensional sheets, allowing their conformation with the cerebellar cortex. A typical corticonuclear compartment is indicated by the projection zone of the "single" Purkinje unit (see ref. 22 for details of the actual projection patterns). The nuclear aftermath of climbing fiber microstrip (or Oscarsson strip) volleys in this compartment is conveyed by the undulating surface superimposed on the nuclear region. Its height at any given point is qualitatively proportional to the degree of nuclear excitation at that location. What the figure demonstrates, in other words, is that climbing fiber microstrip volleys in an Oscarsson strip of the anterior lobe cortex will ultimately lead to a retention--even a reinforcement--of nuclear excitation in the corticonuclear compartment governed by that strip. At the same time, nuclear excitation in mediolaterally

neighboring compartments will be reduced or suppressed.

A mechanism for this rearrangement of compartmental excitation by Oscarsson strip volleys has, of course, also been worked out[22]. The brief silencing of Purkinje cells following their climbing fiber responses (cfr's) yields a significant "release" of cerebellar nuclear excitation within the compartment containing an active Oscarsson strip. That released nuclear activity is transmitted to various precerebellar reticular nuclei to be reflected back to the cerebellar cortex (on so-called "slow" mossy fibers). The excitation then spreads mediolaterally via the parallel fibers, elevating the Purkinje inhibition in neighboring corticonuclear compartments.

In the development of the theory in subsequent sections the physiological details of how climbing fibers achieve the redistribution of compartmental activity will not be of much consequence. Thus, the redistribution phenomenon will be treated as an "axiom" whose antecedents are not particularly important. There will no doubt be some, however, who will find it impossible to consider that climbing fibers could promote the net excitation of those portions of the cerebellar nuclei they directly influence, at the expense of surrounding nuclear regions. After all, do not climbing fibers cause violent discharges of Purkinje cells and consequent sharp inhibition of the nuclear targets of those cells?

Both the "inhibitory" and "excitatory" hypotheses of climbing fiber effects on the cerebellar nuclei have been defended by various investigators in the past. Yet their arguments are based upon

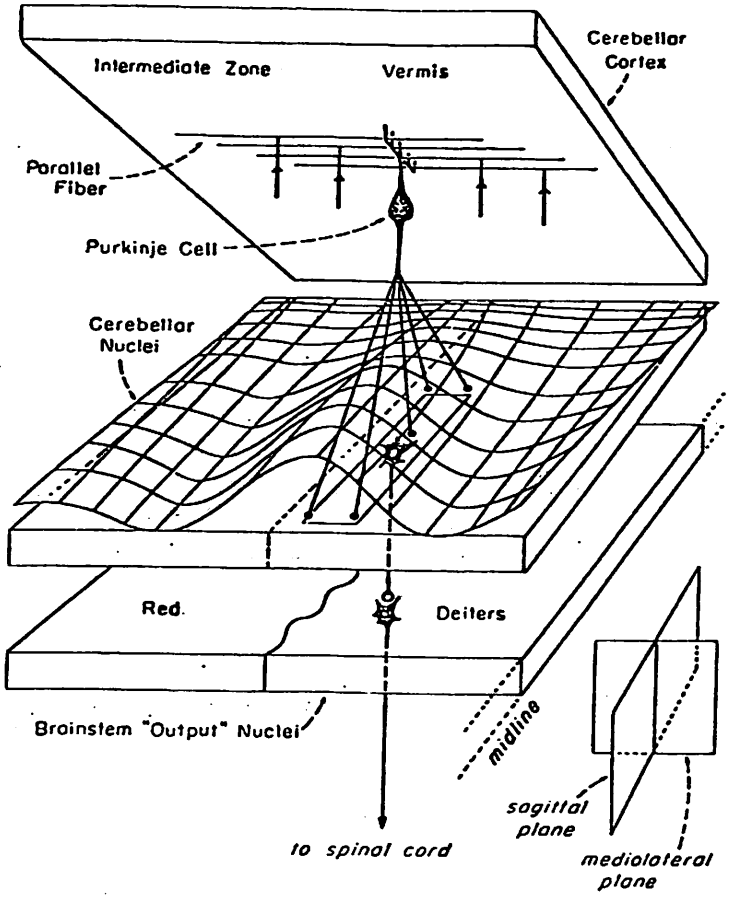

FIGURE 2

Schematic conception (after Boylls[22]) of cerebellar nuclear spatial activity patterning following volleys in an Oscarsson climbing fiber strip. Height of the surface indicates relative degree of nuclear excitation. A ridge of activity is left in the nuclear region within the corticonuclear compartment containing the active strip, while inhibited valleys develop in compartments mediolaterally flanking the strip.

single-unit observations in acute preparations; and it is well known (see ref. 22 for review) that levels of reticular excitability and the duration of Purkinje silencing following the cfr, both of which may have profound qualitative influences upon the cerebellar complex response to climbing fiber inputs (Boylls, unpublished), are strong functions of anesthetic species and levels, and state of consciousness (e.g., sleep vs. waking). Is there, then, a way to assess climbing fiber action upon some "simple" motor behavior--one whose anatomical substrate is known sufficiently well to allow the deduction of the true physiological impact of the olivary system on cerebellar outflow? Yes, there is. The "behavior" is the vestibulo-ocular reflex of rabbits, which is modified by outflow from the cerebellar flocculo-nodular lobe. A description of the reflex and its modification by climbing fiber activity (with respect to the flocculus) is given in the Appendix. But to summarize briefly:

Flocculus climbing fibers are driven by moving visual targets. Using an hypothesis by Ito (see Appendix) that the fibers set the "gain" of the vestibulo-ocular reflex, the author[208] advanced a means of deducing the apparent impact of their activity on flocculus inhibition by observing direction specificities of targets producing such activity. In other words, by examining the "wiring" of the reflex it was possible to conclude that if climbing fiber volleys were intended to increase flocculus inhibition of certain vestibular nuclei or decrease the latter's outflow (as many would expect), then they should respond to visual stimuli moving in one particular direction;

if, instead, the fibers responded to movement in the opposite direction, then one could surmise that climbing fiber activity operationally reduces flocculus inhibition (or increases nuclear output). The latter outcome would support the present theory, of course.

Subsequent experiments have in fact shown that climbing fiber direction specificities are such as to support the inhibition-reduction doctrine (see Appendix). As this text is written, N. H. Barmack is conducting a more direct investigation of flocculus climbing fibers using discrete olivary lesions and stimulation. Thus far, his results (Barmack, personal communication; Appendix) also accord with the idea that climbing fiber activity results in the relative elevation of excitation in nuclear areas it influences directly.

The vestibulo-ocular data support only the conjecture that Oscarsson strips do not serve to suppress cerebellar nuclear excitation within their own compartments: The more remote effects--suppression of adjacent compartments--seen in simulations[22] have yet to be examined behaviorally. It is conceivable, however, that the vestibulo-ocular reflex just might be useful in looking for this phenomenon, too (see Appendix).

A second major observation made in the previous report[22], and which will become a second "axiom" here, is that climbing fiber-induced activity distributions in the compartments of the cerebellar anterior lobe persist for significant intervals of time following their creation. By a "significant interval" is meant a period of say, several orders of magnitude larger than the membrane time

constants of cells constituting the cerebellar complex. In section 3.2 the interval will be postulated to be (minimally) the time required to complete a step cycle in both homolateral limbs in a given gait. Now the existence of such "short-term memory" in the cerebellar complex was already argued (section 2.4), and the evidence will not be recapitulated. It has been shown elsewhere[22] that reciprocal, excitatory connections between the cerebellar and certain reticular nuclei could easily be agencies for the retention of cerebellar activity patterns in a purely dynamic fashion--i.e., without "plastic" changes in the physiological or anatomical parameters of the cerebellum. On the other hand, it will make little difference to the theory below if plasticity exists. Also, the association of cerebellar short-term memory with the function of climbing fibers is not meant to be construed as rejecting the importance of such memory to the operation of mossy fibers in regulating cerebellar output. This subject is currently being investigated (Boylls, in preparation); a few of the preliminary results are mentioned later (section 5).

In order to complete certain of the deductions to be presented, some additional provisos will have to be added to the two "axioms" above. These will be stated in the appropriate sections. Even so, one can still make a surprising amount of progress in constructing a plausible role for climbing fiber activity in locomotion using only the present axioms. The principal conclusion is stated in the next section (3.1.2).

In summary:

Climbing fiber volleys in Oscarsson strips will be considered here to have two fundamental physiological consequences in the cerebellar anterior lobe complex:

1. Cerebellar nuclear excitation within the corticonuclear compartment controlled by an active strip will be accentuated relative to nuclear excitation in neighboring compartments.

2. Such distributions of activity among compartments will be retained for significant intervals of time.

3.1.2 The Relationship of Oscarsson Strip Activation to the Tuning of Structural Prescriptions for Agonist Linkages

As might be guessed from the title of this section, a very definite role for anterior lobe climbing fiber activity in anterior lobe locomotor modulation will now be proposed. Specifically, it will be held that:

> During locomotion, climbing fiber volleys organized within Oscarsson strip zones of the cerebellar cortex facilitate the tuning of the structural prescriptions for the agonist muscle linkages of locomotor synergies.

In other words, it is predicted that climbing fibers are involved in such tasks as promoting shifts from proximal to distal muscle usage, or setting up asymmetric biases on homologous muscles, as occur when animals shift from alternate- to bilateral-step gaits (section 2.1.4).

But before treating such phenomena (sections 3.2, 3.3), the rationale of this structural-tuning hypothesis must be explored.

Actually, the conjecture follows as a straightforward application of the encoding scheme for anterior lobe linkage tunings (structural and metrical prescriptions) described in sections 2.3.2, 2.3.3, and 2.3.4, and of the physiological consequences of Oscarsson strip volleys presented in the previous section (3.1.1). Structural prescriptions of muscle linkages are encoded by means of the relative amounts of excitation distributed among the descending tracts influencing those linkages, as was proposed in section 2.3.2. The excitation distribution among descending tracts in turn has an encoding as an activity distribution among the various sagittal corticonuclear "compartments" of the cerebellar anterior lobe (described in section 2.3.3). By one of the two "axioms" stated in section 3.1.1, climbing fiber volleys organized according to Oscarsson strips are very effective at creating or altering the relative amounts of activity within compartments. On the other hand, even the most precisely localized of ascending mossy fiber tracts (DSCT, CCT) appear to "smear" their information across several compartments[57] (see section 5 for some implications of that organization). Therefore, Oscarsson strip climbing fiber inputs would seem selectively to deal with the structural prescriptions of linkages. That they must be agonist linkages in the locomotor context is a point already brought forth in section 2.3.4.

The retention of compartmental activity distributions set up by climbing fibers--the other "axiom" of section 3.1.1--also has

some bearing upon the structural-tuning interpretation of climbing fiber operation. Given that the structure of loccmotor muscle usage appears to be a function of gait, rather than of the step cycle (section 2.1.4), it follows that the structural prescription for agonist tuning is something which, theoretically, could survive in a short-term memory from one step cycle to the next, so long as gait were unchanged (cf. the discussion of next-cycle modulation in section 2.4). This, however, is not as strong an argument for climbing fiber structural tuning as that given above: The <u>metrical</u> prescriptions computed by the cerebellar anterior lobe probably also make use of short-term memory (Boylls, in preparation; see section 5).

Experimental tests of the climbing fiber/structural prescription relationship will not be proposed until the end of this report (section 4.2), since deductions useful for the construction of such tests have not yet been presented (sections 3.2, 3.3). Nonetheless, it should be heuristically evident that this proposition would explain a number of existing, and rather notorious, physiological and behavioral observations on climbing fibers: Physiologically, it is well known that when activated from peripheral afferents, climbing fibers respond after rather long latencies and will not respond to stimuli repeated much faster than 10/sec (see refs. 5, 22 for review). Thus, it is difficult to see the spino-olivocerebellar system as part of an "on-line" feedback control mechanism, although some have tried. But if climbing fibers are instead responsible for programming step-cycle-invariant, structural prescriptions for agonist muscle linkages,

then response latency is essentially irrelevant and the 10 hz "band-pass" is more than adequate. This will become more clear once an association between spino-olivocerebellar volleys and activation of spinal stepping circuitry has been established (sections 3.2, 3.3). Of course, other hypotheses have been advanced which attempt to account for climbing fiber physiology. Armstrong[5], for example, has suggested that climbing fibers may be part of a long-latency "reflex" system designed to use information from a previous step cycle epoch to modify the present step cycle. His suggestion is thus akin to that of Melvill Jones' explanation of next-cycle adaptation (section 2.4) and is subject to the same criticism--namely, how to reconcile fixed reflex latencies with the wide range of step cycle timings. The popular hypothesis that the climbing fiber "teaches" the cerebellum its duties during locomotion (and other actions[1,2,20,143]) is one whose conjectured physiological substrate can almost always be modified to account for existing findings. But the deficits which appear immediately when climbing fibers are interfered with or eliminated seem difficult to reconcile with an exclusive teaching function for climbing fibers (section 4.2 and Appendix; see also refs. 22, 23).

Behaviorally, it has been extremely difficult to correlate climbing fiber discharges with any immediate attribute of ongoing movement[139,211,212,213] (Grimm and Rushmer, in preparation), either motor or sensory (however, in the cerebellar flocculus correlations have been observed in connection with the vestibulo-ocular reflex; these are treated in the Appendix and ref. 23). Perhaps that failure stems

from investigators looking too closely at the motor and sensory events which comprise an act, while paying little heed to the motorsensory requirements of different <u>classes</u> of action. If the ideas presented here are correct, climbing fiber volleys become salient during locomotion only when a change in the tuning of muscle linkage structure is required--i.e., following the assumption of a new gait (actually, a new gait category, as will be explained in section 3.2). However, the tasks thus far presented animals for the purpose of examining climbing fiber activity have involved either the overtrained repetition of the same action, or at best, mild variations thereof. Unfortunately, what constitutes a "different act" from the standpoint of climbing fibers may not be at all what is "different" to the eye, making the construction of appropriate tests of climbing fiber function difficult. An effort will be made in a subsequent section (3.3) to specify which actions might be equivalent with respect to anterior lobe climbing fibers, thereby indirectly indicating boundaries between truly different actions.

Thus, the olivocerebellar system and its climbing fibers are a mechanism for exerting a "tonic" structural bias upon the usage of muscles. This notion may extend well outside the anterior lobe to other cerebellar regions. An example of "structural bias" as might apply to the vestibulo-ocular reflex and the cerebellar flocculus is given in the Appendix. Another report[23] examines structural bias with respect to the cerebellar hemispheres and the parametric stabilization of movement. Unfortunately, a deeper understanding of the biasing

effect is not really possible without considering the cooperative functions of both climbing and mossy fibers. Climbing fibers may actually be constructing a sort of spatial mask, consisting of more or less excited corticonuclear compartments, through which rather diffuse mossy fiber activity is sieved (to mix metaphors). The mask or sieve "is" the structure of muscle linkages used in the current act; the mossy activity passing through represents both feedback and internal (efferent command), feed-forward information on, in essence, the forces developed or to be developed by those linkages--their metrical prescriptions. The dynamic mask of compartmental activity functions to route mossy metrics into the linkages, weighted according to muscle structure. Climbing fibers, as it were, provide a "programmable reflex" capability at the cerebellar level; but such one-phrase summaries are equally one-dimensional. There will be more said about climbing and mossy fiber cooperation at the conclusion of the report (section 5), and it is not particularly important to understand "masks and sieves" now. What is important is to realize that the statements made here about the muscle effects of climbing fiber action in locomotion do have, and should be understood within, a wider context into which mossy fiber contributions enter.

To summarize:

1. Judging from their Oscarsson-strip effects on the spatial distribution of activity in the sagittal compartments of the cerebellar anterior lobe, it appears that climbing fiber function is best associated with the tuning of the structural prescriptions of agonist

muscle linkages in locomotor synergies.

2. The short-term memory capacity of the anterior lobe complex (its retention of compartmental activity distributions) allows the programming of structural prescriptions which are invariant over individual step cycles, as appears to be actually true in locomotion; structure is a function of gait, rather than of steps.

3. Climbing fiber activity might be better interpreted as biasing the structure of muscle usage for entire acts consisting of many movements. It is probably an error to attempt a correlation of that activity exclusively with the on-line programming of individual movements within an act.

3.2 Oscarsson Strips Associated with the Execution of Particular Gaits: Predictions

The relationship derived in the previous section (3.1) between climbing fiber activity and the structuring of locomotor muscle usage is, generally speaking, too abstract to allow the construction of experimental tests (but see section 4.2). However, given a few additional assumptions about anterior lobe climbing fiber behavior (see below), it is possible to jump quickly to some rather detailed predictions about which Oscarsson strips modulate which locomotor gaits. The selection of "gait" as the parameter most salient for evaluating climbing fiber activity stems directly from the observation that muscle structure is a function primarily of gait (section 2.1.4). However, this is not to say that every gait has a unique structure,

as will be seen shortly.

The additional assumptions (other than the "axioms" stated in section 3.1.1) to be used to derive gait-dependent Oscarsson strip deployments are, with discussion, the following:

1. The cerebellar anterior lobe modulates both the flexion and the extension phases of the step cycle.

Discussion: This seemingly innocuous conclusion is complicated by the presence of near-normal transfer-flexion (as distinct from extension) in spinal cats (section 2.1.2). Moreover, lesions of the red nucleus reportedly have much less effect upon flexion in mesencephalic locomotion than have Deiters nucleus lesions upon extension[171]. But at the same time, "flexor" brainstem output nuclei (red nucleus, NRG) do have activity episodes correlated with flexion (section 2.3.2) and will indeed cause added flexor contraction if stimulated during this period (section 2.3.4). Therefore, anterior lobe outflow almost surely influences flexion, as well as extension; but it is possible that the potent peripheral reflex inputs used to standardize transfer-flexion (sections 2.1.2, 2.3.1) obscure its cerebellar tuning. Faulty cerebellar outflow is, on the other hand, glaringly apparent in the more "open-loop" performance of extension (section 2.3.1). It would thus be interesting to compare transfer-flexion in deafferented limbs with and without red nucleus or NRG contributions.

2. Climbing fiber-induced alterations in anterior lobe compartmental activity persist for at least the duration of the step cycle.

Discussion: The intent of this proposition is to make formal the association of locomotor muscle structure with parameters governing gaits, rather than individual step cycles. That is, structural prescriptions are assumed to vary little with the nuances of isolated step cycle epochs; and instead, the short-term memory capacity of the anterior lobe is used to store such prescriptions for re-use in several (or many) cycles (cf. the phenomenon of next-cycle modulation; section 2.4). Barmack and Hess (see Appendix) have shown that the effects on eye movement in rabbits produced by a brief climbing fiber volley persist for many seconds. Such a time course for the consequences of anterior lobe cfr's would be adequate to service essentially all but the very slowest locomotor performances. In addition, it is quite conceivable that the storage time constant of the anterior lobe complex is not fixed, but varies with step cycle duration (although always remaining greater than the latter). Section 5 treats the possibility briefly.

3. The distribution of activity among anterior lobe corticonuclear compartments should obey some sort of "hill-and-valley" constraint, such that relatively excited compartments are separated by relatively inhibited zones.

Discussion: This statement merely reflects the basic organization of compartmental activity distributions created by climbing fibers. Since a single excited compartment forces, by lateral inhibition, the suppression of its neighbors (section 3.1.1; figure 2), it follows that excited compartments should be isolated from each other by suppressed

regions. Distributions having contiguous excited compartments will be in disequilibrium. A more technical way of stating the constraint is that efficacious climbing fiber strip activity must fit the spatial frequency passband of the anterior lobe lateral inhibition system (see below).

4. In the common locomotor gaits, the distribution of activity among the various anterior lobe compartments is spatially continuous across the midline.

Discussion: The anterior lobe cortex is continuous at the midline. Consequently, any "saltatory" inequalities among cerebellar nuclear activities on each side of the midline will quickly be smoothed by feedback through the cortex (via the pre-cerebellar reticular nuclei), if not by bilateral "slow" mossy fiber projections and the like.

Given the above assumptions, the derivation of Oscarsson strip activity patterns for different gaits is relatively straightforward. As an aid in the discussion, figure 1 (section 2.3.3) is repeated here as figure 3: One may begin the derivation by noting from figure 3 that each "locomotor" anterior lobe Oscarsson strip influences the facilitation of agonistic muscle linkages for only one of the two step cycle epochs (flexion, extension). Thus, by assumption (1) above, it must be that in a given gait at least two strips are active on each side of the midline. Furthermore, the compartmental activity distributions they produce must all reside simultaneously within the anterior lobe complex, according to assumption (2). In other words, the cerebellum has a complete structural program for the

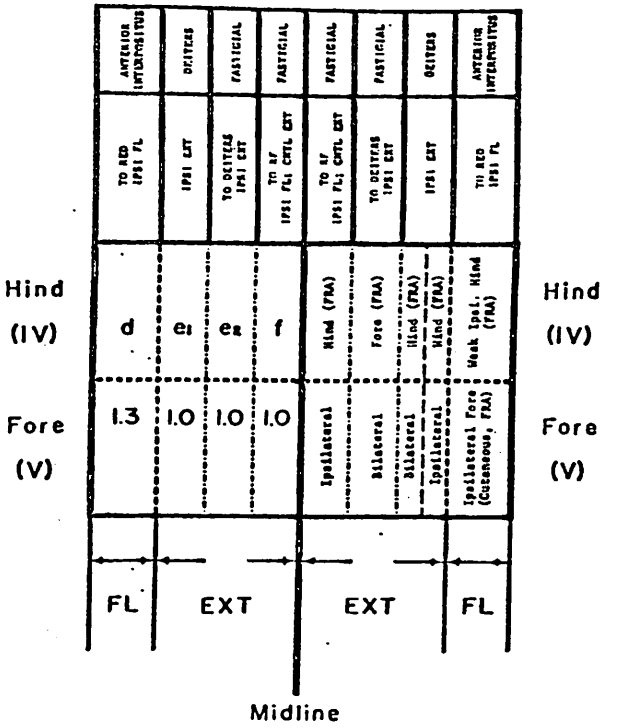

FIGURE 3

Repetition of figure 1 as an aid to discussion. See section 2.3.3 for details.

entire step cycle, in all four limbs, stored within its ongoing activity, regardless of which epochs are currently undergoing execution. This point has an intriguing consequence of its own to be treated in section 5. The present question, however, is how such a structural specification is packed into the anterior lobe compartments. It is at this juncture that assumption (3) is useful:

According to figure 3, there are only four Oscarsson strips on each side of the "locomotor" anterior lobe midline. At least two of these must be active in a given gait (see above). However, according to assumption (3), active strips should be separated from each other. Obviously, therefore, no more than two active strips can be permitted on a given side of the midline; and in fact, it can be seen from figure 3 that strip pairs d-e_2, d-f, and e_1-f are the only admissible co-active combinations. But now one must return to assumption (1) above and ask, does each of the strip pairs affect both a flexor and an extensor corticonuclear compartment? According to figure 3 once again, pairs d-e_2 and e_1-f satisfy the criterion, but pair d-f does not (both strips control flexor compartments). Notice that the two acceptable strip pairs (d-e_2, e_1-f) fall into the same regular spatial pattern of active strips alternating with inactive. This particular sequence conveniently fits the spatial frequency selectivity of the anterior lobe complex, as will be described momentarily.

Having deduced the basic schemes into which locomotor Oscarsson strip activity should fall in each half of the anterior lobe, the next problem is to consider the cooperation of the two halves--that

is, the possible compartmental activity patterns of the complete locomotor anterior lobe. These patterns are easily perceived by taking combinations of the two allowable paired strip distributions in each cerebellar half and splicing them together smoothly at the midline, as assumption (4) above dictates. It will be seen that there are only three qualitatively different ways to do this, as shown in figures 4, 5, and 6:

Each of the figures is an abbreviated version of figure 3--that is, a top view of anterior lobe cortex with landmarks as in figure 3. The wavelike pattern drawn at the top of each diagram qualitatively indicates the level of compartmental activity provoked by activating a given combination of strip pairs in the two cerebellar halves. Thus, peaks of the waves occur above active Oscarsson strips (i.e., excited compartments) and valleys above inactive. Figures 4 and 5 result from combining activation of identical strip pairs in each cerebellar half (pair e_1-f in 4; d-e_2 in 5). Activation of complementary pairs produces figure 6, which, of course, shows only one of the two possible complementary-pair patterns; however, the other pattern is simply the mirror image of figure 6 and does not involve any qualitative differences in the compartments activated. Thus, of the three schemes of anterior lobe strip activation, two yield symmetrical distributions of compartmental activity on each side of the midline (figure 4, 5); one produces an asymmetrical allocation. These symmetry considerations will be important below in determining the gaits for which each pattern is a structural prescription.

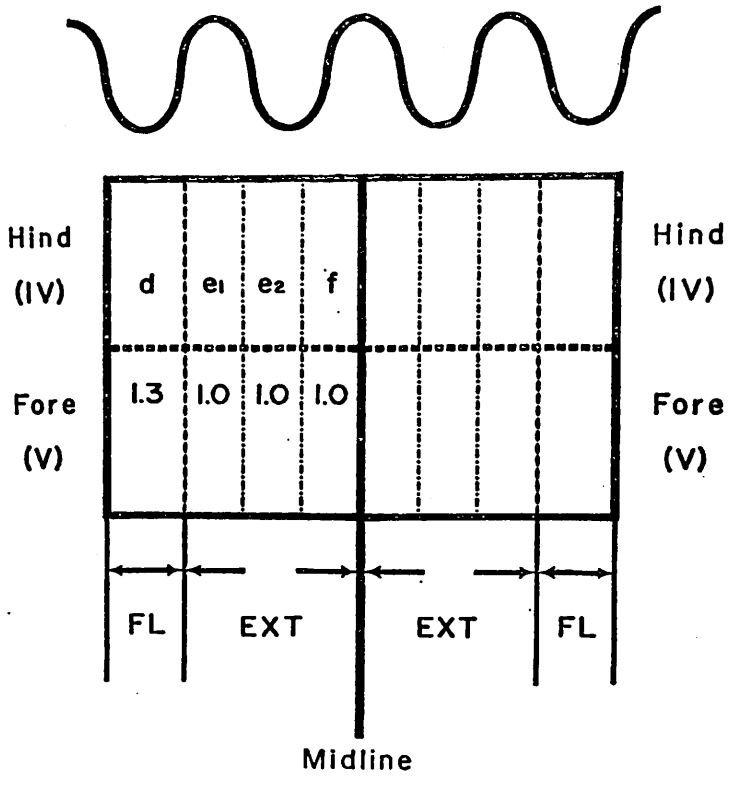

FIGURE 4

One of three possible patterns of anterior lobe compartmental activity which agree with the axioms of this section. Landmarks of the diagram are as in figure 3. The wave pattern indicates compartments whose nuclear regions are either excited (hills) or inhibited (valleys). This particular activity distribution (or linkage structural prescription) has been assigned to the "trot." See text for details.

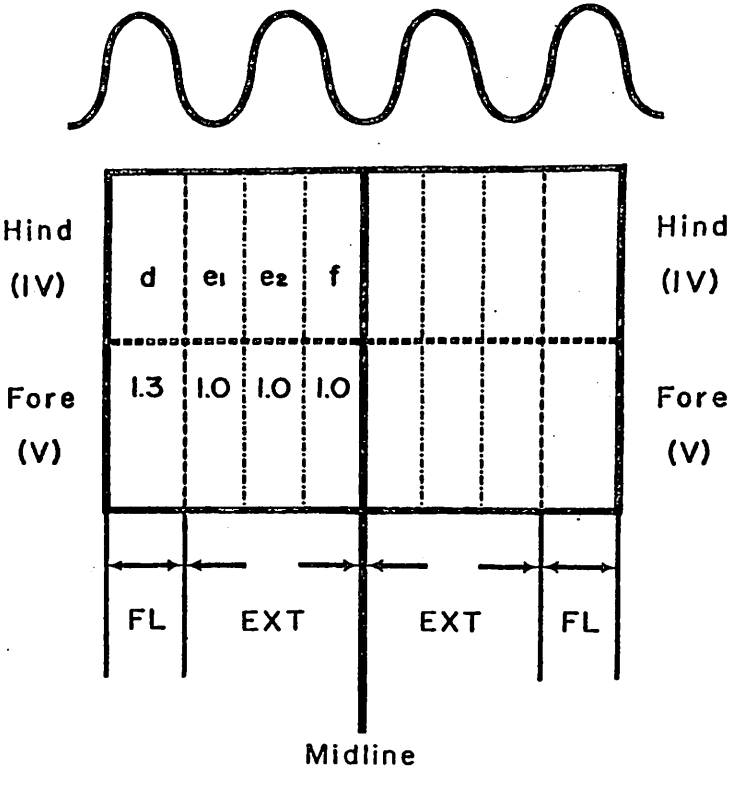

FIGURE 5

A second admissible compartmental activity pattern, designated to be that of the "rack." Compare figure 4.

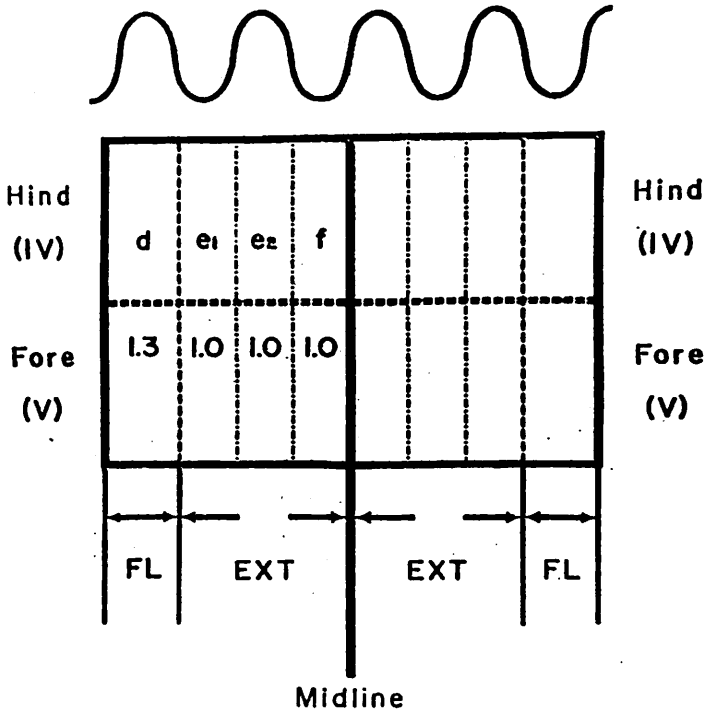

FIGURE 6

The third and final pattern. As against those of figures 4 and 5, it is asymmetric. It belongs to a "gallop" featuring a left-sided rack and right-sided trot.

Before doing that, however, there are some intrinsic features of the patterns worth discussing: The first is the presence of contiguous active or suppressed compartments at the midline in the two symmetric patterns (figures 4, 5), which would seem to violate assumption (3) given above. Actually, only an asymmetric pattern such as in figure 6 avoids this difficulty. But to anticipate later discussion, if, as has been argued, these patterns represent structural prescriptions for locomotor muscle linkages (section 3.1.2), then midline-symmetric muscle usage must be tuned by midline-symmetric prescriptions--i.e., midline symmetric anterior lobe compartmental activity. In view of the other constraints on strip activation given above, the symmetric patterns in figures 4 and 5 must be allowed, lest the large category of symmetric gaits (i.e., the alternate-step gaits; sections 2.1.3, 2.1.4) be without a cerebellar activity scheme for their structural tuning. It is thus concluded that the two midline compartments function as one during symmetric gaits.

A second property of the patterns in figure 4-6 is that the "wavelength" or spatial period of the activity distributions relative to the cortex must differ between the symmetric and asymmetric situations. Looking first at the asymmetric pattern (figure 6), it can be seen that a "best fit" of compartmental activity occurs at a spatial period of approximately 2 mm/c, the average spacing of the active Oscarsson strips. However, to splice compartmental activity symmetrically across the midline such that it still fits the allowable strip-pairs (d-e_2, e_1-f; see above) on each side requires that the period be

lengthened somewhat to approximately 2.5 mm/c (by computer calculation). Now it was shown in a previous theoretical study[22] that a prominent spatial resonance of the anterior lobe complex (thanks primarily to lateral inhibition between compartments) may occur at a period of 2.25 mm/c relative to the dimensions of the cortex. In other words, it is possible that the system is spatially tuned to a point "halfway" between the optimal tunings for the production of either symmetric or assymetric activity distributions, thereby allowing equal acceptance of either. There naturally cannot be too much stock put in this sort of observation, but it still has a certain charm about it.

One at last comes to the question of the specific gaits in which each of the three basic Oscarsson strip (or compartmental) activity patterns might occur. Relying upon data presented in sections 2.1.3 and 2.1.4, it is first possible to conclude that the symmetric patterns of figures 4 and 5 pertain to alternate-step gaits, and the asymmetric scheme of figure 6 characterizes bilateral stepping. As was mentioned above, this is because the muscle structure of alternate-step gaits is symmetric; that of bilateral stepping (gallops) is not. And the symmetry of anterior lobe structural prescriptions (compartmental activity distributions) should mirror the actual muscle usage.

But one can go further than just the gross assignment of gait classes to the strip patterns of figures 4-6, provided some observations of Miller and colleagues[160] are recalled from section 2.1.3: Those workers noted that any given alternate-step gait features one

of only two recipes for hindlimb-forelimb coupling--the "trot" coupling (homolateral limbs out of phase) and the "rack" coupling (homolateral limbs in phase). Both sets of homolateral limbs obey the same coupling recipe. The same two coupling constraints were also found in the bilateral-step gaits--but applied asymmetrically, with one homolateral limb pair functioning according to the "rack," the other according to the "trot." Now observe that, according to the present results, there are two symmetric, but qualitatively different Oscarsson strip patterns structuring the alternate-step gaits; and an asymmetric pattern which has features of one alternate-step scheme on one side of the midline and of the other scheme on the opposite side. The situation suggests, therefore, that:

> The Oscarsson strip patterns of figures 4 and 5 correspond to symmetric gaits characterized by one or the other of the "rack" or "trot" homolateral limb couplings. The pattern of figure 6 occurs in the gallop, where both limb couplings are seen, one on each side of the midline.

Or to state the general principle: The anterior lobe climbing fiber system tunes the structure of locomotor agonist linkages in a homolateral limb pair according to the current coupling constraint (trot, rack) between the two limbs.

Studies on locomotion in spinal cats (sections 2.1.2, 2.1.3) suggest that homolateral limbs are much less strongly coupled by segmental circuits than are hindlimb or forelimb pairs. Consequently, a substantial portion of homolateral limb coordination may rest with

supraspinal centers. The present analysis suggests that the anterior lobe could be such a center, listening via the spino-olivary system to the weak homolateral coupling circuits and tuning homolateral hind- and forelimb agonist structure according to spinal requests for a rack or trot in those limbs. Notice that three of the four Oscarsson strips connected with this process extend across both the "hindlimb" and "forelimb" areas of cortex (figure 3), implying that muscles in both homolateral limbs will be tuned simultaneously by the same signals. One might expect such an information distribution if those climbing fiber signals originate in the homolateral propriospinal system (treated in section 3.3).

To which of the two homolateral limb couplings should the Oscarsson strip patterns of figures 4 and 5 be assigned? There really is no way to choose without some additional information that must be acquired experimentally (see section 3.3). However, the author tends provisionally to assign figure 4 (or more precisely, homolateral strip-pair e_1-f) to the "trot" and figure 5 (strip-pair d-e_2) to the "rack." This feeling is based largely upon personal observations of intact cats performing treadmill locomotion: As others have observed (section 2.1.3), the animals adopt the rack at slow speeds. They also appear to take extraordinary care in stepping, largely out of anxiety it seems. Their stepping appears sufficiently slow to permit voluntary intervention in the ongoing step. These subjective findings suggest that the rack is employed when a cat attempts more precise control over its locomotion than can be got in the trot or walk (the latter

also featuring "trot" limb couplings). Why the rack should offer greater precision (if it really does) is not clear. But supposing that strips d and e_2 (figure 5) are "rack" strips, then one can see from figure 3 that the rack is influenced by climbing fiber information primarily from the forelimbs (treated in section 3.3). There is also an exquisitely sensitive cutaneous input from the forelimb footpads entering strip d[189]. Both facts fit with the idea of forelimbs "feeling out" the way ahead in some sort of precision locomotion task. On the other hand, "trot" strips e_1 and f (figure 4) are controlled by hindlimbs and seem to survive on FRA signals alone. This would seem to indicate a more automatic, secure form of locomotion. And on the third hand, this sort of reasoning may also be utter nonsense--which is why the author can comfortably endorse only the generic association of different strip patterns with different homolateral limb couplings.

As for the gallop pattern of figure 6, if the "rack" and "trot" assignments above should happen to be correct, then the pattern is that of a left-handed rack and right-handed trot. This conforms to either of the "left rotatory" or "left transverse" gallops, depending upon whether the left or right hindlimb leads (data of Miller, et al.[160,161]). Again, this is sheer speculation; but it would be interesting to see if there exist affinities among the left- and right-handed gallops because of a reluctance to change an anterior lobe compartmental activity pattern pertaining to either group, once the pattern has been established.

Thus, the anterior lobe complex "thinks" in terms of coordinating homolateral hind- and forelimb pairs during locomotion. The spino-olivocerebellar system acquires information on whether the rack or trot coupling constraint is to be in force between the homolateral limbs and activates the appropriate pair of Oscarsson strips (d-e_2 or e_1-f). As a result, the distribution of relative excitation among the various descending tracts under cerebellar influence is altered, producing a retuning of agonist linkage structure in both homolateral limbs. Both epochs of the step cycle are simultaneously adjusted; the tuning recipes--the excitation distributions--are retained over the complete step cycles of the hind- and forelimb. Spinal switching selects the times at which this biasing of the agonist linkages will be actually expressed in EMG patterns--in the forces or torques developed among the joints by the linkages. Although it is not treated here, mossy fiber signals arising either from the actual performance or the commands to perform, are also weighted by the structural prescription (again, the activity distributed among cerebellar compartments) as they pass through the cerebellum on their way to the musculature. These signals control the metrical prescriptions of the homolateral limb agonists, the amounts of force developed by the linkages within a particular structural configuration. In other words, the spino-olivocerebellar system essentially tells the cerebellum how to interpret mossy fiber information in accordance with the current coupling of homolateral limbs (Boylls, in preparation). This may still be a confusing picture to some, so an attempt will be made in section 4

to restate these and other thoughts with the help of some figures. Section 4 will also detail features of the structural tunings (e.g., tonic biases on the proximal or distal muscles) represented by the two Oscarsson strip-pairs.

Given the undeniable neural complexity of the "locomotor" anterior lobe and its related nuclei, it may seem silly a priori to claim that its computations are restricted to only three qualitatively different patterns of activity (figures 4-6), corresponding to only two types of homolateral limb coupling. Before considering the proposition it should be understood that the anterior lobe compartmental activity distributions set up by any of the three climbing fiber patterns can be expressed in an infinitude of degrees of "vividness." Nuclear regions influenced by active strips could be only slightly more excited than regions in neighboring compartments; or they might be fully potentiated and the latter completely suppressed. Such a continuum of compartmental excitation can arise if olivocerebellar transmission into Oscarsson strips is itself graded; evidence that it may in fact be is set forth in the next section (3.3; see also ref. 22). Since each Oscarsson strip-pair is associated with a hindlimb-forelimb coupling arrangement, rather than with a specific gait, it follows that each pair has a diverse category of gaits in its domain. Conceivably, then, activity in a given pair might thus be a somewhat continuous function of the specific gaits within its gait category. The structural tuning of the gaits could thus likewise experience

some degree of continuity, although the time course of tuning changes would remain extended over several step cycles.

Even if climbing fiber-induced anterior lobe activity does experience the finer adjustments mentioned above, severe limits on the "topology" of the activity remain. So in that regard, the present theory does stand squarely in opposition to the often expressed belief that the anterior lobe complex is a computer of almost limitless finesse. But then, little inspiration for experimental study has, or could, come from postulates of cerebellar omnipotence. If the organ's functions are indeed so esoteric and elusive, then it is a brave person who would attempt to figure them out. The limited repertoire concept offered here would seem to be much more experimentally optimistic (section 4.2). Furthermore, just because a system, neural or otherwise, has many potential degrees of freedom, one cannot infer that it must necessarily exercise all of its apparent options. Cats doubtless employ at least a hundred of their many hundred muscles in carrying out locomotion. Yet they do not display anything approaching a hundred different locomotor behaviors; they have only a few. Of course, one could certainly <u>think</u> of all sorts of bizarre (and biomechanically feasible) ways for cats to locomote, but they simply do not occur.

Will the cerebellum be able to live up to the high expectations of computational complexity imposed upon it by some investigators? Or will it be discovered that the anterior lobe does its job by invoking only a handful of powerful formulas, formulas carefully worked out over evolution to tune what seem to the eye to be

countless classes of subtle and complex motor skills?

In summary:

By adding four additional assumptions to the two "axioms" of climbing fiber physiology stated in section 3.1.1, it has been possible to show the following:

1. A structural program for the entire step cycle in all four limbs exists within the ongoing neural activity of the anterior lobe complex, regardless of the current step cycle epoch(s) being executed. This program, of course, is in the form of activity distributed among the various anterior lobe corticonuclear compartments and is set up by climbing fiber volleys in Oscarsson strips.

2. Only two strips can be simultaneously active in each half of the anterior lobe. In particular, strips d and e_2, and strips e_1 and f (figure 3) are paired.

3. Only three qualitatively different strip patterns can exist in the "locomotor" anterior lobe as a whole. Two such patterns are symmetric and construct structural prescriptions for alternate-step gaits; the third pattern is asymmetric and deals with the gallops.

4. The strips which are active in a given half of the anterior lobe are dictated by the current coupling, mediated spinally, of the homolateral limbs. Thus, strip-pair d-e_2 becomes active when the coupling is of one type (possibly the rack); e_1-f is triggered by the other coupling (trot). This formula applies to both the alternate- and bilateral-step gaits.

3.3 Origins of Anterior Lobe Olivocerebellar Inputs During Locomotion: Predictions

Observations on the behavior of anterior lobe climbing fibers during locomotion have thus far been limited to a few incidental observations (see below). However, an extensive literature has grown up around various central and peripheral events provoking climbing fiber volleys in acute animals (for review, see refs. 5, 19, 182, 183). This is not a particularly easy literature to understand, since it essentially is in the form of an empirical catalogue. Moreover, one often has the impression that it is simpler to describe the information which does not reach the climbing fiber system than to recount the multitude of influences which do.

Now the present theory of locomotor climbing fiber operation places certain demands upon the data which the spino-olivary tracts should provide. For example, the correlation between the activation of particular Oscarsson climbing fiber strips and the locomotor utilization of certain coupling constraints between homolateral limbs suggests that some spino-olivary inputs may originate in the propriospinal networks coordinating hind- and forelimbs (section 3.3.2). By means of similar reasoning, an attempt will be made below to "derive" classes of peripheral and central signals that should be capable of triggering certain sets of climbing fibers. Without too much rehearsing of details, it will be shown that most, if not all, known climbing fiber trigger-events have a place within the theoretical framework; and some hitherto unexpected

sources of olivary input will be proposed. To improve the suitability of this material as a framework for experimental investigations (acute and mesencephalic cats; section 4.2), comments on olivocerebellar coding mechanisms are also included (section 3.3.4).

3.3.1 Basic Principles Governing Inputs to Anterior Lobe Oscarsson Strips

To understand why certain central or peripheral events trigger anterior lobe climbing fibers, it first seems essential to know what climbing fiber volleys "mean" to the cerebellum when they arrive. Previous discussion (sections 3.1, 3.2) has demonstrated that such volleys within Oscarsson strips may bias the structure of muscle linkages engaged in locomotion as a function of homolateral limb couplings established spinally. Presumably, therefore, the anterior lobe places one or both of the following interpretations upon the activation of an Oscarsson strip during locomotion:

1. The homolateral hindlimb-forelimb coupling associated with the strip (section 3.2) is being potentiated.
2. One or more muscle linkages tuned by the strip's corticonuclear compartment are either being deployed, or are being recruited for deployment.

Said another way, the anterior lobe interprets climbing fiber activity as a corollary either of a demand for motor action or of some motor fait accompli. If this is so, then it seems reasonable to expect that a given peripheral or central stimulus event might be transmitted to the olive and to a particular anterior lobe

Oscarsson strip insofar as the stimulus obeys these governing principles:

a. The stimulus activates spinal homolateral limb coupling circuits associated with the strip.

b. The stimulus recruits a muscle linkage facilitated by the strip.

c. The stimulus arises from the contraction of such a linkage.

Examples of climbing fiber trigger-stimuli satisfying each of the above principles are already extant in the literature: Thus, Miller and coworkers[156,159] noted that hindlimb inputs most effectively influencing homolateral forelimb reflexes via ascending propriospinal pathways fell into the FRA and cutaneous categories; both are also potent activators of Oscarsson strips (figure 3; section 3.2), in agreement with principle (a). The FRA themselves are so named for their facilitation of flexion/crossed-extension reflexes (section 2.1.2)--that is, their firing potentiates particular muscle linkages in accordance with principle (b). The same would be true of cerebral cortical[158] and certain brainstem nuclear (red nucleus)[111,112] "central" signals that are known to activate climbing fibers in the spinocerebellum. Principle (c) is illustrated by Murphy's[162,163] demonstrations of anterior lobe cfr's evoked following muscle stretch. Such inputs will normally arise largely as a consequence of muscle contraction, as would the footpad taps[52,53,189] and other cutaneous inputs (above) that have been shown to trigger Oscarsson strips.

These examples (which will receive more detailed treatment momentarily) make evident some additional considerations about the sources of olivary input: Firstly, any given source of climbing fiber inputs will almost always fit more than one of the above governing principles (FRA information is a good illustration). Secondly, many input sources will activate more than one Oscarsson strip. This automatically is true of sources related to homolateral limb coupling, since each coupling is associated with a pair of strips (section 3.2). It also applies to other inputs whose function is "ambiguous" with respect to muscle linkages which are either contracting or are to be potentiated. For instance, stretches of single muscles are ambiguous because a single muscle could participate in a variety of linkages; and it has been shown that, indeed, "all" Oscarsson strips are activated by single-stretch inputs (see below). Lastly, since a variety of central and peripheral input sources may all bear upon the potentiation of a particular muscle linkage, one must expect convergence of these influences upon the olivary neurons projecting to the Oscarsson strip(s) facilitating that linkage. Convergence of different spino-olivary pathways and cerebral cortical inputs onto olivary cells does take place[155,158,183], a fact which sometimes has been assigned a certain esoteric significance (e.g., the olive could act as a "comparator" of the different inputs[155]). However, the significance could be nothing more than a demonstration of the access a variety of central and peripheral information has to the same muscle linkages. If olivary

neurons are metaphorically akin to anything technological, they minimally (and perhaps maximally) are "OR-gates."

At this juncture it should be easy to see how climbing fiber activity can come to be associated with an immense number of qualitatively distinct peripheral and central stimuli which often seem to have little or nothing in common. The nodal points of these disparate events are the various muscle linkages (and the coupling circuitry of the cord); and it may be submitted that the events in and of themselves are virtually inscrutible without considering the motor consequences which they provoke and/or in which they arise. Asanuma has appreciated this point in his studies of "reflexes" mediated via motor cortex[13,14]: He has observed that a cutaneous stimulus presented to some point on a limb will activate a linkage of muscles at several joints which then act to bring the limb into increased contact with the stimulus ("positive feedback" of sorts). Conversely, the pyramidal tract neurons which facilitate individual muscles of such linkages have very wide cutaneous receptive fields representing all the points "their" muscles could advance toward a stimulus. The neurons also receive inputs from other sensory modalities reflecting joints moved, additional muscles contracted, and the like. Thus, pyramidal tract neurons are "multimodal, wide-field" cells in terms of their sensory responses, as olivary units are described to be. So also are motoneurons--only they scarcely are ever referred to in these terms since their functions are so well known.

Induction applied over the catalogue of known spino-olivocerebellar inputs has thus far failed to produce a detailed explanation of either what the spino-olivary apparatus does, or why it receives such inputs. Perhaps it is high time to employ more direct laboratory techniques (cf. Appendix; section 4.2) assessing the impact of climbing fiber activity on motor behavior, as has been done here with theoretical methods. It is, after all, axiomatic that one can never know for certain why any neural system receives a certain class of information unless one first has a fairly good idea of what outputs the system is to produce.

To summarize:

Based upon the muscle linkage effects of activating a given Oscarsson climbing fiber strip, it is probable that peripheral or central inputs will trigger the strip if they also:

1. Activate spinal homolateral limb coupling circuits associated with the strip; and/or
2. Recruit a muscle linkage facilitated by the strip; and/or
3. Arise from the contraction of such a linkage.

These governing principles can be used to deduce sources of olivocerebellar signals to the anterior lobe. They also explain both the diversity of known climbing fiber trigger events and also the convergence of seemingly unrelated peripheral and central inputs upon the same olivary neurons.

3.3.2 Sources of Olivocerebellar Inputs. I. From Commands for Locomotor Action

According to two of the three principles governing anterior lobe climbing fiber input sources (section 3.3.1), various Oscarsson strips should be activated by inputs either potentiating homolateral limb coupling mechanisms at spinal levels and/or facilitating the contraction of particular muscle linkages. Quite a number of potential central and peripheral inputs to the spinal olive are suggested by these criteria, as well as several distinct anatomical arrangements of the olive with other structures. In figure 7, four such arrangements are illustrated. Each shows the same set of structures wired up in a qualitatively different way; all wiring shown is excitatory (for clarity): Thus, at the bottom of every diagram is a box representing the spinal cord. Inside it are shown the flexor (F) and extensor (E) motoneuron pools for a homolateral hind- and forelimb (contralateral limbs are not represented). A spinal interneuronal network (SIN) mediates the segmental reflexes of each limb (only a hindlimb SIN is shown); it supposedly also contains stepping generator(s) for laterally paired limbs (section 2.1.2). Connecting the homolateral limbs are propriospinal tracts (PSP). The indicated hind-to-fore tract is shown facilitating forelimb extension when the hindlimbs flex; however, such details of propriospinal influences, aside from being ill-known (section 2.1.3), are of secondary importance (see below). At the top of each drawing in figure 7, cerebellar anterior lobe circuitry is

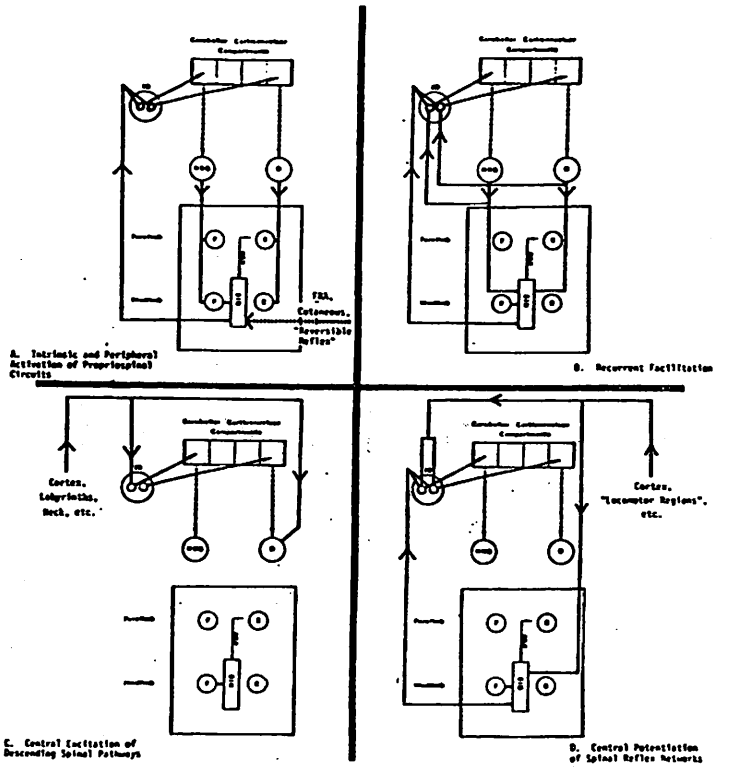

FIGURE 7

Assorted strategies by which anterior lobe Oscarsson strips can be activated by inputs calling for locomotor action. Abbreviations: IO = inferior olive; NRG = nucleus reticularis gigantocellularis; D = Deiters nucleus; F = flexor motoneuron pool; E = extensor motoneuron pool; PSP = propriospinal pathway; Text explains details of connections.

indicated. Regions in the inferior olive (specifically, in the dorsal and medial accessory olives; section 2.2.2) are portrayed, by way of example, to project into Oscarsson strips controlling two anterior lobe compartments, one facilitating the reticularis gigantocellularis nucleus (NRG) and limb flexors, the other the Deiters nucleus (D) and limb extensors (cf. figure 3).

Before discussing the specifics of the wiring schemes in figure 7, it should be said that this set of configurations is not meant to be exhaustive, but only representative of contexts in which climbing fiber inputs could arise. And essentially all arrangements would bear upon any given instance of locomotion, hence the convergence of diverse inputs upon olivary neurons (section 3.3.1). Of course, it is conceivable that interactions other than simple summation could occur among different inputs within the olive (section 3.3.4; ref. 22). The possibility is not entertained here, but it surely merits experimental investigation.

a. Climbing fiber inputs from intrinsic propriospinal mechanisms. In view of the results of section 3.2, these are perhaps the easiest spino-olivary input sources to predict: Recall that Oscarsson strip-pair d-e_2 (referring to figure 3) in the anterior lobe should be active when the homolateral hindlimb-forelimb pair is coupled according to one of the two constraints, rack or trot, seen in cat locomotion; strip-pair e_1-f will be aroused when the other coupling is used. The decision as to the proper coupling is of course made by spinal circuitry, in particular, the propriospinal

system (section 2.1.2). As noted in section 3.2, this observation is consonant with the bridging of both hind- and forelimb lobules of the anterior lobe by the more medial Oscarsson strips. Now interestingly enough, it can be seen from figure 3 that strip-pair e_1-f receives peripheral inputs exclusively from the hindlimbs, and strip-pair d-e_2 almost exclusively from the forelimbs (the rostral part of d does receive a weak hindlimb influence). Given the posited relationship of each strip-pair with the propriospinal system, this input pattern suggests:

1. That pair e_2-f is activated whenever information is passed from hindlimb to forelimb on the ascending propriospinal tracts; and

2. That volleys occur in pair d-e_1 when signals pass caudally on the descending propriospinal tracts.

In section 3.2 strip-pair d-e_1 was rather arbitrarily assigned to the "rack" homolateral limb coupling, and pair e_2-f to the "trot." So discounting a possible exchange error in these assignments, one is led to a further conclusion:

> The ascending propriospinal system, and information from the hindlimb, are essential to the governing of the trot coupling of homolateral limbs. Conversely, the rack is governed by the descending tracts and forelimb signals.

Here, then, is an interesting switch: A theory for a portion of the cerebellum has unexpectedly given birth to a corollary proposition

on spinal cord organization. It seems that there should exist a hierarchy of control among the limbs which is altered as a function of the way that they are coupled. The coupling itself presumably emerges out of a decision as to which of the ascending or descending propriospinal systems should be dominant. This suggests competition between the two, as Miller has suggested in a more general context[161]. One consequently may envision that each propriospinal circuit has a hard-wired connection with inferior olivary regions projecting into "its" strip-pairs, thereby allowing the dominant circuits to create the structural biases on cerebellar outflow appropriate to the current locomotor performance (a fact which leads to an extremely simple experimental test; see section 4.2). Such a connection is shown in figure 7a, wherein the ascending propriospinal system is portrayed transmitting to anterior lobe compartments (specifically, strip-pair e_1-f; figure 3) facilitating the Deiters nucleus and NRG; the added "FRA," "cutaneous," and "reversible reflex" inputs are treated in the next subsection. There naturally may be much more "processing" in the propriospinal connection with the olive (for instance, the ability of a dominant network to block spino-olivary transmission from all other networks, as indicated in recent work by Sjölund*). There may also be a variety of spino-olivary tracts involved. Conveniently enough, however, it may be that the cerebellar projection

*Sjölund, B., "Information carried to the cerebellar cortex by the ventral spino-olivocerebellar paths (VF-SOCP's)," Abstract, 7th International Neurobiology Meeting, Göttingen, September 1975.

from small olivary regions is already organized into geometrically regular "lattices" of multiple strips which include the propriospinal strip-pairs (see next subsection).

It is to be expected that propriospinal inputs to anterior lobe Oscarsson strips will ultimately reflect processes intrinsic to the spinal cord--that is, they will remain following deafferentation and abolition of descending activity. In this respect they will parallel inputs from the ventral spinocerebellar tract, a mossy fiber pathway[9,10,11]. To the author's knowledge, the propriospinal system has never before been suggested as a source of climbing fiber input--and yet, if the present conclusions are even approximately correct, this system may in some sense be fundamental to climbing fiber operation in the "locomotor" anterior lobe.

b. Climbing fiber inputs from peripheral signals activating spinal reflexes. Inputs from the FRA and cutaneous afferents have been known for some time to be routed to various anterior lobe climbing fiber strips (cf. refs. 5, 19, 155, 182, 183, and figure 3). The potentiation by such inputs of various spinal reflexes, including those related to stepping (sections 2.1.2, 2.1.3, 2.3.4), has recently led some investigators to look directly at correlations of cerebellar activity with reflex triggering. Thus, clonus has been found to provoke rather generalized, rhythmic olivary bursting in precollicular cats[37]; and cutaneous inputs elicit Purkinje cell reactions in fish only if they are strong enough to induce reflex movement[186]. It therefore is easy to accept an association of

climbing fiber activity with the peripheral recruitment of reflex circuitry. However, at the moment this association remains far too vague.

A large part of the vagueness stems from the poorly defined spinal reflex actions which FRA and cutaneous inputs are supposed to provoke. As mentioned in section 2.1.2, the FRA are traditionally linked with Sherringtonian flexion/crossed-extension in laterally paired limbs--in short, with the spinal generator for alternate-stepping in a limb pair. Similarly, cutaneous inputs are associated with the bilateral extensor thrust of the gallop (footpad signals; section 2.1.2), or with tactile placing and more generalized facilitation of alternate-stepping (2.3.4). As a result, it is tempting to look for a correlation between anterior lobe climbing fiber activity and the operation of stepping generators at paired limbs. One might expect experimentally, for example, that footpad "gallop" inputs will activate a different set of Oscarsson strips than will FRA "alternate-step" events. But on the other hand, if the findings of the previous subsection are correct, then the strips triggered by either FRA or cutaneous signals will depend entirely upon their impact in the homolateral propriospinal networks--upon the multisegmental reflexes between hind- and forelimb. Reflex relationships between opposed limbs are irrelevant.

Propriospinal facilitation of forelimb reflexes by hindlimb nerve stimuli does appear to take place primarily when the latter exceed FRA threshold[156,159] (see also section 2.1.3). One should

realize, therefore, that FRA inputs do not produce spinal effects restricted only to the segments in which they are received, and that climbing fiber strips may in fact be activated by the FRA because of their propriospinal influences. Likewise, cutaneous inputs given the hindlimb in DOPA-nialamide, high spinal cats will facilitate stepping movements of the forelimbs (van der Meché, personal communication; see below). Figure 7a illustrates both cutaneous and FRA signals entering the hindlimb propriospinal system and at the same time giving rise to activation of an anterior lobe strip-pair (further details are given in the previous subsection). Perhaps the time has arrived to define a class of "propriospinal reflex afferents" with which to label Oscarsson strips in diagrams like figure 3.

It is possible to use the association of propriospinal mechanisms with pairs of Oscarsson strips to devise another, but complementary, method of characterizing peripheral strip inputs: Figure 8 illustrates, on two hemi-anterior lobes, the strip-pairs ostensibly activated by the homolateral "trot" and "rack" propriospinal coupling circuitry, as derived above (previous subsection). Note that each strip-pair falls into a regular "lattice" wherein active strips alternate with inactive. The existence of such lattices was predicted on purely mathematical grounds in an earlier report[22] (they fit the spatial frequency selectivity of the anterior lobe lateral inhibition system; section 3.1.1). Very recently, Courville* has been able to show, using autoradiography, that fairly

*Courville, J., "Distribution of olivocerebellar fibers demonstrated by a radioautographic tracing method," Brain Res. 95, 253-263 (1975).

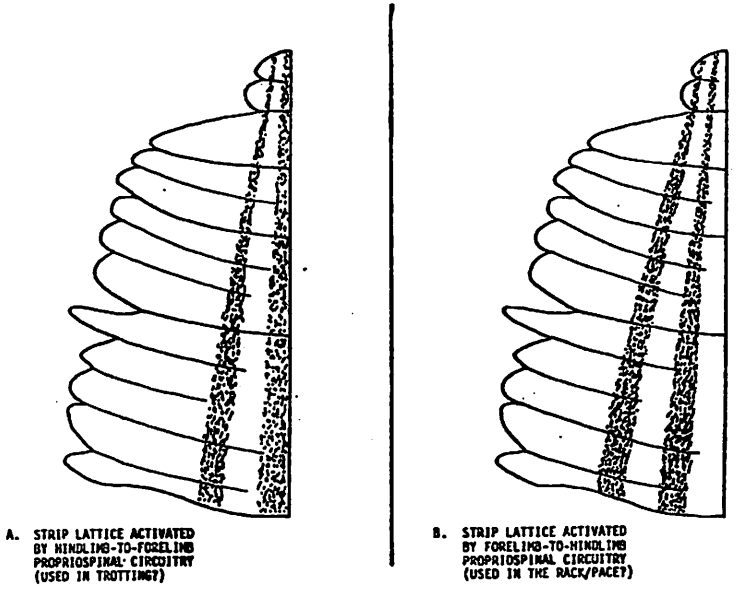

FIGURE 8

The hypothetical coinnervated Oscarsson strip lattices activated by the "rack" and "trot" propriospinal coupling mechanisms.

small sectors of the cat inferior olive do indeed project into anterior lobe lattices similar to those in figure 8. The actual lattices may have somewhat narrower strips and gaps than figure 8 indicates; and still smaller olivary regions may innervate the individual strips in a lattice (Armstrong, personal communication). But nevertheless, it is conceivable that the theoretical propriospinal strip-pairs are built into the olivocerebellar projection geometry.

Now recall from section 3.2 that an active propriospinal strip-pair, or lattice, will excite descending spinal pathways modulating both flexor and extensor muscle linkages in the two homolateral limbs. So if one were to trigger a lattice using some peripheral signal while a cat locomoted, the immediate effect would be to reinforce whatever homolateral limb movements were just then being executed--irrespective of whether the movements were flexions or extensions. Acting by way of the cerebellum, then, this hypothetical peripheral input would produce a "reversible reflex" response in both homolateral limbs, a response paralleling the reversible reflexes of spinal animals (section 2.3.4). Of course, the latter are usually describec only in single limbs, while the conjectured cerebellar "reflex" would involve two limbs in a seemingly "propriospinal" coupling. But interestingly enough, Miller and van der Meché (van der Meché, personal communication) have recently observed reversibility in the hind-to-forelimb propriospinal reflexes of high spinal cats (DOPA-nialamide). These considerations naturally lead to the following

hypothesis:

> A prime source of peripheral signals to both the spino-olivocerebellar system and the propriospinal networks may be those inputs participating in "reversible" spinal reflexes.

As mentioned above, this alternative characterization of climbing fiber peripheral inputs complements, rather than replaces, the FRA/cutaneous viewpoint. It is even possible that FRA/cutaneous and reversible reflex inputs are one in the same.

While consideration of the immediate impact of climbing fiber activity on locomotor movement is convenient for the derivation of relationships such as the one just described (reversible reflexes), the prolonged time course of the climbing fiber influence must not be overlooked: Lundberg[133] has pointed out that spinal reflex circuits have the regenerative capacity to convert very brief peripheral triggering stimuli into a prolonged bout of movement. This is especially true when those circuits are noradrenergically potentiated for stepping, in which case such stimuli release a sequence of alternating movements. Now if this is the situation at spinal levels, where movement is generated, it would seem that a similar process should take place in the cerebellum (and other central centers), where movement is modulated. That is, a spinal trigger-stimulus should result in the creation of descending modulation whose time course reflects that of the ensuing spinal motor sequence. One way this might come about, of course, would be for the cerebellum to

produce its own temporal sequence of flexor/extensor modulatory activity in time with that of the movements being executed; and in fact, certain spinocerebellar mossy fiber inputs to the anterior lobe do appear to engender such periodic outputs, but only because the inputs themselves are periodic; the sequential stepping mechanisms of the spinal cord are essentially "borrowed" by the cerebellum (see section 5 for discussion). But an entirely different sequence-modulating strategy is inherent in the spino-olivocerebellar system. Here spinal movement-triggering inputs are transmitted into lattices of climbing fiber strips whose corresponding anterior lobe compartments govern all the movements of the sequence; the serial order in which the movements are executed is nowhere represented. Rather, the resulting compartmental activity alterations persist in time long enough for all the represented movements to be played through at the spinal level (with that activity "read-out" into agonist muscle linkages by spinal switching, as appropriate; sections 2.3.4, 2.4). In more abstract terms, then, the spino-olivocerebellar apparatus permits the locomotor system to use peripheral (or central) information arising at an isolated moment during execution of a sequential motor act to tune not just the movements currently under way, but also all subsequent movements in the sequence. The act is centrally or peripherally manipulated as an holistic structure, rather than as a collection of disjoint motor events dispersed in time. This principle--actually no more than a generalization of the linkage/synergy paradigm (section 2.3.1) extended to temporal sequences of

linkage deployments--has obvious significance for such topics as next-cycle adaptation (section 2.4), the "open-loop" pre-programming of movement, and the central schemata whereby action is represented. These points will be briefly taken up in section 5 (see also ref. 23).

c. Climbing fiber inputs originating by recurrent facilitation from the anterior lobe complex. Both the cerebellar nuclei and their brainstem nuclear targets facilitate the contraction of particular locomotor muscle linkages (section 2.3.3). It thus follows from the principles stated in section 3.3.1 that all these nuclei may have ways to re-excite the Oscarsson strips governing "their" cortico-nuclear compartments.

Two ways of effecting that recurrent facilitation via the climbing fiber system are illustrated in figure 7B: The first involves direct collateral connections between anterior lobe output nuclei and the appropriate inferior olivary regions, as are exemplified in 7B by hypothetical projections from the Deiters and NRG nuclei to the olive. Those particular pathways do not yet seem to have been demonstrated. However, Jeneskog[111,112] has studied in some detail a projection from the red nucleus to the olive which does appear to activate Oscarsson strips in the paramedian lobe, strips recurrently influencing the red nucleus by way of the anterior interpositus and dentate cerebellar nuclei. Direct projections from the cerebellar nuclei to the olive (reviewed briefly in ref. 22) have already been known anatomically for some time; and more recent

evidence* suggests that such projections may allow an individual cerebellar nucleus rather specific control over its own climbing fiber input. Unfortunately, it has not proved easy to study the cerebello-olivary pathway electrophysiologically (Armstrong, personal communication).

A second way whereby cerebellar outflow might provoke returning climbing fiber activity is through the potentiation of spinal interneuronal networks which themselves have olivary connections. This possibility is also shown in figure 7B, wherein the NRG and Deiters nuclei are shown projecting into the propriospinal system via spinal interneuronal networks. It is known qualitatively that supraspinal centers do influence the manifestation of long propriospinal reflexes (cf. ref. 161 for brief review), although details of any cerebellar participation in such phenomena are not available. But it is well established that all brainstem "output" nuclei modulated by the anterior lobe do at least produce ancillary facilitation and depression of simpler segmental reflexes, along with more direct effects on motoneuron pools (surveyed in ref. 30). In fact, it is quite likely that the former is the more important process involved in cerebellar potentiation of agonist linkage contraction (Grillner, personal communication). One must expect, then, that spino-olivary transmission should feel supraspinal

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*Martin, G. F., Henkel, C. K., "Cerebello-olivary fibers: An analysis of their origin, course and distribution using horseradish peroxidase, autoradiographic and degeneration techniques," Abstract, Society for Neuroscience 5th Annual Meeting, New York, November, 1975.

influences insofar as the latter recruit spinal (specifically, propriospinal) reflex systems. To give a particular example, an "extensor" descending tract, say, the lateral vestibulospinal tract, which facilitates "pro-extension" reflexes (1a excitation from extensors, 1b crossed excitation from opposed flexors, contralateral FRA excitation, etc.) and suppresses "anti-extension" reflexes, will also enhance activity in ascending spino-olivary tracts projecting to "extensor" Oscarsson strips. It may also suppress transmission into "flexor" strips, but this will depend upon the effects, if any, produced in propriospinal reflexes; as has already been determined (earlier subsection), these influence lattices comprising both extensor and flexor strips.

The modulation by any central brain structure of its own afferent input invariably conjures up ideas about "selective attention," "corollary discharge," and the like. Specialized versions of these concepts have been proposed for some time with respect to the supraspinal control of activity in ascending spinocerebellar pathways. Most proposals have dealt with various mossy fiber systems, although the arguments are so structured as to be more or less equally applicable to the climbing fibers (implying that some refinement is required). It is possible, however, that the cerebellar efferent supervision of the spino-olivary system can be explained with much simpler notions, as has been done here.

d. Climbing fiber inputs as a corollary of non-cerebellar, central excitation of descending spinal pathways. In the mesencephalic

cat, the cerebellum provides most of the input to the brainstem output nuclei projecting to the cord. However, in intact animals the cerebral cortex, labyrinths, neck proprioceptors, and a number of additional structures also have direct effects on those nuclei. Consequently, one would predict that all these areas should provoke climbing fiber activity in the anterior lobe compartments governing the nuclei they excite. Figure 7C illustrates a typical example. Details of these influences lies outside the scope of the present report, but the Appendix and refs. 5, 19, and 183 may be consulted for review.

e. Climbing fiber inputs as a corollary of non-cerebellar potentiation of spinal reflexes. This final category of climbing fiber input sources has two principal members. The first is the cuneiform nucleus, or "locomotor region" of the mesencephalon (section 2.2.2). Stimulation of this area should provoke enhanced climbing fiber activity throughout the "locomotor" anterior lobe, in view of its facilitation of "all" spinal locomotor mechanisms. It is also known that the cuneiform area projects directly to the cat medial accessory olive[56] (section 2.2.2). Presumably, other "locomotor regions," such as that in the posterior hypothalamus (section 2.2.1), might also directly affect the olive.

The second reflex-potentiating source of climbing fiber activity is once more the cerebral cortex. Details of the relationship will again not be treated here, but it is worth pointing out one of its interesting consequences: Figure 7D portrays, in part,

cortical connections which potentiate spinal locomotor reflexes and simultaneously excite inferior olivary regions modulating the muscle linkages so aroused. At the same time, the spinal reflex centers themselves activate the olive. There thus rather naturally occurs a convergence of spinal and cerebral cortical inputs within the olive--perhaps upon the identical olivary neurons. As mentioned in section 3.3.1, such experimentally demonstrated convergence has sometimes been assigned a special meaning--the "comparison" of spinally-evoked movement with descending central commands. But it should now be obvious that this view could be quite misleading. Cortical, or spinal, or peripheral, or whatever inputs will superimpose in the olive if they all pertain to the contraction of the same muscle linkages.

In summary:

Oscarsson climbing fiber strips of the anterior lobe may be activated by exogenous inputs either potentiating homolateral limb coupling circuits and/or recruiting particular muscle linkages. From these principles, one can derive the following sources of olivocerebellar input:

1. The intrinsic propriospinal mechanisms. Specifically, it is found that:

   a. The ascending (hind-to-forelimb) pathways will influence strip-pair e_2-f (figure 3), and will also govern the "trot" homolateral limb coupling using primarily hindlimb signals.

   b. The descending (fore-to-hindlimb) pathways will activate strip-pair d-e_1, and will govern the "rack" coupling using primarily forelimb cues.

There thus exists a "dominance" hierarchy between the homolateral limbs, which shifts as a function of the current coupling pattern between them.

2. Peripheral inputs. These may fall into the FRA or cutaneous categories, insofar as they facilitate propriospinal reflexes. They also comprise the category of inputs involved with "reversible" reflexes, which may be identical with the FRA/cutaneous class. In any case, such inputs activate "lattices" (strip-pairs) of Oscarsson strips associated with the propriospinal mechanisms they potentiate. As such, they set up structural prescriptions for all locomotor movements in both homolateral limbs. Thus, the temporally extended sequence of locomotor limb movements is telescoped into a single active Oscarsson strip lattice, thereby permitting adjustment of all elements of the sequence as a structural whole.

3. The cerebellar nuclei and their brainstem targets. These will activate strips of their "own" anterior lobe corticonuclear compartments, both by direct collaterals to the olive and by spinal reflex potentiation.

4. The cerebral cortex, labyrinths, neck proprioceptors, etc. At the same time that these inputs are directly exciting the cerebellar and brainstem "output" nuclei, they also activate the anterior lobe strips governing those nuclei.

5. The cuneiform nucleus (and other "locomotor" regions). By direct olivary projections and the overall potentiation of spinal locomotor circuits, these facilitate activity in all "locomotor" Oscarsson strips.

6. The cerebral cortex (again). It facilitates climbing fiber activity in its role as a controller of spinal reflex arcs. Strips will be activated which potentiate the movements so released.

3.3.3 Sources of Olivocerebellar Inputs. II. From Results of Locomotor Action

The contraction of a given locomotor muscle linkage leads to an assortment of sensory consequences in muscles, joints, and skin. Many of these cues, by virtue of their participation in long proprioceptive reflexes, will promote climbing fiber volleys in particular Oscarsson strips (or lattices) in the anterior lobe (section 3.3.2). However, it is quite possible that spinal reflex or muscle linkage potentiation is not the sole criterion for admission of a peripheral input into the olivocerebellar system. As suggested in section 3.3.1, a strip may be activated by the sensory aftermath of the deployment of a linkage it governs. Certain known anomalies of olivocerebellar transmission (see below) may be better accounted for by this principle than by that of reflexive linkage recruitment, although at present the rationale is highly speculative:

Suppose that an Oscarsson strip is affected by some peripheral signal as the result of a muscle linkage contraction modulated by the strip. This would seem to require the presence of mechanisms

in the spino-olivocerebellar channel which first "interpret" the signal in terms of linkages and then direct it into the appropriate strip(s). Ignoring for the moment what such mechanisms might be (see below), it is evident that certain signals should be more readily interpreted than others. For instance, cutaneous inputs will usually arise from the contraction of a rather restricted, multi-joint collection of muscles that either enhance or decrease the contact of skin with an external stimulus (cf. the motor cortical "reflex" described in section 3.3.1). But information from the proprioceptors of individual muscles may be interpreted in the context of many different linkages; the narrowing down of the relevant linkages for a given action requires additional data and some decision-making. One thus might construct a scale of muscle-linkage "ambiguity" on which to rank peripheral inputs, with cutaneous signals less ambiguous than muscle proprioceptive. The ambiguities of other peripheral cues (e.g., from joint proprioceptors) probably lie between those of skin and muscle. Given the association of Oscarsson strips with particular muscle linkages, one can easily predict, then, that:

> The number of Oscarsson strips influenced by a given peripheral input may, in part, be inversely related to the muscle-linkage ambiguity of the input.

This "ambiguity principle" suggests, in particular, that proprioceptive inputs from individual muscles should produce rather widespread activity in many Oscarsson strips; the organization of

the activity into strips might actually be obscured. On the other hand, discrete cutaneous events should lead to localized volleys in recognizable strips. And indeed, Murphy and colleagues[162] have found in unanesthetized, curarized cats that stretch of either a single flexor or extensor of the forelimb digits will evoke Purkinje climbing fiber responses over a broad extent of anterior lobe lobule V (the "forelimb" lobule; figure 3), in the intermediate zone; no "strips" could be resolved. By comparison, Roberts and Rushmer[189] noted that taps given the forelimb footpad evoked climbing fiber volleys entirely restricted to a unique, narrow, paravermal strip (decerebrate cats). Climbing fiber activity distributions lying somewhere between these two extremes has been observed by Strata and coworkers* following stimulation of the posterior knee joint nerve (decerebrates).

Now the findings mentioned above only suggest a connection between the muscle-linkage ambiguity of a peripheral input and its ability to trigger circumscribed climbing fiber activity. Seeming counterexamples also exist: Oscarsson, for example (cf. refs. 155, 182, 183 for review), has discovered at least one spino-olivocerebellar pathway (the dorsolateral) that responds primarily to distal limb cutaneous inputs and yet appears to innervate quite a number of intermediate zone climbing fiber strips. Consequently, ascertaining the validity of the "ambiguity principle" will require an experimental

*Belcari, P., Carli, G., Strata, P., "The projection of the posterior knee joint nerve to the cerebellar cortex," J. Physiol. 237, 371-384 (1974).

investigation of the hypothetical mechanisms which supposedly "interpret" peripheral inputs in terms of the results of muscle linkage contraction. Such an experiment, based upon work already done by Murphy (see above), is described in section 4.2.

Assuming that the ambiguity principle can be established experimentally, what might be the neural mechanisms that resolve ambiguity--that assign peripheral inputs to the consequences of particular muscle linkage contractions, thereby allowing the proper Oscarsson strips to be triggered? For unambiguous inputs, there of course is no need for any elaborate processing, and these may be steered directly from peripheral afferents into the proper inferior olivary sectors. Perhaps it is this contingent of inputs which is represented in the more direct spino-olivary pathways (from the dorsal column nuclei[5,21,183] and portions of the ventral funiculus [184]). However, the ambiguous inputs--notably, the information from muscle proprioceptors--must be considered collectively and a "decision" reached about the muscle linkages to which they pertain. Perhaps the olive could perform this function itself. But to be even more speculative for a moment, it seems more attractive to consider that peripheral inputs are linkage-interpreted in the same circuits where linkages are constructed--in the intrinsic "reflex" networks of the spinal cord. A spinal locomotor mechanism may, in other words, do more than assemble a given muscle linkage in the efferent sense; it may also "recognize" (see below) that a particular collection of afferent signals is coming from that linkage (or the joints it

governs). Put more abstractly:

> Spinal interneuronal networks may function as "feature detectors" for certain extero- and proprioceptive inputs destined for the spino-olivocerebellar system. A "feature" is defined to be the set of immediate sensory consequences stemming from the contraction of a particular muscle linkage; and the "feature detecting" network can itself produce the contraction of that linkage.

However fantastic this proposition may sound, it may well amount to little more than a recasting, in a "sensory" framework, of the more acceptable hypothesis (section 3.3.2) that climbing fiber activity ensues when peripheral inputs potentiate spinal locomotor circuits. This is if the "feature detection" or "recognition" process is itself identifiable with such potentiation--as, for example, when the aggregate stretch of flexors elicits a flexion reflex in a chronic spinal animal[194]. The question is experimentally addressable in the test of the ambiguity principle proposed in section 4.2.

Now admittedly, there is probably little reason to consider spinal "feature detection" in understanding the control of mesencephalic locomotion; the kinesthetic "perceptions" of the preparation are academic. But this probably is not true in the situation of free locomotion in intact animals, let alone still more voluntary performances. There some sort of internal "body image" is likely constructed, within which both the results of, and plans for, motor

action are conceived. This image is no more a list of the behavior of individual receptors than is the central specification for an act a list of commands to individual muscles. The formulation of commands in terms of muscle linkages would seem to require that at least some sensory reports be written in the linkage language, through the use of linkage-feature extraction applied to the corpus of receptor data. When it is viewed as a sensory system, the spino-olivary apparatus provides such reports, albeit to the cerebellum rather than to higher levels. Even so, section 5 will discuss how this information on locomotor "features" (linkages) can be seen as altering what amounts to the "body image" of the anterior lobe complex, and thereby its "perception" of motor performance. Perhaps this use of the psychological vocabulary will prove naive and objectionable; however, it is at least possible to assign physiological processes to elements of that vocabulary in the cerebellar microcosm and from that obtain, perhaps, a few notions about what to look for at "higher levels."

To summarize:

Volleys in an anterior lobe Oscarsson climbing fiber strip may be produced by peripheral inputs stemming from the contraction of a muscle linkage potentiated by the strip. Such inputs may fall into essentially any modality, but the spatial distribution of the evoked climbing fiber activity is governed by the muscle-linkage "ambiguity" of the inputs: The number of Oscarsson strips activated by a given input is inversely proportional to the degree to which

that input can be interpreted as having resulted from the contraction of a unique muscle linkage. From this "ambiguity principle," it may be deduced that proprioceptive cues from individual muscles will give rise to widespread climbing fiber volleys; discrete cutaneous inputs will lead to a more focussed activity distribution; and information from individual joints will produce some intermediate activity map.

If the ambiguity principle is correct, then mechanisms for interpreting peripheral inputs in muscle-linkage terms must exist. While unambiguous inputs could reach the olive directly, more ambiguous information may undergo "feature detection" in spinal locomotor circuits, where the "features" are sensory consequences of linkage contractions produced by those circuits. "Feature detection" may be identical with peripheral reflex potentiation of linkages. As such, it is of secondary importance in understanding mesencephalic locomotor control. But linkage-feature detection may have significance when one considers the construction of perceptual "body images" involved in more voluntary performances.

3.3.4 Coding in the Spino-Olivocerebellar Pathway

Experimental tests (section 4.2) of the conclusions reached in previous portions of this report obviously require knowledge of what "activation" of an anterior lobe Oscarsson strip actually entails during locomotion. Since that activation has been claimed to occur, in particular, when certain spinal locomotor circuits are potentiated (section 3.3.2), one might expect that simple correlations might

appear between individual climbing fiber responses and the more "reflexive" movements of the step cycle (paw placement[5], initiation of transfer-flexion, etc.). However, Purkinje unit recordings from the anterior lobe intermediate zone in both mesencephalic[174] and intact (McElligott, personal communication) walking cats have yet to reveal such correlations--even though the mossy fiber-induced, "simple spike" discharges of many units are well correlated with stepping. But then, these disappointing results are fully in keeping with the history of climbing fiber investigations in animals trained to make voluntary movements (section 3.1.2; see also Appendix). Thus, climbing fiber strip "activation" almost certainly means something besides a volley time-locked to an external event.

The previous report on the physiological theory of climbing fiber function[22] described three mechanisms encoding spino-olivary information into "activation" of Oscarsson strips: The first, of course, is topographical. Information is routed into particular olivary zones and Oscarsson strips as a function of its spinal or peripheral origin (cf. the strip lattices associated with different propriospinal circuits; section 3.3.2). The second involves the regulation of electrotonic coupling between olivary neurons, where it exists. Strong coupling produces synchrony among the discharges of neurons projecting into the same strip and also may elevate the repetition rate of olivary bursts; both quicken the redistribution of "background" activity in anterior lobe compartments (figure 2 and ref. 22). The third mechanism was not examined in the earlier report and will instead be treated here. It has to do with the possible

subdivision of Oscarsson strips into a collection, or continuum, of narrower "microstrips":

Oscarsson strips of the "locomotor" anterior lobe (figure 3) are approximately 1 mm wide. However, experiments employing both electrical and "natural" stimulation have on occasion revealed climbing fiber volleys lying in much narrower (0.2-0.4 mm) sagittal microstrips within the Oscarsson bands[5,57,155,226]. Some autoradiographic evidence for an olivocerebellar microstrip projection is also available (Courville, personal communication). These microstrips appear to have some functional significance, for it has been observed that they can "migrate" within their confining Oscarsson strip as a function of the location on a limb where either a nerve[57] or tactile (Roberts, personal communication) stimulus is delivered. What is the significance of this microstrip encoding mechanism?

Microstrip encoding may basically be a ploy for avoiding the limited "bandpass" of the spino-olivocerebellar system: It is true that for microstrip activation to have maximum cerebellar nuclear effect, the relevant olivary neurons should fire synchronously and at the highest burst repetition rate (presumably made possible by electronic coupling; see above). However, it is also well known (ref. 22; section 3.1.2) that individual olivary neurons will not follow peripheral stimuli delivered at frequencies much higher than 10/sec, which is also approximately the frequency at which they synchronously burst under harmaline (section 4.2)[42,123,124,129]. Now the production of significant activity alterations in anterior lobe

compartments can be shown to require activation of most or all of the microstrips within an Oscarsson strip[22]. So suppose that the limb inputs which appear to have private channels into particular microstrips (above) were actually distributed throughout the olivary pool projecting into an entire Oscarsson strip; or alternatively, suppose the entire pool were electrotonically coupled. Then peripheral transmission into the Oscarsson strip would be limited by the 10 hz bandpass of the microstrips--the majority of limb inputs would encounter a refractory olive. But with the private channel scheme, the time-averaged "density" of microstrip volleys in the Oscarsson strip might be much higher for the same set of inputs; signals from different parts of the limb could not interfere with each other through refractoriness. At the same time, the consequent alterations in anterior lobe compartmental activity may be produced more rapidly because of the higher density of climbing fiber volleys. Consequently,

> One may identify "activation" of an Oscarsson strip with an increase in the synchrony and burst repetition rate of climbing fibers within each of its component microstrips. However, the bursting of neighboring microstrips will probably remain essentially uncorrelated in most situations.

A corollary of this proposition, of course, is that electrotonic coupling (and other synchronizing mechanisms such as, perhaps,

recurrent olivary collaterals[5]) should be restricted to neurons innervating the same microstrips--and should not normally extend to the neuron pool associated with an entire Oscarsson strip. Thus, in guinea pigs Bell and Kawasaki* found little correlation between spontaneously occurring Purkinje climbing fiber responses in cells more than approximately 0.6 mm apart mediolaterally. Barmack and Hess (personal communication; see also Appendix) saw no obvious synchrony among visually driven olivary neurons of the dorsal cap, projecting to the cerebellar flocculus (rabbits). And Armstrong, et al.[8] observed that an Oscarsson strip can be innervated by neuron colonies in different (albeit neighboring) anatomical divisions of the olive, which would seem to cast doubt on the synchronization, by electronic coupling, of all climbing fibers in such strips.

If the above statements have any validity, then it may be difficult indeed to detect, by direct recording from the cerebellar cortex, the "activation" of an Oscarsson strip during locomotion. One would have to show microstrip synchrony and an overall increase in the "density" of climbing fiber volleys per unit time. If the entire Oscarsson strip were synchronously active, then rather simple field potential analysis might serve to detect it (Armstrong, personal communication); but, as described above, such whole-strip synchrony may not be a usual occurrence. Some methods of avoiding these problems are given in section 4.2. Incidentally, to the author's knowledge

*Bell, C. C., Kawasaki, T., "Relations among climbing fiber responses of nearby Purkinje cells," J. Neurophysiol. 35, 155-169 (1972).

no recordings have been published of neurons <u>afferent to</u> the "spinal" olive (i.e., spinal interneurons, brainstem and dorsal column nuclear units, etc.). Such data might well give some further insight into the temporal properties of olivocerebellar coding. For example, do olivary afferents mimic the bursting of the olive itself? Or are they more "tonic," with the bursting entirely the product of intrinsic olivary processes (involving recurrent inhibition, electrotonic coupling, and the like)? A recent study (Collewijn, in press) of units in the rabbit accessory optic tract nucleus, which <u>may</u> innervate the olive dorsal cap, has revealed very "tonic" discharges modulated in a strictly analogue fashion with moving visual inputs.

A final property of the spino-olivocerebellar channel deserves mentioning, and that is its insensitivity to the <u>temporal order</u> in which peripheral (or central) inputs are presented to it. This is especially clear in relation to the microstrip encoding process described above: An efficacious Oscarsson strip activation, in terms of redistributing the activity in anterior lobe compartments, requires more frequent, synchronous volleys in each of the component microstrips. But the order in which the microstrips are triggered is essentially immaterial to the compartmental outcome. This is simply because of the extended time course of the nuclear effects of climbing fiber inputs, which tends to "integrate" and blur the results of successive microstrip volleys. The phenomenon only becomes interesting when one realizes that this makes the olivocerebellar system blind to the time sequencing of movement. That is to say:

The various microstrip-activating motor events (reflex potentiations, cutaneous signals, muscle stretches, etc.) that occur during a given instance of locomotion could be freely permuted in time with no change in the resulting distributions of anterior lobe, "background" compartmental activity.

This conclusion, of course, is in keeping with the mapping of a complete locomotor movement sequence into a single lattice of Oscarsson strips (section 3.3.2). Such a lattice contains no information about the temporal order in which the movements are to be executed. Obviously, order-independence may have considerable bearing upon the design of experiments that are to show differences in climbing fiber activity with different types of movement. Even if one could get around the problems of detecting microstrip synchrony and so forth that define Oscarsson strip "activation," it may be that some movement sequences which appear quite different to the eye are actually "equivalent" with respect to the olivocerebellar system; no qualitative changes in climbing fiber activity would be produced by changes from one "equivalent" sequence to another. In the example of locomotion, all gaits executable with the same hindlimb-forelimb couplings are equivalent with respect to the Oscarsson strip lattices involved (section 3.2); one would have to force a change in coupling to see a very dramatic change in the pattern of climbing fiber volleys. What does this say about attempts to produce correlations of climbing fiber activity with episodes of more voluntary movement, where the

"equivalencies" between movements are unknown? Even if correlations could be seen (and they have not been; section 3.1.2), how could they be interpreted functionally?

Unfortunately for experimentation, the spino-olivocerebellar pathway may encode its information in a rather complex way, but a way which is completely consonant with its theoretical role of adjusting the "tonic" structural bias on the musculature for extended periods of movement. Even if that theory is incorrect or incomplete, it still seems that a slightly more sophisticated view of the climbing fiber system must be evolved to permit the rapid unraveling of its secrets. Continued trial-and-error searches for the "right movement" are exactly that--a trial and an error.

In summary:

The spino-olivocerebellar system encodes its information in three basic ways:

1. By the location of a target Oscarsson strip.
2. By the location of microstrips within an Oscarsson strip.
3. By increasing the synchrony and burst repetition rate of climbing fibers within a microstrip, probably through strengthening electrotonic coupling between the appropriate olivary neurons.

The effective "activation" of an Oscarsson strip requires synchrony and repetition rate increases in most or all component microstrips. However, neighboring microstrip discharges will largely remain uncorrelated.

By virtue of the extended time course of the nuclear effects

of climbing fiber activity, the olivocerebellar system is insensitive to the temporal order in which its inputs arrive. A number of distinct movement sequences may thus be "equivalent" with respect both to the climbing fiber activity associated with them, and to the structural modulation produced by the olivocerebellar system.

3.4 Climbing Fibers and the Cerebellar Posterior Lobe: Speculations

According to the results of various classical studies (cf. refs. 34, 45, 187), the vermis and paramedian lobule of the cerebellar posterior lobe are as much a part of the "locomotor" cerebellum as is the anterior lobe. However, there is very little known about the posterior areas. The sagittal corticonuclear compartmentalization of the anterior lobe appears to continue posteriorly, such that the anterior and posterior vermis share fastigial and Deiters influences, while the anterior intermediate zone shares interpositus with the paramedian lobule[221] (but see refs. 38, 219); lesions or stimulation of the posterior vermis or paramedian lobule produce effects somewhat similar to those associated with the corresponding anterior lobe regions[33,34]. Paralleling this corticonuclear organization, it has been observed that certain Oscarsson climbing fiber strips of the anterior lobe have continuations into the posterior[6] and are innervated by the same spino-olivocerebellar pathways[7].

The above evidence might suggest that the posterior lobe is but a continuation of the anterior. However, the two regions have at least three distinct differences that may be of functional

significance: The first is that the posterior lobe cortex is mediolaterally discontinuous at the boundary between the vermis and paramedian lobule[38,220], which is not true for the vermal-intermediate zone boundary in the anterior lobe. It is conceivable that this discontinuity will decouple any lateral inhibition between vermal and paramedian corticonuclear compartments, such that the "hill-and-valley" patterns of climbing fiber-induced nuclear excitation (figure 2; section 3.1.1) characteristic of the anterior lobe may not pertain to the posterior. A second anterior/posterior distinction lies in the topography of limb representation. As was shown in figure 3, the hindlimb is influenced by more rostral anterior lobe areas (lobule IV) than is the forelimb (lobule V). But the topography of the posterior lobe is the mirror image of this, with the forelimb region rostral to the hindlimb. This head-to-head somatotopic organization in the locomotor cerebellum would probably have no intrinsic significance if the anterior and posterior lobes functioned independently. Yet the sharing of the same climbing fiber systems by the two regions (above) suggests some form of interaction between the two. A speculation on that interaction and how the somatotopy may play a part in it will be given in a moment. The third contrast between anterior and posterior lobes involves the likelihood that the muscle linkage influences of the two are distinct, rather than "redundant." It has been suggested[45] that a more explicit representation of muscle structure exists posteriorly, with the vermis dealing primarily with axial and proximal muscles and the paramedian lobule with distal.

Pompeiano[187] has also examined muscle linkage facilitation produced by the anterior and posterior portions of the interpositus nucleus (which are anatomically distinct and are primarily governed by the anterior intermediate and paramedian cortical zones, respectively). He reports that "homologous" regions of the two nuclear portions can facilitate opposed linkages, although the result is questionable at present.

Unfortunately, besides the data sketchily presented above, there is little else known about the properties of the posterior lobe in cats, especially with respect to locomotion. It therefore is probably foolish to speculate at any length on posterior lobe function; however, in the interest of at least opening discussion on this part of the cerebellum, a few comments might be in order: In the previous theoretical study on climbing fiber physiology[22], it was pointed out that lateral recurrent inhibition may be expressed among cerebellar nuclear regions lying <u>within</u> a single sagittal cortico-nuclear compartment as well as <u>among</u> neighboring compartments. The "lateralization" of the inhibition would in this situation not be due to parallel fiber activity, of course, but rather to the supposed geometry of the corticonuclear projection: On the basis of then-existing evidence[22], it was thought that rather small patches of cortex distributed projections throughout the rostrocaudal extent of a compartment, thereby producing sagittal inhibitory fields similar to those created mediolaterally by parallel fiber excitation. The presence of lateral inhibition along both the sagittal and mediolateral

axes suggested that the "locomotor" cerebellum might be very receptive (with respect to the creation of nuclear excitation distributions) to patterns of Oscarsson strip climbing fiber activity fitting the sort of "checkerboard" arrangement shown in figure 9. As can be seen, the activity remains confined to strip "lattices" mediolaterally (cf. sections 3.2, 3.3); but the entire rostrocaudal length of a strip is not activated as a unit. There are regularly spaced breaks corresponding to "valleys" of nuclear inhibition produced by the hypothetical sagittal inhibition system. If such a checkerboard climbing fiber template is applied to the corticonuclear compartments shared by the anterior and posterior lobes, one possible result is that illustrated in figure 10. Here it has been assumed that Oscarsson strips can be "broken," in terms of their activation, at somatotopic boundaries on the cortex. The number of breaks required is reduced by the head-to-head topographic scheme; or alternatively, the topographic organization may be related to the anatomical mechanisms producing sagittal lateral inhibition.

Unfortunately for the above conjecture, ongoing anatomical work (Courville, personal communication) has given preliminary indications that the compartmental corticonuclear projection might not, in all probability, produce the necessary sagittal lateral inhibition. It appears that the projection in the parasagittal plane is akin to so many "pie wedges," with rostralmost cortical regions restricting their influences to rostralmost parts of the fastigial and interpositus nuclei and progressively more caudal lobules projecting with little

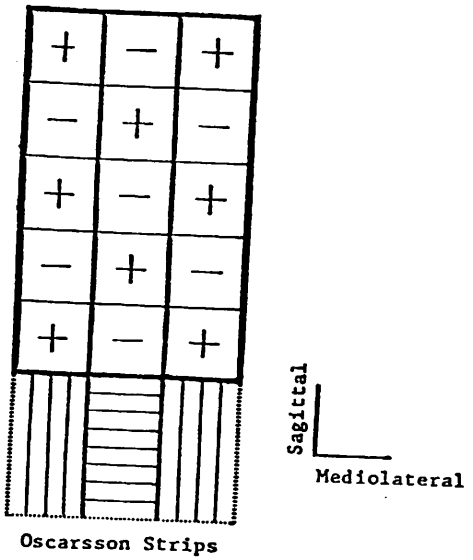

FIGURE 9

A "checkerboard" pattern (after Boylls[22]) of active (+) and inactive (-) Oscarsson strip segments that is best suited to the forces of lateral inhibition in both the mediolateral and sagittal planes.

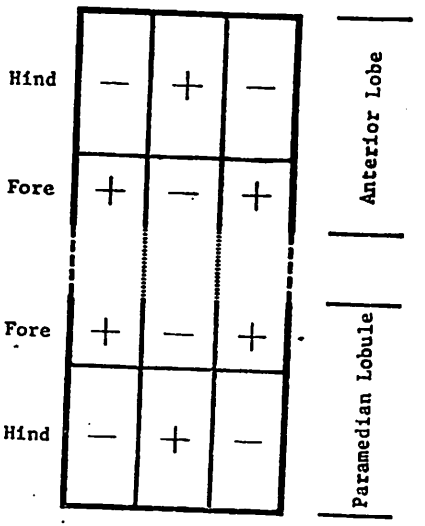

FIGURE 10

A possible application of the checkerboard climbing fiber strip pattern (figure 9) to the anterior and posterior lobes. See text for constraints.

overlap, to increasingly caudal nuclear sectors. In short, broadcast sagittal inhibition from discrete cortical regions is unlikely. As an alternative, one might look to the effects of the sagittally oriented cortical interneurons (basket and stellate cells), but that requires a good deal more thought.

This discussion must consequently close on an unsatisfactory note, even though it does seem almost certain that the anterior and posterior cerebellar lobes cooperate in the modulation of locomotion. Perhaps it will not be long before studies appear which do range over the entirety of the "locomotor" cerebellum.

To summarize:

The cerebellar posterior lobe (posterior vermis, paramedian lobule) shares corticonuclear compartments and Oscarsson climbing fiber strips with the anterior lobe. However, it does differ from the latter in the physical continuity of its cortex, in its somatotopic organization, and (probably) in its influences on the structure of muscle linkages. It is barely possible that the interactions between the anterior and posterior lobes may involve some form of sagitally directed lateral inhibition expressed over cerebellar nuclear regions within a corticonuclear compartment. However, the matter cannot be resolved here.

4. Discussion

This report, if one recalls the Introduction (section 1), has set itself two tasks: The first was to develop a practical theory

for how the climbing fiber system of the cerebellar anterior lobe assists in the regulation of locomotion in cats, while the second was to illustrate a deductive attack on that problem using a general motor control paradigm--the postulates on muscle linkages and synergies developed by Bernstein[15,16] and later workers[73,83,208]. The work has produced rather precise conclusions on the generic relationship of olivocerebellar activity to the tuning of locomotor muscle usage (section 3.1), on the Oscarsson strip distributions of that activity as a function of gait category (section 3.2), and on the peripheral and central sources of climbing fiber signals (section 3.3). At the same time, the Bernstein paradigm has itself been refined and significantly augmented. Discussion below will concentrate primarily upon the climbing fiber theory, commencing with an overview and then proceeding to a synopsis of the theory's "axioms" and principal conclusions. While basic elements of the Bernstein view will also be treated, its more exotic aspects will be reserved for section 5 (see also ref. 23).

4.1 Locomotor Functions of the Anterior Lobe Olivocerebellar System

4.1.1 Overview

According to the present results, a cat's anterior lobe climbing fiber system is a mechanism for introducing prolonged biases into the "structure" of locomotor muscle usage. It does this primarily as a function of the spinally determined coupling of homolateral limbs, i.e., in response to internally, rather than peripherally, generated signals. Loosely speaking, then, climbing fiber activity adjusts the "carriage" of

a locomoting animal according to the gait it has assumed. Or to abuse the language still further:

> The olivocerebellar complex is an act-specific, "postural" mechanism--an intrinsic system for pre-programming the proximal-distal, adductor-abductor, rostral-caudal, and ipsilateral-contralateral contraction balances among muscle groups executing complete motor acts.

If the above ideas are correct, then the behavioral effects of anterior lobe climbing fiber volleys may be remarkably similar to those created by influences from the vestibular apparatus and neck proprioceptors. The latter also effect holistic "postural" skewing of the contraction proportions within multijoint muscle linkages, and thereby modify an animal's carriage or the "directionality" of its locomotion (as when turning the head of a locomoting thalamic cat causes the entire animal to turn in the same direction[134]). This parallelism suggests that climbing fiber afferents might have evolved in fish from a subset of specialized vestibular, lateral line, and even visual inputs that were part of an early cerebellar regulator of body attitude. Indeed, in the phylogenetically ancient vestibulocerebellum of rabbits (and, likely, other mammals), visual and vestibular climbing fiber inputs have survived and appear to elicit vestibulo-ocular effects mimicking extended changes in the "tonic" discharge level of the vestibular (VIII) nerve (see Appendix).

Climbing fibers of the modern anterior lobe are not part of a surrogate vestibular system, of course. They do not govern ongoing

action as an immediate function of peripheral events, and their muscular influences probably have a much longer "time constant" than do vestibular forces. But it does seem meaningful to say that their activity may help establish a stabilizing milieu for locomotion by assuring that the carriage of an animal is best adapted to carrying off a particular gait. A crouch, for example, would be ill-suited to the gallop. The olivocerebellar apparatus could thus be viewed as an internal, anticipatory stabilizer of locomotion, pre-tuning the "posture" of a performance. On the other hand, vestibular, neck, visual, and other influences presumably fill in the differences between such idealized postures and the realities of the environment (such as in walking uphill). This notion of "internal stabilization" becomes important when one realizes that the external stabilizers, such as vestibular reflexes, often oppose active movement and consequently can be actively suppressed during it (e.g., in mesencephalic locomotion[178]). Yet clumsiness does not ensue. Conversely, the carriage of locomoting rats with total olivary lesions, but which are otherwise intact, is bizarre (to be discussed in section 4.2). Another report[23] treats these and other aspects of internal stabilization more fully.

In the past, theoreticians--and not a few experimentalists--have assigned ·o the climbing fiber a very indirect role in movement regulation. The work of Marr[20,143] and Albus[1,2] in particular has held that the olivocerebellar system is involved primarily in executing novel performances, where it acts to condition cerebellar responses to mossy fiber inputs. As such performances become habit, mossy inputs alone are left as the

critical determinants of cerebellar outflow. It is comparatively common, of course, to find experimental correlations between anterior lobe mossy fiber activity and attributes of ongoing movement (cf. refs. 9, 10, 11, 174 for locomotion). Since this is not true of climbing fiber discharges (sections 3.1.2, 3.3.4; ref. 22), the popularity the "indirect" theories have enjoyed is easy to appreciate. They also have blended the allure of plasticity with the seeming precision and finality of mathematics.

However, as against the "indirect influence" philosophy, the present theory sees the olivocerebellar system as contributing immediately, specifically, continuously, but subtly, to all types of movement; and a number of remarkable experiments (described in the Appendix and in sections 4.1.3, 4.2) have recently been performed which support this view: All have demonstrated that well-controlled lesioning and/or stimulation of the climbing fiber pathway leads immediately to clear-cut motor disturbances. Unfortunately, the work has not yet been sufficiently refined to reveal explicitly the functions of anterior lobe climbing fibers. The experiments proposed in section 4.2 have two purposes, one of which is to help remedy that situation. Their other goal will be to evaluate the theory presented here in comparison with alternative proposals on the direct motor influences of climbing fibers (see sections 4.1.3, 4.2). Now it should be said in conclusion that the likelihood of more indirect climbing fiber effects, such as might involve plasticity, is not to be ruled out. But to dwell upon such possibilities in search of the key functions of the olivocerebellar system may not be particularly profitable[22].

In summary:

This report has demonstrated that the anterior lobe olivocerebellar system may help to establish the appropriate "postures"--the structural biases on muscle linkages--for particular locomotor performances. It does this primarily by using cues provided by the intrinsic spinal circuits programming those performances. Thus, one could consider the anterior lobe climbing fibers to be part of an internal "stabilizing" mechanism which ensures that the carriage of an animal is appropriate to its gait. It is possible that this internal stabilization role evolved from an earlier time when climbing fibers were part of a vestibulocerebellar system that used external signals to regulate body attitude.

The present theory treats the climbing fiber as having a direct influence on the course of essentially all movement (at least in locomotion); but the influence is subtle. Recent evidence supports this philosophy, although experiments delineating anterior lobe climbing fiber function more precisely have yet to be performed.

4.1.2 Essential Theoretical Postulates

a. The muscle linkage principle and the controllable parameters of linkages. Of all "axioms" for the present work, none has been so important as Bernstein's principle of the muscle linkage[15,16]. It permits one to turn the statement, "the cerebellum modulates movement," into something more quantitative, because it suggests candidates for the controllable parameters of movement through which such modulation could be expressed.

The muscle linkage principle teaches two closely related things: The first is that the most primitive, independently governable actuators of movement are rarely individual muscles, but rather aggregates of muscles, often distributed over many joints. The second is that, at some level, such aggregates are constrained to act as a unit--which is what turns the aggregate into a linkage. In more Bernsteinian terminology, the motor controller makes use of muscle linkages which reduce the "controllable degrees of freedom" presented by the skeletomuscular system. Characterizing the cerebellar contribution to movement thus requires specifying a set of muscle control parameters which not only can express multijoint adjustments in the behaviors of many muscles, but can also permit the portrayal of linkage constraints among muscles. Obviously, these parameters will have to deal with more than the firing frequencies and recruitment states within isolated motoneuron pools.

To attempt to satisfy the above requirements, the present study has defined control parameters for agonist linkages based upon the following hypothetical constraints on the (integrated) EMG of linked, locomotor muscles:

1. In a given muscle, EMG timing (burst onset and duration) will be, to some degree, independent of EMG amplitude.

2. The ratios of EMG amplitudes in coactive, linked muscles will remain roughly fixed relative to the time frame and the absolute amplitude of individual contractions.

Constraint (1) has been adequately discussed in the "two-process hypothesis" of section 2.4, where the idea of spinal "sampling"

of a potential EMG profile was introduced. Of course, (1) is also readily tested experimentally by routine correlation procedures.

Constraint (2) embodies the distinction between independent metrical and structural prescriptions for linkage activity--defining, respectively, its overall amplitude and proportioning throughout the linkage. The validity of (2) for cat locomotor linkages is unknown (cf. sections 2.1.4, 2.3.1). However, the constraint has been examined quite recently within the context of human postural stabilization[165] (Nashner, unpublished): Quietly standing subjects were confronted with sudden ankle rotations from a moving platform (described further in section 2.4). Recovery from these perturbations was found to involve near-synchronous EMG activity of various ankle, knee, and hip muscles; and despite wide fluctuations in the absolute integrated EMG levels in those muscles from one ankle rotation trial to the next, the computed activity ratios among muscles (or structure) remained very nearly constant. Over a succession of trials the ratios could change (for reasons that are presently being investigated; Nashner, in preparation), but it seemed clear that the structure of this "postural stabilization linkage" was invariant with respect to the time frame of a single trial and the EMG amplitudes achieved. Similar quasi-invariant structure may account for the behavior of the human "respiratory synergy" studied by Gurfinkel'[96], and for Kots' observations of fixed wrist/elbow velocity ratios in human arm movements[121]. Checking constraint (2) in a locomoting cat would not be difficult if, modulo constraint (1), a reasonable number of instances exist wherein the EMG's of linked muscles overlap in time. Many limb extensors probably

satisfy this requirement; the flexor situation may be more complex[59].

Constraints (1) and (2) above transform linkage EMG patterns into simple vector quantities. By way of illustration, suppose linkage $\vec{L}$ involves three muscles (or three muscle groups at different joints). Then one could write down its EMG portrait at time t as the three-component vector:

$$\vec{L}[m(t), \{S(t')\}, \{\tau,D\}] = m(t)[s_1(t')u(t-\tau_1,d_1),\ s_2(t')u(t-\tau_2,d_2),\ s_3(t')u(t-\tau_3,d_3)]$$

where $u(t,d) = 1,\ 0<t<d$

$= 0$, elsewhere

and $t' \propto \frac{t}{K}$, $K>>1$

and with the following identifications:

i. The scalar m(t) (non-negative) is the linkage metrical prescription, or multiplier of all EMG activity in the linkage;

ii. The set $\{S(t')\}$ (positive elements) is the linkage structural prescription, the collection of EMG ratios among the linked muscles which changes but slowly with respect to t, the "real time" of movement;

iii. The set $\{\tau,D\}$ (positive elements) is the timing prescription, determining the onsets (τ's) and durations (d's) of EMG bursts in each muscle--or in other words, describing the operation of "spinal switching" (section 2.3.4).

If $\vec{L}$ were to be used to model a locomotor linkage, then m(t) would be replaced by a periodic function, as would the sampling function, u(t,d). It would be an interesting experimental (and mathematical) exercise, in fact, to attempt to reconstruct a continuous m(t) from the sporadic samples provided by the EMG bursts (having first obtained $\{S(t')\}$, of course; see above).

A corollary of constraints (1) and (2) is that the parameter sets m(t), $\{S(t')\}$, and $\{\tau,D\}$ are independent of each other. But what of the elements <u>within</u> sets $\{S(t')\}$ and $\{\tau,D\}$? Do they constitute independent variables? Note from the expression for $\vec{L}$ that if such were true, a linkage could display <u>any</u> instantaneous "snapshot" of EMG's in its muscles. Even though EMG proportioning among the muscles would have to remain fairly constant among successive snapshots, this still would represent myriad degrees of freedom in linkage programming. Consequently, it is worth noting one less obvious result of the present work: <u>The elements of $\{S(t')\}$ are ~~not~~ independent; locomotor linkage structure is itself subject to constraints</u>. The conclusion follows from the identification of $\{S(t')\}$ with excitation ratios among nuclear zones in different anterior lobe corticonuclear compartments, coupled with the observation that such ratios are restricted by lateral inhibition among compartments (sections 2.3.2, 2.3.3, 3.1.1, and subsections below). One should thus be able to express structure as a function of fewer variables than there are muscles in a linkage. For example, suppose the s's in $\{S(t')\}$ for a limb linkage can be indexed by x, $0 \le x \le 2$ where x denotes the location of a muscle. Let $x = 0$ indicate the most proximally-acting muscle, and

x = 2 the most distal. Then the structure of the linkage might be constrained by:

$$\{S(t')\} = \bigcup_{0 \le x \le 2} s(x,t')$$

where $s(x,t') = [1 - f(t')] + f(t')x$, $0 \le x \le 2$, $-1 \le f(t') \le 1$,

and $f(t')$ represents a single, independent structural variable. This says that the linkage can be continuously tuned from a primarily "proximal" ($f(t') = -1$) to a primarily "distal" ($f(t') = 1$) bias, but prohibits dominance of muscle between these extremes of location. The mysterious $f(t')$, of course, is ostensibly a black-box characterization of olivocerebellar activity. Now whether this particular form of structural constraint suits cat locomotion is immaterial, although a case of sorts for it will be made in section 4.1.3. The important points are to recognize the possibility of such restrictions and to look for them experimentally (again, a fairly easy task). The same is true with respect to possible dependencies in the elements of $\{\tau,D\}$, about which nothing is known.

An EMG-oriented description of linkage control has obvious shortcomings. Perhaps the worst is that it usually is impossible (except under isometric conditions) to translate EMG patterns into muscle force. As a result, one cannot use the formulation of the linkage principle given here to say anything very precise about either the dynamics of movement or about the central use of dynamical feedback. To remedy that situation, Fel'dman's*

*Asatryan, D.G., Fel'dman, A.G., "Functional tuning of nervous system with control of movement or maintenance of a steady posture. I. Mechanographic analysis of the work of the joint on execution of a postural task," Biophysics 10, 925-935 (1965).

nonlinear spring characterization for the control of agonist muscles at single joints is being employed to develop a new description of linkage control in terms of more conventional "state variables" (Boylls, in preparation. To Fel'dman's model are being added certain features of agonist-antagonist interaction and of parametric adjustment of the resultant dynamics (stiffness, damping, etc; cf. refs. 99, 101). The jump to multi-joint linkages is made simply by applying constraints similar to (1) and (2) to the Fel'dman control variables at each joint, including the parametric controls. Indeed, it appears that the latter could in part be computed in portions of the cat cerebellar hemisphere using the identical linkage format found in the anterior lobe[23].

A good deal has been heard about constraints and invariances in this discussion, because these are the essence of the Bernstein linkage paradigm. For some, they might also be the stuff of skepticism. The linkage paradigm by no means represents a conventional engineering approach to the control of motor performance, because the brain is not viewed as having the capacity to transfer an existing state of the musculature into any other arbitrary state, however biomechanically sound. But then, what purpose would such a capacity serve? Most such unconstrained states would have no behavioral utility. Hence, the linkage paradigm rather naturally assumes that evolution has economized the motor system's task through constraints restricting its operation to the domain of behaviorally useful muscle deployments. And if that is so, then it should also be no surprise to find the computations performed by some central structures to be similarly restricted in nontrivial ways--as, for example, in the three basic spatial formats found here for climbing fiber-induced anterior lobe activity

(sections 3.2, 4.1.3). The argument extends to the processes of skill acquisition and other motor learning problems, in that if the "style" of the motor controller is to operate within constraints, learning should be similarly structured. Plasticity might be expected to alter constraints somewhat, but it will not abolish them. As a result, certain dynamically complex tasks will be much more easily acquired than other, seemingly "simple" actions, if the former fit existing constraints better than the latter. Theorizing on the central mechanisms of motor plasticity has dwelled upon the construction of "universal" movement sequence generators and the like--artifices deriving from context-free information theory. Perhaps, instead, theoreticians should be addressing the possibilities of special-purpose plasticity to accompany a special-purpose motor system.

By now it should be obvious that acceptance of the linkage principle's elementary tenets leads one rather innocuously into a more radical philosophy of motor control than is presently in vogue. Skepticism is thus entirely in order, all the more so if it will spur a continued experimental search for linkage constraints in different acts--for what could loosely be called "constants of the motion." As in physics, such constants might well be found to bind up all the relevant dynamical information about movement.

b. Encoding of structural and metrical linkage tunings as activity distributions among anterior lobe corticonuclear compartments. The two-process hypothesis of section 2.4 removes the cerebellar anterior lobe from the business of timing locomotor EMG bursts (the responsibility of spinal circuits) and gives it a role exclusively in governing EMG amplitudes--in tuning the structural and metrical prescriptions of linkages.

The present "axiom" is the critical bridge between cerebellar physiological process and the computation of those prescriptions. Simply enough, it states:

1. That the cerebellar anterior lobe is partitioned into corticonuclear compartments, each compartment consisting of one or more nuclear zones (in the cerebellar or vestibular nuclei) inhibited by a unique sagittal band of cortex;

2. That excitation of the nuclear region in a given compartment will, at the appropriate times in the step cycle, potentiate contraction of limb flexor or extensor linkages (but not both);

3. That the contraction ratios of muscles in a linkage (i.e., linkage structure) is tuned through the ratios of excitation among cerebellar nuclear regions potentiating that linkage, but lying in different compartments; and

4. That the overall linkage contraction level (m(t) in the previous subsection) is proportional to the overall excitation distributed over the same nuclear regions.

There is assumed to be, in other words, a natural isomorphism between the spatial patterning of cerebellar compartmental activity and the spatial properties of muscle linkage contraction, and between the overall amplitudes of both patterns and contractions.

The evidence supporting the first two assertions above has been amply reviewed both here (sections 2.3.2, 2.3.3) and elsewhere[22]. Propositions (3) and (4) become reasonable provided two preconditions can be satisfied: The first is that a given muscle linkage should be structurally biased

in distinctly different ways by nuclear regions in different anterior lobe compartments; the second is that the linkage effects from such regions should superimpose on the linkage. This amounts to saying that any two seemingly "redundant" descending spinal pathways receiving from the cerebellum (e.g., the rubro- and lateral reticulospinal tracts, both potentiating flexion; section 2.3.2) should actually focus their facilitation on different muscle groups within a linkage and should not occlude each others' actions. Experimental examination of the hypothesis would be straightforward.

When taken with the linkage constraints described in the previous subsection, propositions (1)-(4) lead to a most important corollary on the nature of anterior lobe computation:

> The physiological processes of the anterior lobe must take place within at least two distinct time frames: Neural interactions establishing the excitation ratios of nuclear regions in different corticonuclear compartments (i.e., creating the structural prescriptions of muscle linkages) should operate within a time frame that is "slow" relative to interactions governing the generalized excitation of all compartments (metrical prescriptions). In fact, the time frame of the latter should be that of movement itself.

During locomotion, in other words, the "DC level" of a spatial activity pattern residing in the compartments of the anterior lobe (e.g., the pattern of figure 2, section 3.1.1) is expected to fluctuate temporally in synchrony with the step cycle. But that pattern will also have a life of

its own, changing but slowly over a number of cycles. Thus, at the single unit level, what one sees is the fast, level-setting process in the cyclical activity of Purkinje[174] or cerebellar nuclear[175] neurons. The question is, will the activity ratios of neurons in distinct compartments (governing the same linkages) be found to be so quickly mutable? If not, how would one account physiologically for two quite different time courses of events within the same cerebellum (remember, plastic processes are not being considered)? Only further experiment can answer the first question, but the second is considered below, and in sections 4.1.3 and 5.

c. Physiological effects of climbing fiber volleys on anterior lobe compartmental activity. This final set of postulates is the last link in the logical chain between the olivocerebellar system and the regulation of certain locomotor properties. The postulates have been rehearsed at some length both here (sections 2.3.3, 3.1, Appendix) and elsewhere[22], including proposals for their experimental examination. They merely will be restated here.

It is assumed that:

1. Nuclear zones within neighboring corticonuclear compartments of the anterior lobe recurrently inhibit each other via portions of the reticular formation and the cerebellar cortex;

2. The olivocerebellar projection is organized according to a set of sagittal Oscarsson strips whose boundaries coincide with those of the compartments;

3. Volleys in a given Oscarsson strip, if they meet certain criteria (section 3.3.4), will disinhibit the nuclear region within their own

compartment. That will in turn lead to nuclear inhibition in neighboring compartments;

4. Since the recurrent inhibition of (3) is regenerative, the resulting compartmental activity patterns will persist for a "long" time relative to, say, the step cycle.

The previous subsection raised a question about physiological mechanisms for long time-course, spatial patterning processes versus short time-course, level-setting processes in the anterior lobe: According to the postulates above, the chief architect of activity distributions (ratios) among corticonuclear compartments--lateral recurrent inhibition--is, conveniently enough, also that responsible for securing quasi-invariance of those distributions over time. Now the climbing fiber system produces its temporally extended effects upon movement because it can address compartmental lateral inhibition selectively. It has that effect because climbing fiber inputs are spatially restricted to single compartments, as can readily be shown analytically[22]. How, then, might the anterior lobe respond to spatially extensive inputs, "diffuse" signals subtending a number of compartments? The question is irrelevant, of course, to the climbing fiber system. As section 5 will describe, however, it may be through precisely such "diffuseness" that certain mossy fiber pathways are able to trigger the posited "fast" physiological processes that rapidly alter overall compartmental activity and determine the metrical prescriptions for muscle linkage contractions. Paradoxically, the cerebellar networks involved are the same, lazy lateral inhibition mechanisms important to climbing fiber function. But such networks may reveal quite a different personality when

confronted with inputs lying outside their spatial "bandpass" (section 5).

To summarize:

The "axioms" of the present work comprise various assumptions about the controllable parameters of locomotor agonist linkages, the encoding of some of those parameters in the outflow of the cerebellar anterior lobe, and the impact of climbing fiber volleys upon that outflow. Fundamental among these assertions is that the constellation of integrated EMG amplitudes in a linkage is constrained in certain nontrivial ways. In particular, it is held that amplitude ratios among linked muscles change but slowly with respect to the time frame of ongoing movement. Such a quasi-invariant "structural prescription" permits absolute linkage contraction levels to be specified by a single scalar "metrical prescription" multiplying the activity in all muscles. The anterior lobe deals independently with both structural and metrical linkage prescriptions, while spinal circuitry imposes a pattern of EMG timing "slots" upon the structural/metrical recipe for EMG amplitude.

A natural isomorphism is assumed to exist between muscle linkage structure and the spatial distribution, or ratios, of activity in the corticonuclear compartments of the anterior lobe. A similar relationship should hold between the magnitude of overall compartmental activity (or the "DC level" of compartmental spatial activity patterns) and linkage metrical prescriptions. Thus, two time frames must characterize anterior lobe physiological processes: Spatial patterns of compartmental activity (structural prescriptions) will change slowly relative to the baseline levels of that activity (metrical prescriptions).

Lateral recurrent inhibition among the nuclear zones in different corticonuclear compartments is the neural mechanism chiefly responsible both for regulating compartmental activity ratios and assuring their quasi-invariance over step cycles. Through its spatially restricted, Oscarsson strip projection patterns, the olivocerebellar system plays upon this lateral inhibition; climbing fiber volleys thereby have a prolonged effect upon ongoing movement. It may be that the more rapid time frame of cerebellar processing is addressed through more "diffuse" inputs, as typified in certain mossy fiber pathways.

4.1.3 Essential Results

a. Climbing fiber volleys bias the structure of locomotor muscle linkages over extended periods of time. This, of course, is the most fundamental result of the present report and has already been discussed at length. It follows as a straightforward consequence of the postulates recounted in the previous section. Postulates or not, however, it is rather surprising that the association of the anterior lobe climbing fiber with some sort of "postural" mechanism (section 4.1.1) has not previously been suggested by others. The utter refractoriness of the olivocerebellar system when compared with other cerebellar afferent pathways, its intuitive (and demonstrated) inability to "keep up" with movement in a believably continuous fashion, would seem rather blatantly to point to processes which regulate the overall milieu of action. One need know nothing of muscle linkages to at least consider the idea. And indeed, from rough correlations between the frequency of climbing fiber bursts and the amount of muscle

tonus in different stages of sleep (cats), Strata* did propose that the olivocerebellar system might regulate a more "tonic" (albeit unspecified) aspect of movement. But the few investigators who have at least accepted a direct climbing fiber role in movement have tended to identify that role explicitly with the brief impact made by climbing fiber discharges upon individual cerebellar neurons. In particular, Llinás** has hypothesized that the olivocerebellar pathway contributes a "phasic operator" to motor performance--a force that presumably might assist in, say, starting or finishing an action, or in producing rapid movements or mid-course corrections. Lack of linguistic precision is the chief problem with this view; but it also seems difficult to reconcile with the significant conduction delays in the spino-olivary pathway, the low "bandpass" of the olivary relay (section 3.3.4), and the absence of climbing fiber discharge correlation with movements seeming to have clearcut "phasic" components by any definition (e.g., refs. 139, 211; Grimm and Rushmer, in press).

Luckily, the present theory seems to have no trouble assimilating the known quirks of the olivocerebellar system (section 3.1.2), while retaining the "phasic" cellular responses prized by Llinás. The latter are, after all, a fact of cerebellar physiology. However, those responses could merely be the opening shot in the slow spatial patterning process by which lateral inhibition among anterior lobe compartments creates the structural prescriptions for muscle linkages. It has been shown rather

*Marchesi, G.F., Strata, P., "Mossy and climbing fiber activity during phasic and tonic phenomena of sleep," Pflügers Arch. 323, 219-240 (1971).

**Llinás, R., "Neuronal operations in cerebellar transactions," in Schmitt, F.O. (ed.), The Neurosciences: Second Study Program, Rockefeller U. (New York, 1970), pp. 409-426.

graphically elsewhere[22] just how difficult it would be to see such slow processes in conventional single-unit records. They may well be much more easily demonstrated directly in the behavior of the mesencephalic cat (section 4.2).

b. The structural prescriptions generated by the spino-olivocerebellar system are constrained in parallel with constraints on gait. According to the findings of section 3.2, climbing fiber activity in the "locomotor" anterior lobe should be found to be localized to certain "lattices" of coactive Oscarsson strips. Only two such lattices exist on each side of the midline, and which of the two is active on a given side should prove to be a function of the current hindlimb-forelimb gait coupling (rack or trot) on that side. The result of these constraints is that only three basic lattice activity patterns will ever appear in the complete anterior lobe during locomotion (figures 4-6; section 3.2): Two patterns are symmetric and correspond, respectively, to the walk/trot and to the rack. The third, asymmetrical pattern (made up of a trot lattice in one half of the anterior lobe and a rack lattice in the other) appears in the gallops. Each of these lattices sets up a different set of structural prescriptions for the muscle linkages executing locomotion, of course, so one is led directly to the more general conclusion that the spino-olivocerebellar system constitutes an "act-specific, 'postural' mechanism (section 4.1.1) through whose intervention an animal's carriage is tuned optimally for the gait it is executing. It is also easy to deduce from these results that a primary source of ascending spino-olivary signals must be the propriospinal system (section 3.3.2). Many of the peripheral

inputs known to activate climbing fibers, particularly those from the FRA and the skin, may do so because they also collaterally affect the intrinsic propriospinal circuits (indeed, the olivocerebellar system could likely function on "internal" information alone).

If these ideas are correct, then one should be able to observe experimentally that the structure of muscle usage varies according to the hindlimb-forelimb coupling adopted by a locomoting cat (and not, incidentally, according to the couplings of opposed limbs). What might those structural changes look like? Or in other words, what are the structural prescriptions represented by figures 4-6? Unfortunately, it is not easy to answer that question, because the structural effects of the different descending spinal pathways receiving from the anterior lobe are not well known (but could be readily ascertained; section 4.1.2). The author suspects that proximal (and axial) versus distal muscle dominance may be one of those structural quantities determined by the currently active anterior lobe lattice: If, for example, the rack is a more "precise" gait than is the trot, as was weakly argued in section 3.2, then it may be that the d-e_2 "rack" lattice shown in figure 5 shifts EMG activity distally relative to the effects of the e_1-f lattice (figure 4). But it may also be true that the structural alterations of locomotion entail changes in the balance between adductors and abductors (resulting in wide- or narrow-based gaits) or in the rostrocaudal distribution of muscle contraction (positioning the center of mass). In addition, it should be remembered that locomotor structure, while constrained according to the climbing fiber latticework, is still continuously tunable through changes in the synchrony within, and burst frequency of, the microstrips constituting the

lattices (section 3.3.4).

The inability to predict how structures should be assigned to hindlimb-forelimb couplings in no way inhibits experimental test of the proposition, as hinted above. And this is just as well, for the idea that anterior lobe computation is subject to the severe restrictions derived here is probably not one friendly to the intuition of most investigators (cf. section 3.2). The proper way to think of these restrictions, however, is not in terms of the degree of paralysis a cat must suffer in order to accommodate the cerebellum presented in this report. Rather, one must think in terms of how to rein in 800 or more muscles so that they are a cat.

c. The olivocerebellar system treats locomotor movement sequences holistically. When one first begins considering how central structures such as the cerebellum might modulate motor performances, it is natural to assume that such modulation is delivered exclusively on a movement-by-movement basis. Thus, in the locomotor situation, one might expect the anterior lobe to deal with each flexion or extension of the step cycle at the time it is spinally generated, while remaining oblivious to either past or upcoming cycles. This assumption is very much part of the popular belief in the cerebellum as a high-speed "computer" of movement[47,48,49,54]. It is also inherent in the standard laboratory practice of seeking correlations between discharges in single cerebellar units and motor events immediately preceding or following those discharges; and of course, such correlations do exist (provided one is not studying climbing fibers!). So far as it goes, then, the movement-by-movement hypothesis

is reasonable.

The problem is that the hypothesis may not go quite far enough: Recall once again that two time courses likely characterize physiological transactions in the anterior lobe. It is the "fast", metrical prescription process, governing the overall amplitude of linkage EMG's, that is usually seen with the single microelectrode. On the other hand, according to the present findings, the structural prescriptions of those linkages will remain as quasi-invariant spatial patterns of anterior lobe compartmental activity for periods of several step cycles. Indeed, the prescriptions for every movement constituting the current locomotor act must coexist in this activity, even if some of those movements are not under execution (a result entirely compatible with the existence of "spinal switching"; section 2.3.4). The complete locomotor movement sequence in time thus has a structural representation in space--the cerebellar cortical space demarcated into Oscarsson strips. Thus, by activating different strip lattices, each of which deals with flexions and extensions in both hind- and forelimbs (one strip apiece), spino-olivocerebellar signals can manipulate the locomotor sequence as a whole. In fact, this would be true even if volleys occurred only in single strips (instead of lattices) by virtue of the lateral inhibitory interactions between compartments.

It is not too far-fetched to say that the activation of a climbing fiber lattice creates for the anterior lobe an "image" or "plan" of the complete motor behavior produced by the intrinsic spinal locomotor circuits to which the lattice is related. Out of this image emerge the possibilities for next-cycle modulation and the feed-forward utilization of present information to tune future movement (section 2.4). Actually,

these properties are incipient in the "reversible" reflexes and like responses of the spinal animal (section 2.3.4), all of which seem to represent a generalization of certain stimuli to the end of tuning the entire step cycle rather than its individual epochs. It is fitting that some of the same stimuli might form a major peripheral input to the olivocerebellar apparatus (section 3.3.2). There is something of a paradox in how the climbing fiber system can at once "lag behind" ongoing movement physiologically--and yet at the same time be far ahead of that movement. But such may be the idiosyncrasy of any motor mechanism which follows a schedule of acts, rather than of pieces of action.

Another significant peculiarity of the climbing fiber "image" of performance is that the times things are to happen--in particular, the serial order of locomotor flexions and extensions--have no representation (section 3.2.2). All gaits sharing the same hindlimb-forelimb coupling constraints are equivalent from the viewpoint of an Oscarsson strip lattice, regardless of the temporal permutations of the constituent movements. In specifying the structure for linkages executing each of these movements, then, the olivocerebellar system is actually defining quasi-invariant relationships among the movements, independently of their sequencing. It is saying, for example, that a certain kind of forelimb flexion requires a complementing extension whenever either might occur--and indeed, that a certain style of forelimb stepping must be answered with appropriate hindlimb actions. But one recognizes in this situation a most interesting analogy with the muscle linkage itself, in that the "relationships" among linked muscles--i.e., their EMG ratios or structural

prescription--are also quasi-invariantly defined independently of when they contract (section 4.1.2). Putting the analogy more formally:

> Locomotor acts are programmed as linkages of movements, or linkages of muscle linkages. The "structure" of an act-linkage defines the relationships among its movements and is programmed by a lattice of Oscarsson strips. Timing "slots" for its movements (analogous to those of muscle EMG bursts) are specified by spinal stepping circuitry. The "metrical prescription" for the act-linkage can probably be identified with its energy output. For locomotion, this is governed by the noradrenergic executive.

Now whether the linkage "operator" can be applied once again to yield linkages of acts is moot (and probably irrelevant to the anterior lobe). But the process has gone far enough to allow some telling insights into how complex movements might be represented at higher levels of the brain in terms of an "image" of the relations between their components. It was to such an image, and its evolution into actual movement through the supplying of metrical and timing prescriptions, to which Bernstein was referring when he wrote (more than thirty years ago), "movements are not chains of details but structures which are differentiated into details"[16] (emphasis his). The relational concept will be mentioned once again briefly in section 5; it is discussed at greater length elsewhere[23].

d. The control of locomotion is arranged hierarchically. A hierarchical control system emerges when mechanisms attempting to control a process directly are themselves controlled by fewer parameters than

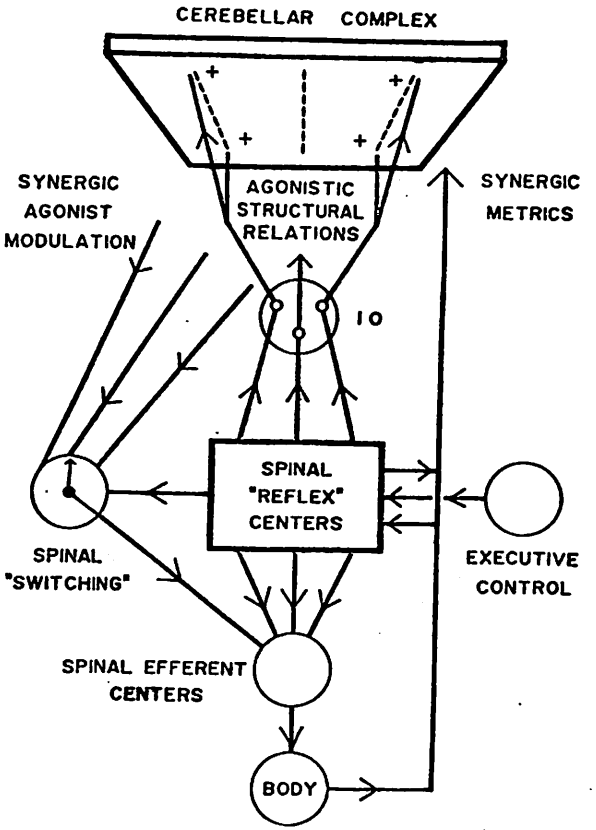

FIGURE 11

Synopsis of the locomotor control hierarchy. Details in text.

described the original process. Consequently, despited its hackneyed connotations, the term "hierarchy" arises quite naturally from both the muscle linkage paradigm and the phenomena surrounding mesencephalic locomotion.

A schematic sketch of the locomotor hierarchy is given in figure 11: As can be seen, the diagram is somewhat distorted in an effort to preserve anatomical relationships which are not at all reflective of the flow of control. Thus, at the very top of the control hierarchy (but not of the figure), one finds the noradrenergic executive of the brainstem (section 2.2). But the next lower level, which the executive activates with a single signal, is at the very bottom of the anatomical setup--in the spinal "reflex" circuits that hold the intrinsic locomotor algorithm:

The operation of the intrinsic spinal networks will no doubt prove to be a good deal more complex than almost anything that happens in the cerebellum. Aside from providing plans for the locomotor sequence to the spinal efferent centers (motoneuron pools) and gating, via spinal "switching", the influences of supraspinal areas into those centers, the spinal circuitry must decide on the gait to adopt. The decision-making process might entail competition among circuits programming different gaits, as was suggested in a general way some time ago by Pyatetskii-Shapiro and Shik* (see also section 2.1.3). If the somatotopy of the anterior lobe Oscarsson strip lattices is any indication, such competition may be typified by a dominance struggle between circuitry of the hindlimbs (which "advocate" the trot) and the forelimbs (rack; see section 3.3.2). But the present work has indicated that decision-making could

*Pyatetskii-Shapiro, I.I., Shik, M.L., "Spinal regulation of movement," Biophysics 9, 525-530 (1964).

also involve elements of "feature detection", wherein spinal circuits identify the proprioceptive or cutaneous aftermath of their own activation (section 3.3.3). In any event, the results of the spinal decision are transmitted to the inferior olive ("IO" in figure 11) and thence to a particular lattice of Oscarsson climbing fiber strips. The result is the appropriate structure for the locomotor agonist linkages (or for the locomotor act-linkage itself; see previous subsection). For completeness in figure 11, a pathway contributing to the anterior lobe computation of metrical prescriptions is also shown. Actually, there are many such pathways, all part of the mossy fiber system; these will be mentioned in section 5.

Except for the entry point of the simple noradrenergic executive command, the mesencephalic locomotor control hierarchy is a closed system, with the spino-olivocerebellar apparatus supplying part of that closure (figure 11). The author has resisted the impulse, so common in other theories, to ship off various inexplicable functions to "higher centers." Here is hoping that the results of the experiments proposed in the next section will not make him wish he had.

In summary:

Most fundamental of this report's results is that the spino-olivocerebellar system tunes the structure of locomotor muscle linkages. The conclusion differs markedly from the idea that climbing fiber function is identifiable with the immediate responses of cerebellar units to climbing fiber volleys (the "phasic operator" hypothesis). Suitable experiments might help resolve the issue.

A second concept introduced here is that the anterior lobe's computations of structural prescriptions are constrained in parallel with the spinal constraints on limb coordination. In particular, each of the two homolateral hindlimb-forelimb couplings will be assigned a structure (modulo some degree of continuous tuning) through the activation of its "own" lattice of Oscarsson strips. At present, the assignment of structures to couplings cannot be predicted, but the proposition that such an assignment is meaningful is more fodder for the laboratory.

The existence of climbing fiber lattices, coupled with the quasi-invariance of the structural prescriptions they establish, leads to a third proposition--that the olivocerebellar system manipulates the locomotor movement sequence as a complete entity. Climbing fiber activity may actually be envisioned to establish an "image" of the spinally generated performance, thereby fostering the faculty of using feedback from present action to tune future movement (next-cycle modulation). However, the climbing fiber image contains information only about the relationships between locomotor movements, independently of the timing of those movements. Hence, a locomotor act is itself organized like a linkage wherein "movements" have replaced muscles, and whose structure is prescribed by a climbing fiber lattice.

Lastly, the locomotor control system in the mesencephalic cat is a hierarchy closed except for the entry point of the noradrenergic executive. The anatomical arrangement, though, neither reflects the flow of control through the hierarchy, nor the complexity of computation at each of its levels.

4.2 Methods for Experimental Test

4.2.1 General Remarks

The experiments outlined in this section by no means exhaust the issues raised in this report. Instead, they are intended only to illustrate that most of the results here can indeed be taken into the laboratory without further ado. Consequently, it has been decided to give but one protocol in detail, leaving the remainder as sketches. That one detailed study, however, is meant to be a "crucial experiment," in the sense that if the results are not qualitatively as predicted, the present theory should probably be discarded (although it might be interesting to figure out what went wrong).

All experiments are designed to be performed in the mesencephalic cat receiving locomotor region stimulation in the usual fashion (section 2.2.1). In a previous study[22], it was suggested that administration of noradrenergic potentiators might substitute for the electrical stimulus, but this has proved infeasible (the cats will not walk; Zajac, personal communication). Other physiological cautions have been delivered elsewhere[22].

4.2.2 Critical Experiment: Does the Olivocerebellar System Tune the Structure of Locomotor Muscle Linkages?

Whether or not one seriously entertains any of the conclusions presented here, the subtlety of the climbing fiber's influence upon movement is undeniable. It is likely, therefore, that the most rapid progress

in discovering its function will be made by direct interference of some sort with the olivocerebellar system. The historical problem with this approach has been how to control the "interference" sufficiently so that the effects can be unambiguously interpreted: Mettler[154,167] attempted to lesion the inferior olive in cats and monkeys and claimed that no deficits were produced that could not be laid to damage of surrounding structures; however, that damage was so extensive and the deficit sufficiently severe that the olivary contribution to the latter might not have been distinguishable. Somewhat more careful lesion work in cats has been done by Wilson and Magoun[225] and by Murphy and O'Leary[163]. In both studies deficits appeared which resembled those following cerebellectomy, only less severe. Very recently, Llinás and colleagues* have perfected a very exciting biochemical technique that, in rats, apparently kills all inferior olivary neurons exclusively. The locomotor result is an animal which "mud-walks," to use the authors' phrase--progression is slow, and biased toward hyperflexion. This elegant demonstration does at least indicate that the olive has a role to play in locomotion; but there is some question as to whether lesion studies can offer the control necessary to the examination of the present theory.

Stimulation of the climbing fiber system, although rarely tried in behaving animals until just recently (cf. ref. 185), seems to offer much better chances of refinement: Thus, Armstrong (personal communication) has been able to activate discrete anterior lobe Oscarsson strips from the olive in acute cats. Barmack (in press; see Appendix) has achieved a

*Llinás, R., Walton, K., Hillman, D.E., Sotelo, C., "Inferior olive: Its role in motor learning," Science 190, 1230-1231 (1975).

similar result in the awake rabbit flocculus using microstimulating pulse trains (see below). It thus seems feasible to attempt the activation of individual Oscarsson strip lattices in the mesencephalic cat, and to examine the effects of that activity upon locomotor muscle structure in the following way:

The present study predicts that climbing fiber volleys in a particular Oscarsson strip lattice of the anterior lobe will produce prolonged (seconds-long) alterations in the EMG ratios among the muscles of locomotor linkages. Suppose, then, that one considers a particular lattice, say, the "rack" lattice of figures 5 (section 3.2) and 8B (section 3.3.2), and a particular linkage--the linkage of hindlimb flexors. Now according to the chart of compartmental muscle influences in figure 3 (section 3.2), when the "rack" lattice is activated, the flexor linkage will be facilitated primarily by the red nucleus, while the reticulospinal flexor pathway will be disfacilitated. Supposing for the sake of argument that the reticulospinal system has a largely "proximal" structural bias, and the rubrospinal a distal, then the EMG effect of rack lattice activation should be to produce an extended shift of EMG activity into the more distal flexors as the cat walks. Perhaps the animal may "prance." Thus, to examine this experimentally, one would locate the inferior olivary region projecting into the lattice, and stimulate there while observing the EMG picture and, possibly, cellular responses in the cerebellar or brainstem nuclei.

Speaking more practically, the olivary area innervating the "rack" lattice could be located by antidromic field potentials (i.e., by stimulating, say, a zone of strip d), and the stimulus would be the brief,

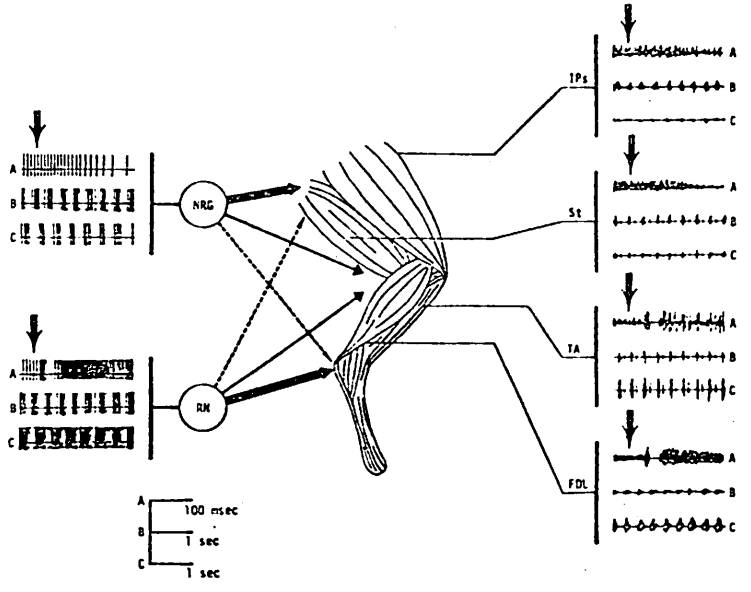

FIGURE 12

Simulated data from a proposed experiment involving stimulation of the inferior olive in the mesencephalic cat. Experiment examines structural changes evoked in a hindlimb flexor linkage and in ratios of activity in descending spinal pathways caused by activating a particular Oscarsson strip lattice. EMG's on right (Abbreviations: IP = iliopsoas; St = semitendinosus; TA = tibialis anterior; FDL = flexor digitorum longus). Nuclear unit discharges on left (Abbreviations: NRG = nucleus reticularis gigantocellularis; RN = red nucleus). Heaviness of arrow to muscle denotes degree of structural "emphasis" of nucleus on that muscle. For protocol and explanation of traces, see text.

high-frequency, low current pulse train found effective by Barmack (above). The experiment would probably be carried out in two stages, as illustrated by figure 12: Here one sees a cat hindlimb (center), "fake" EMG records from four muscles of its flexor linkage on the right, and equally "fake" single unit (extracellular) records from the red (RN) and reticularis gigantocellularis (NRG) nuclei on the left. Heavy and light arrows from the nuclei to the muscles indicate hypothetical nuclear structural affinities. Traces A in all records portray the result of a stage 1, "acute" experiment in a non-locomoting mesencephalic cat. What has been done is to stimulate the cuneiform locomotor region and then to extend the cat's hindlimb until a goodly level of reflex tonic contraction has developed in the flexors. The limb is then fixed and the olivary stimulus given at the arrow in all records. Looking first at the single-unit responses, it can be seen that the RN and NRG units have initially been firing at approximately the same frequency, but that the olivary stimulus results in the RN becoming dominant over the NRG. Reflecting this, the structure of the flexor linkage is altered from a more or less even tempered distribution of EMG over the muscles to a distinctly distal bias. Incidentally, the mechanism of the burst-silence-rebound, initial response of the RN and associated muscles to the olivary stimulus is covered in another report[22].

Stage 2 of the above experiment finds the cat walking on a treadmill. Traces B in the EMG and single-unit records illustrate what might be the typical locomotor picture--bursts of a certain amplitude in synchrony with step cycles--the situation before any olivary shock is given. If, however, the identical stimulus given in traces A is now delivered

to the cat, then a short period after the stimulus the new motor pattern is shown by traces C. One can see, at least qualitatively, that it is the ratio of both contractions and cellular activities which is altered to produce the nominally "prancing" cat. Comparison of traces B and C also provides a good illustration of the difference between the rapidly changing metrical prescription for this linkage (seen especially in the stepping bursts of the neurons) and the very much more static structural prescription inherent in the activity ratios.

Now, as has been mentioned earlier (section 4.1.3), the exact structural alterations produced by activating the "rack" lattice may not correspond to the picture of figure 12; these cannot be predicted. However, the figure should provide some intuition as to what to look for. And of course, should the experiment actually be done, a number of controls (e.g., sectioning of the restiform body to interrupt climbing fibers) would be performed to ensure that any effects really are due to the olivocerebellar system. It may also be possible to do this experiment using a biochemical stimulus, which eliminates some rather obvious sources of artifact (and substitutes others). It is well known that the olivocerebellar system is susceptible to a number of drugs (e.g., refs. 42, 123, 124, 129, 130, 141).

4.2.3 Other Experiments

The experiment of the previous section, or one similar to it, is at present the most important to the theory here. Still, there are a few others which deserve mentioning and which will now be sketched out

briefly below:

a. A test of the correlation between climbing fiber activity and muscle structure by direct observation of climbing fibers. If one attempts to correlate individual climbing fiber responses with individual locomotor movements, then it is almost certain that no sure relationship will be found--as, in fact, appears to be the case (McElligott, personal communication). Individual movements are not the concern of the olivocerebellar system. Instead, however, suppose one were to assume that the climbing fiber/structural prescription relationship exists. The the correlations one should be seeking would be between integrated EMG ratios over successive step cycles and the long time-course processes triggered by climbing fiber activity in the cerebellum. This suggests that one do an experiment in the mesencephalic cat (or an intact animal) wherein Purkinje climbing fiber responses (cfr's) are recorded during locomotion. But rather than these cfr's going into a peri-movement histogram, as is usually done, they instead would be convolved with a decaying exponential function which ostensibly mimics the slowly varying ratios of anterior lobe compartmental activity. This convolution would then be compared with variations over time in locomotor linkage structure computed from the EMG. After a number of time constants have been tried with the same data, an interesting matchup might suddenly appear. It could also be mentioned that the compartmental activity patterns ostensibly created by the olivocerebellar system during locomotion might be visualized using several fairly new techniques for assessing RNA turnover[110] or metabolic demand[115, 193] of cerebellar units.

b. A test of the connection between certain anterior lobe strip lattices and the operation of the propriospinal system. This admittedly would be a difficult demonstration to attempt. One would start by examining locomotor muscle structure as a function of homolateral hindlimb-forelimb coupling, versus structure as a function of paired limb coupling. The former should show the stronger correlation. After this, one would wish either to intervene in the propriospinal system (perhaps by stimulating propriospinal tracts and recording evoked cfr distributions in acute cats) or to go directly to an anatomical study. Certainly the lattice organization of the olivocerebellar projection is itself an intriguing subject for further scrutiny.

c. A test of the "ambiguity principle." It will be recalled from section 3.3.3 that the "ambiguity principle" relates the number of Oscarsson strips activated by a peripheral stimulus to the muscle linkage "ambiguity" of that stimulus--that is, the degree to which the stimulus can be interpreted as having arisen from the contraction of a single linkage. The more ambiguous the stimulus, the more strips aroused. Now not all stimuli are expected to obey the principle. But the results of Murphy[162,163] (see section 3.3.1) suggest that muscle proprioceptive information might, in that the stretch of a single muscles in an awake, paralyzed cat results in "diffuse," rather than striplike, anterior lobe climbing fiber activity. The obvious test of the ambiguity principle, then, is to repeat Murphy's experiment--but to stretch a number of muscles in a linkage <u>simultaneously</u>. This combined afference is unambiguous and should, therefore, lead to a resolution of the diffuse, single-muscle

response into a single strip (or strip lattice). Any sudden focussing could be quite dramatic; and it would provide a first hint that intrinsic spinal networks could serve as somatosensory feature detectors as well as producers of movement.

The above proposals seem to represent an adequate sampling of the experimental possibilities indicated by the present work; and they only touch a few highlights. Buried in the text are quite a few other nuggets to be assayed. Hopefully, however, the one "critical" experiment outlined above will be tackled soon. Its results, in large measure, will determine the merit of others set forth here.

5. Conclusion: Implications of the Climbing Fiber Theory for the Function of Mossy Fiber Systems, and for the Higher Order Mechanisms of Motor Control

From the specific results of this report has evolved the more general theme that the spino-olivocerebellar system is a mechanism for "holding together" a motor act--for developing cohesion between the separate pieces of a performance however they might be dispersed in time. It does this by defining quasi-invariant relationships among those pieces; relationships as simple as the ratios of integrated EMG among linked muscles, or as complex as the complementing of step cycle epochs among limbs. In this cohesion, one can now catch a glimpse, perhaps, of that elusive faculty known as cerebellar motor coordination.

The coordination the climbing fiber brings to movement issues from the "image" of a performance created in the anterior lobe by climbing

fiber activity. This image is a very real thing, an encoding of movement structure in ratios of activity among different anterior lobe compartments. To conclude this report, it seems fitting to examine very briefly the implications of the olivocerebellar movement image for the other great cerebellar afferent system--the mossy fibers--and also for concepts of how "voluntary" movement is organized at cerebral levels. Of necessity, the discussion will be very speculative. It will also be very informal, with references supplied only where critical. The material is treated in much greater rigor in other studies (ref. 23; Boylls, in preparation).

5.1 Mossy Fiber Contributions to Locomotion

Lateral recurrent inhibition among cerebellar (or vestibular) nuclear regions appears to embody one of the most basic, intrinsic computations of the anterior lobe (referring, of course, only to the mediolateral plane). As mentioned in section 4.1.2, the prolonged physiological effects of climbing fiber volleys stem from their spatial restriction. They excite the lateral inhibition system optimally and so take advantage of its inherent regenerative properties.

Recently, a preliminary theoretical analysis (Boylls, in preparation) has been done of anterior lobe responses to the more diffuse inputs characteristic of certain mossy fiber systems (see below). As it happens, the anterior lobe's spatial dimension is irrelevant to such inputs. The cerebellar complex can be reduced to a simple "lumped" circuit involving single cerebellar nuclear, pre-cerebellar reticular, and Purkinje cells which together can be shown to make up a differentiating network of sorts

(incoming inputs excite the nuclei, but that excitation is quickly checked by Purkinje inhibition; see also similar comments by Thach[213]). In other words, the cerebellar nuclear output to a diffuse input will be quite "phasic." This, incidentally, is independent of how the input enters the cerebellar complex (to a first approximation). Such phasic responses have in fact been elicited in cat interpositus neurons by muscle stretch signals arriving on one of the more diffuse mossy fiber systems[136,137].

Now recall that the structural prescriptions of locomotor muscle linkages are tuned by spatial patterns of anterior lobe compartmental activity, while metrical prescriptions depend only upon the overall level of that activity. This, and the observations above, suggest the following conjecture:

> The time course of anterior lobe responses to afferent inputs differs as a function of their spatial extent. Inputs restricted to single compartments contribute to the prolonged, spatially patterned outputs governing muscle linkage structure. However, multi-compartment, "diffuse" inputs quickly alter overall compartmental activity levels, permitting rapid changes in the metrics of linkage contraction.

The above proposition is only that; it requires considerably more investigation. But if it proves to be roughly correct, then one can draw some interesting inferences about the movement contributions of different mossy fiber systems:

There are two broad categories of ascending mossy fiber pathways, based upon sources of input and cerebellar termination geometry: The

"intrinsic" pathways, typified by the spino-reticulocerebellar (SRCT), ventral spinocerebellar (VSCT), and rostral spinocerebellar (RSCT) tracts, appear fundamentally to report upon spinal interneuronal events--notably those in spinal stepping circuits (cf. refs. 9, 10, 11). Their axons appear to branch widely within the anterior lobe to terminate in a number of compartments. By contrast, the "peripheral" mossy fiber pathways, the dorsal spinocerebellar (DSCT) and cuneocerebellar (CCT) tracts, transmit peripheral information almost exclusively and have very punctate (single compartment) terminal zones. From this information alone, and the conjecture above, one is led immediately to the hypothesis below:

> The metrical prescriptions for locomotor linkage contractions are determined primarily by the "intrinsic" mossy fiber pathways (VSCT, RSCT, SRCT) and ultimately by the spinal stepping circuitry itself (along with the inputs affecting that circuitry). On the other hand, fine tuning of linkage structure is provided by the purely extrinsic signals arriving in the "peripheral" mossy tracts (DSCT, CCT).

In other words, via the VSCT, RSCT, and SRCT the spinal locomotor circuits may be developing a feed-forward, speedup signal in the anterior lobe in order to foster the more prompt contraction of the muscles they control. The actions of the DSCT and CCT, however, may somewhat parallel those of the climbing fibers in providing next-cycle modulation of muscle structure. Thus, if a locomoting cat should, say, encounter an obstacle while flexing a limb, the "intrinsic" mossy systems will probably cause

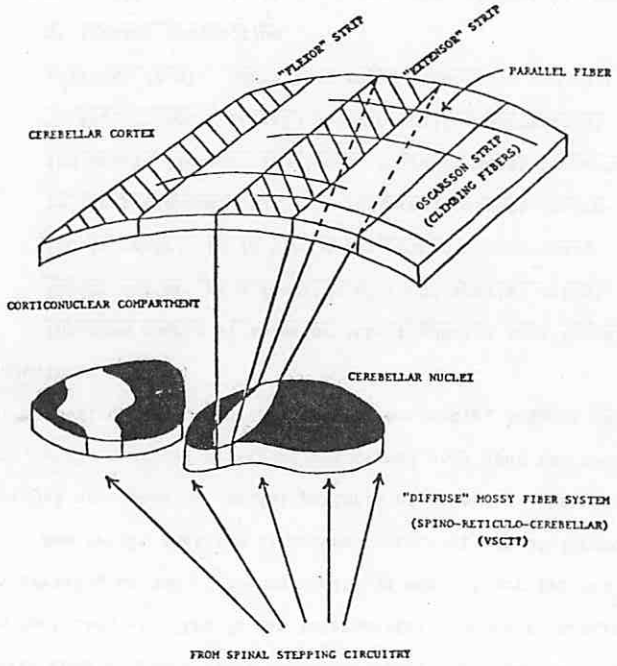

FIGURE 13

Interaction between the cerebellar structural "image" of a locomotor act and information from the diffuse, "intrinsic" mossy fiber system. The active Oscarsson strip lattice (stripes) has created the image as a pattern of excited (light) and inhibited (dark) nuclear regions in different compartments. The mossy activity is preferentially routed into the excited regions. Thus, the linkage metrical prescription it represents is weighted by movement structure before entering the musculature. See text.

the anterior lobe to deliver an immediate multiplication of all forces in the flexor linkage so as to carry the limb over the obstacle. But at the same time, the "peripheral" systems will alter somewhat the structure of flexion so that, perhaps, the cat increases its distal flexion for the next few steps.

Of course, all of the above transactions are designed to take place within the context of an already-existing spatial pattern of compartmental activity created by the olivocerebellar apparatus--the structural "image" of the locomotor act. Figure 13 attempts to convey how that image might interact with incoming mossy fiber inputs: Here one can see an active climbing fiber lattice (stripes) which has disinhibited cerebellar nuclear regions in its own compartments. Other regions are inhibited by lateral inhibition. When diffuse mossy fiber excitation from the "intrinsic" pathways encounters the nuclear activity pattern, it is fairly obvious that it will pass more freely through the excited areas than the inhibited; or in other words, the pattern functions as a "sieve" of the diffuse mossy fiber signals, steering their facilitation into certain nuclear regions (and descending pathways) at the expense of others. Since the nuclear activity pattern or image defines the structure of the locomotor act, it follows that what occurs in the anterior lobe is the weighting of the diffuse mossy fiber metrical prescription by the structure of the muscle linkages into which it is to flow. "Peripheral" mossy inputs, not shown in figure 13, affect this process by introducing small changes into the cerebellar "sieve."

One should now have a fairly good idea of how the anterior lobe's image of the locomotor act, provided by the olivocerebellar system, could

serve to unify the disparate movements called forth by the spinal stepping circuitry. The last question to be raised here is whether such an image can be identified in "volitional" movement.

To summarize:

Preliminary results indicate that the time course of anterior lobe responses to inputs of any sort is inversely proportional to the spatial extent of the input. With respect to the mossy fiber systems, then, it would seem that the diffuse, "intrinsic" pathways (VSCT, RSCT, SRCT) cause the anterior lobe to generate feed-forward, metrical facilitation of locomotor linkage contractions based upon the output of the spinal stepping generators. The much more punctate, "peripheral" mossy tracts (DSCT, CCT), on the other hand, allow external cues to make small, but prolonged adjustments in the structure of those linkages. Naturally, both sets of mossy systems function within the compartmental activity "image" of the locomotor act created by the olivocerebellar apparatus.

5.2 Climbing Fibers and the Central Representation of "Voluntary" Motor Performances

The conscious planning of volitional movement, and the perception of its sensory consequences, would both appear to lie well outside the domain of the anterior lobe climbing fiber system; and that is probably correct. Still, the present analysis of the system suggests that the cerebellum engages in rudimentary forms of both "planning" and "perceiving" in coordinating locomotion. A quick look at how it does this might suggest a few new ways to view the much more advanced processes of the

cerebrum:

a. The anterior lobe's "plan" for a locomotor act is a set of time-independent relationships among its components. Activity in a lattice of Oscarsson strips creates a structural prescription for an act-linkage in the anterior lobe--a set of freely permutable movements having quasi-invariant "relationships" among themselves (section 4.1.3). These relationships, of course, are defined in terms of comparisons between the structural prescriptions of the muscle linkages executing the movements.

Interestingly enough, many years ago Bernstein[16] proposed that the central representation of voluntary movement was "topological", i.e., written in terms of how motor elements are arranged relative to each other, rather than relative to an absolute coordinate system. Bernstein's idea is obviously captured in the lattice; and in fact, so also is a corollary--the notion that there exists a representation of movement which is independent of the musculature used to execute it: The climbing fiber lattice defines flexions or extensions for all limbs, so that one can say that the lattice represents a style of "absolute" flexion or extension executable by any limb. One can indeed define the idea of an act without ever speaking about which of the many muscular machines might carry it out.

To actually execute a movement, however, requires that a machine be selected. In the locomotor situation, the selectional process is bound up in the spinal creation of timing "slots" for EMG's and movements themselves. Is there such a separation of selection-timing from an action plan in voluntary movement? Is the selectional process itself represented relationally? One could in some sense say that a spinal locomotor generator

represents a temporal relationship between motor events, but this seems unsatisfactory. For now, the central representation of selection/timing must remain a mystery (for further observations, consult refs. 191, 204).

b. The anterior lobe "perceives" its inputs in terms of the performance it has planned. How the anterior lobe interprets a mossy fiber input--that is, the response it produces following the input--is very much a function of the compartmental activity state left by volleys in climbing fibers. A change of climbing fiber lattice activity results in a complete rerouting of a fixed mossy fiber signal into a different set of descending pathways and muscle groups (section 5.1). Thus, one could say that the image of movement created by the olivocerebellar system operates in a way analogous to the hypothetical "body image" supposedly resident in such centers as the parietal cortex: Both images represent perceptual frameworks within which to interpret sensory data.

In this regard, it is worth noting the theoretical correlation between activation of Oscarsson-strip lattices and the arousal of spinal "reflex" centers, notably the propriospinal mechanisms: The body image of the anterior lobe is constructed from but a few recipes tied to the hard-wired movement producing machinery of the cord, and all perceptions are related to this handful of reflexive reference points. Several years ago, Melzack and colleagues[94,153] conducted a series of intriguing experiments on the perception of human arm position in cases of "phantom limb" versus the normal situation. The phantom limb is a phenomenon which appears following amputation where, in a nutshell, the amputee continues to feel the lost arm and to perceive it in a certain position. By means

of brachial plexus blocks, Melzack[153] was able to induce the same state in intact subjects. Rather surprisingly, he found that the great majority of phantom limbs were perceived in only one of two positions--either in a state of flexion-adduction or extension-abduction. Saltatory jumps between these two positions were also noted, over which the subjects had no control. Having noted these findings, Melzack[94] conducted another study in which normal, unanesthetized subjects were asked to plot the perceived position of one of their arms which rested, without moving, out of their view (under an opaque shield directly in front of them). Upon first placing the arm in this position, the subjects' perception of it was quite accurate. However, with the passage of time, the arm was felt to "migrate" until it achieved one of the two positions found in the phantom limb situation. This most interesting experimental series does suggest that not only is the central body image organized in terms of a few "standard positions, but also that those positions are related to the endpoints of movements produced by classical spinal reflexes.

On this hypothesis (which is explored in greater depth elsewhere[23]), the present report is concluded. It has been a considerable odyssey, if not oddity, to have sailed from problems of Purkinje cells[22] to vistas of volition. Perhaps, then, it is time for a brief pause in activity.

In summary:

The anterior lobe alters its interpretation of mossy fiber inputs according to the "body image" supplied it by the olivocerebellar system. Of course, the latter is intimately related to the production of a

handful of spinally generated movements. It comes as some surprise, then, to find that the conscious body image may well be organized along similar lines.

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APPENDIX

THE PHYSIOLOGICAL FUNCTION OF THE CLIMBING FIBER ASSESSED BY MEANS OF THE VESTIBULO-OCULAR REFLEX*

A.1 Introduction

The preceding theory of climbing fiber operation during locomotion rests heavily upon the following two physiological "axioms": (a) Climbing fiber volleys must act to accentuate cerebellar nuclear excitation within corticonuclear compartments controlled by active Oscarsson strips, at the expense of excitation in neighboring compartments; and (b) such compartmental excitation distributions must persist for significant periods of time. These axioms have been derived from a model[5**] which attempted to adhere to known anatomical and physiological parameters of the anterior lobe complex and its climbing fibers. Nonetheless, one would still like some independent means, preferably experimental, for determining whether the axioms are "in the ballpark." Such information may well be available in studies of the vestibulo-ocular reflex (VOR) in rabbits, and the purpose of this Appendix is in part to present some of the relevant data and the deductions therefrom (section A.2). Thus far, the evidence bears only upon the "nuclear excitation" portion of axiom (a); but some additional ways to use the

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*The author is especially indebted to Dr. N. H. Barmack for thoughtful discussion of this material and for permission to cite unpublished data.

**Note that this appendix has its own set of references.

VOR to examine other features of both axioms will be proposed (section A.3). All discussion here is very much intended to be informal--a thorough review of the VOR literature is well beyond either the scope or needs of the present report.

A.2 Facilitation of the Vestibular Nuclei Through the Action of Climbing Fibers

The primary purpose of the VOR appears to be the stabilization of the eyes' fixation point against any movements of the head[3,25]. In the rabbit, Ito[15,16,18] has painstakingly worked out a portion of the circuitry controlling the VOR in the horizontal plane, with special emphasis upon the role of the cerebellar flocculus (a sector of cortex in the extreme posterior region of the cerebellum). His VOR circuit diagram, for the structures modulated by the left flocculus (complementary circuitry exists for the right flocculus, of course), is illustrated in figure A (adapted from ref. 16): The figure represents excitatory influences among the various components by white bold arrows and inhibitory by black (ignore momentarily the small arrows to and from the "IO"). The VOR is expressed in movements of the two eyes (circles with black "pupils") which are separated by the midline (M). Each eye is pulled towards M by a medial rectus (MR) muscle and away from M by a lateral rectus (LR). The muscles receive innervation from the oculomotor and abducens nuclei, respectively (not shown), which in turn are innervated by certain vestibular nuclei. A portion of the medial vestibular nucleus (MV) acts to excite the ipsilateral MR and the contralateral LR. Consequently, when excited MV will pull the

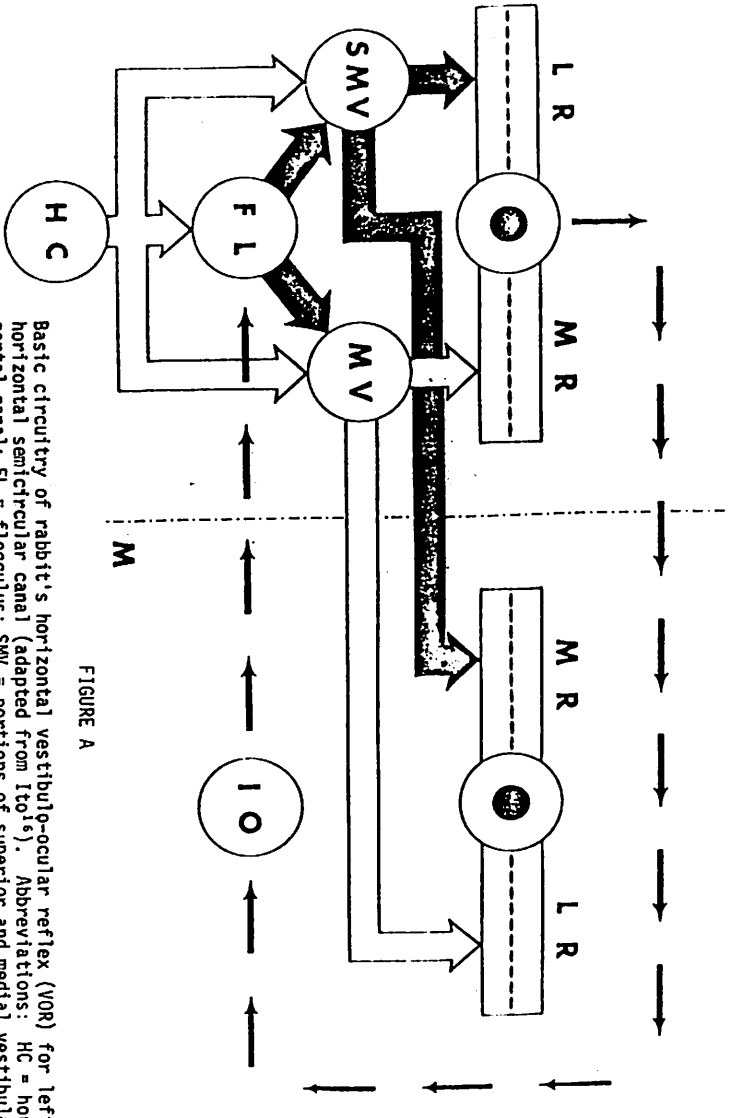

FIGURE A

Basic circuitry of rabbit's horizontal vestibulo-ocular reflex (VOR) for left horizontal semicircular canal (adapted from Ito[16]). Abbreviations: HC = horizontal canal; FL = flocculus; SMV = portions of superior and medial vestibular nuclei; MV = other portions of medial vestibular nucleus; LR = lateral rectus muscle; MR = medial rectus muscle; IO = inferior olive (dorsal cap region); M = midline. Thick black and white lines denote inhibitory and excitatory pathways, respectively. Broken arrows indicate visual "feedback" pathway through contralateral olive to flocculus. Relevant oculomotor nuclei are not shown (see text).

eyes conjugately to the right. Another portion of the medial vestibular nucleus, along with the superior vestibular nucleus (SMV, collectively), "inhibits" (via the unseen motor nuclei) the ipsilateral LR and the contralateral MR. In other words, SMV also facilitates rightward eye deviation. Now the horizontal semicircular canal (HC) excites both SMV and MV. Its signals will therefore lead to conjugate rightward eye deviation, and reciprocal activation of the LR and MR in each eye. The HC itself is excited by head turning to the ipsilateral (left) side. Thus, the rightward eye displacements HC produced under those conditions will tend to hold the fixation point of the eyes. That, of course, is the essential VOR function.

To the basic VOR circuit of figure A is added simultaneous SMV and MV inhibition from the flocculus (FL). The inhibition is developed by Purkinje cells out of HC excitation entering on mossy fibers. Now given some sort of standard HC stimulus, it seems evident that by increasing the inhibition developed by the flocculus in response, the VOR could actually be nullified. Conversely, the VOR could be accentuated by suppressing flocculus inhibition. Therefore, it appears reasonable to conclude that, other factors remaining constant, the amplitude of the VOR should be directly proportional to the level of HC-induced inhibition from the flocculus. In theory, therefore, one could regulate VOR amplitude by adjusting that inhibition.

Is VOR amplitude subject to adjustment? Yes, it is. A number of factors affect amplitude, but the most interesting are those connected with vision. Ito[14] pointed out that the VOR might well be

visually calibrated, in keeping with its purported function of stabilizing gaze; and in fact, experiments using prisms or mirrors to reverse or otherwise alter the apparent rotation of the visual world as the head rotates have demonstrated that VOR amplitude will indeed adapt appropriately. In humans[13] or animals[24,27], fixation stabilization is gradually achieved over a period of days, although a substantial portion of the correction may be complete within a few hours.

Does the flocculus have any part in these visually-provoked VOR adjustments? Robinson[27] found that in cats with flocculo-nodular lesions, VOR adaptation does not occur. In a series of studies, Maekawa, Simpson, and Ito[12,20,21,22,28] have discovered (in rabbits) that visual stimuli do indeed reach the flocculus, and that they do so primarily upon climbing fibers. Moreover, the fibers respond to horizontal retinal image "slip"[12,28] (as do olivary neurons projecting to the flocculus; Barmack, personal communication). This, of course, is what one would expect for a system which measures fixation stability. Thus, there is strong, albeit circumstantial, evidence that the visually mediated adjustment of horizontal VOR amplitude may in part be carried out in the rabbit by means of the flocculus and its climbing fibers.

If one assumes that climbing fibers do influence VOR amplitude via the flocculus, then they presumably do so by adjusting flocculus inhibition of the vestibular nuclei (figure A). But how? There seem to be two generic approaches to the question. The most popular by far is to invoke some form of the Marr-Albus theory of classical

conditioning of Purkinje cells[1,4,23]. This theory holds that climbing fibers plastically alter the effectiveness of parallel fiber synapses such that HC inputs produce more or less inhibition, according to whether VOR gain is to be lowered or raised. The second approach is to assume that climbing fibers have an important, immediate effect upon eye movements independent of what HC inputs are doing; plastic effects (which are certainly present in the VOR; see above) are not to be ignored, but are in some sense secondary to this primary climbing fiber operation.

It is all too easy to lapse into polemics about either of these conceptions of climbing fibers. Yet it is also "easy" (but not technically so!) to tell which is the more important by simply eliminating climbing fiber activity from the VOR circuit. If an exclusive Marr-Albus "training" hypothesis were correct, one should see no immediate eye movement effects (VOR adaptation would, of course, be disrupted). Barmack and Simpson (unpublished) have made unilateral, histologically controlled lesions restricted to that portion of the inferior olive projecting to the flocculus (dorsal cap) in chloralose anesthetized rabbits. No eye movement effects (and no VOR) are evident until the animal recovers, whereupon the eyes exhibit a slow, conjugate drift horizontally (the direction of the drift will be treated momentarily). When the VOR is elicited, this drift is superimposed upon it. In this elegant demonstration, then, one can clearly see that climbing fiber activity <u>does</u> have an immediate impact upon eye position stabilization, ostensibly by regulating the level of flocculus

inhibition and/or excitation in the vestibular nuclei (SMV, MV in figure A). But to repeat, Barmack's result and the "immediate impact" conception of climbing fiber function do not exclude plastic phenomena appearing after some extended period. However, plasticity would seem ancillary to the day-to-day tasks of the olivocerebellar system.

Climbing fibers act "instantly" in the governing of eye movements. But once again, how? To state the question in simplistic terms, do flocculus fibers become active to decrease or to increase excitation of the vestibular nuclei to which the flocculus projects? Many would vote for the former, citing the nuclear inhibition implicit in the cfr. The author's anterior lobe theory depends upon the latter (section A.1; axiom (a)). Two methods of attacking the problem may be considered, both of which rely upon the correctness of the circuitry shown in figure A. The first method, the indirect approach, was proposed some time ago by the author[29]:

Suppose that climbing fiber feedback of moving visual targets (see above) is indeed designed to correct fixation "slippage" during the VOR by adjusting flocculus inhibition (or vestibular nuclear excitation) Figure B (from ref. 29) illustrates the consequences of either insufficient or excessive VOR amplitude ("gain") upon fixation slippage when a rabbit turns its head to the left, so as to excite the HC of figure A (only the ipsilateral--left--eye is shown in figure B; the view is from above the head, and the line through the head is the midline). In the upper portion of figure B, VOR amplitude is too

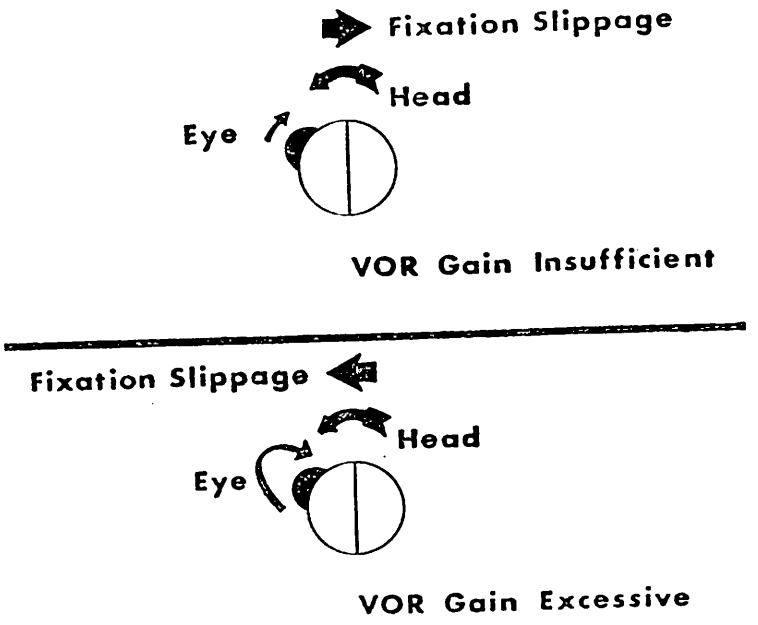

FIGURE B

Effect of insufficient or excessive VOR "gain" (or amplitude) upon direction of slippage of fixated retinal image. View is from above rabbit's head. Only left eye is shown. Text gives details.

low; the eye counterrotates less than the head and fixation slips from left to right (postero-anteriorly for the rabbit). Slippage in this direction would thus imply excessive flocculus inhibition, or insufficient vestibular nuclear (MV, SMV in figure A) output. Similarly, slippage from right to left (antero-posteriorly) under the same conditions would occur with insufficient inhibition (seen in the lower portion of figure B). Therefore, the question of the climbing fiber effect upon flocculus inhibition of the vestibular nuclei can be put in terms of any direction specificity of flocculus cfr's to moving visual stimuli. That is, if they respond to say, antero-posteriorly moving targets, they must signal a condition of excessive VOR amplitude or insufficient flocculus inhibition--and would presumably then act to increase that inhibition. Both Ghelarducci, et al.[12] and Simpson and Alley[28] did find a certain direction specificity in rabbit flocculus cfr's, but it was in the postero-anterior direction (63% of cfr's in both sets of experiments). Barmack (personal communication) recorded fields from the "floccular" portion of the olive and found an even more dramatic postero-anterior specificity. By the above hypotheses, then, it seems that climbing fibers are driven by visual signals which call for a reduction of flocculus inhibition--or an increase of vestibular nuclear excitation.

Barmack (personal communication) has attempted a second, more direct assessment of climbing fiber influence on VOR circuitry by direct olivary stimulation (unanesthetized rabbits). With reference to figure A (i.e., left side of the animal), stimulation of

the contralateral olive drives both eyes to the right; lesioning (see above) causes the eyes to drift to the left. In other words, the contralateral olive and the ipsilateral climbing fibers it controls have the same qualitative effect upon the VOR as does the ipsilateral horizontal canal: Both have the operational effect of exciting the vestibular nuclei. Now Ito[17] has reported inhibition by olivary or optic disk stimulation of vestibular nuclear excitation evoked from nerve VIII. The conflict with Barmack's results may be superficial, however: Ito may have seen only the transient inhibition caused by Purkinje cfr's, while Barmack's effect could stem from post-cfr nuclear rebound[5].

As it happens, there are other data on climbing fiber activity during the rabbit VOR which are nicely explained by the "vestibular excitation" (or flocculus inhibition suppression) hypothesis: Some time ago, Baarsma and Collewijn[2] found that when visual stimuli are removed from rabbits, the amplitude of the VOR drops to about one-half its normal value. Restoration of vision promptly returns the amplitude to normal. This suggests that the "gain" of the VOR tends to sag without visual feedback. With that in mind, consider the findings of Ghelarducci, et al.[12] (also in rabbits), who recorded flocculus cfr's in a series of circumstances involving head rotations combined with visual cues. Their results can be presented with reference to figure A. It was first noted that if an animal's head is rotated relative to a fixed visual target (light slit), cfr's occurred primarily during ipsilateral movement (that is, to the left in figure A). By the deductions presented above, this presumably comes about because

decaying VOR gain causes postero-anterior fixation slippage when the head turns ipsilaterally (figure B), triggering the fibers. The resulting added excitation of the ipsilateral (i.e., left) vestibular nuclei "takes up the slack" in the VOR and stabilizes the retinal image.

What happens if the light slit moves with the head? Postero-anterior slip will now occur if the eyes move from right to left (figure A), or in other words, if the head rotates contralaterally. This is precisely when Ghelarducci, et al.[12] found flocculus cfr's to increase. Notice that this moving-slit situation requires the VOR to be suppressed in order that the slit be fixated. Firing the climbing fibers during contralateral rotation causes excitation (by the above hypothesis) of the ipsilateral vestibular nuclei, and that excitation is pitted against excitation of the contralateral nuclei by the contralateral HC. The opposing forces thus offset each other, resulting in little or no VOR (Note: Lisberger and Fuchs[19] have also observed increased simple spike, or mossy fiber, activity occurring in the contralateral flocculus under these circumstances in monkeys; this may reduce the controlateral HC "pull" on the eyes, thereby adding to the gain-reduction process). It would be exceedingly difficult to explain this behavior of cfr's by claiming that they help suppress the vestibular nuclei: One would expect them to fire during ipsilateral rotations if that were the case.

Finally, what happens in the situation of no visual input? This is another "low-gain" situation for the VOR, according to Baarsma

and Collewijn[2] (see above). Not surprisingly, then, Ghelarducci and colleagues[12] found that cfr's fired during contralateral head movements, just like in the moving-slit situation. Of course, this also implies that inputs other than visual affect flocculus climbing fibers! The source of these inputs is not known; but Ferin, et al.[10,11] observed that cfr's in cat vermis (the flocculus was not studied systematically) could be driven by both caloric and galvanic stimulation of the HC. Climbing fiber activity affects the vestibular nuclei in the same manner as excitation from the vestibular nerve (see above). So it is not particularly revolutionary to find both similarly influenced by the labyrinth.

It may seem difficult to keep track of the various situations in which flocculus climbing fiber activity will occur. Actually, however, there are two "laws" which appear to subsume much of the known data: The first, already stated and discussed above, is that the effects of climbing fiber activity parallel those of the ipsilateral HC (which, of course, does not imply that climbing fiber and HC excitation are inevitably simultaneous; cf. the low VOR gain situations described above). The second rule, which applies to visual inputs, is that climbing fiber activity assists the production of optokinetic reflexes. That is, climbing fibers create ipsilateral vestibular nuclear excitation which drives the eyes in the direction of a moving visual target. This is obvious from figure A and the postero-anterior direction specificity of ipsilateral flocculus cfr's. A target moving slowly, say, from left to right will induce cfr's on the left side,

exciting the left vestibular nuclei, and thereby promoting the rightward tracking of the eyes. It is probable that such climbing fiber activity is not the sole arbiter of optokinetic responses, since smooth pursuit tracking can occur with targets moving faster than the "cutoff" velocity of many visually evoked cfr's (but see ref. 28). At times, though, it may be useful to incorporate the olivocerebellar system into the optokinetic reflex substrate at least figuratively, and then speak of cooperation or competition between it and the VOR. This may be especially appropriate in the current worries about VOR plasticity. There is at least some precedent for associative reinforcement of distinct spinal reflexes (see ref. 6 for discussion).

If the above deductions and data are correct, then it seems that at least one part of one "axiom" employed in the preceding investigation of locomotion may have some truth in it. Climbing fiber volleys within an Oscarsson strip in the anterior lobe may indeed result in the relative excitation of nuclear regions in that strip's corticonuclear compartment. The contention has of course not been "proved" and may well be exceedingly difficult to prove in any direct way, especially if neural population effects (rather than individual cell idiosyncrasies) are involved. Moreover, the seeming excitation of vestibular nuclei by flocculus climbing fibers is only what takes place operationally. One is given no idea whether, say, Purkinje silencing following the cfr[5] is involved (although it is tempting to point out that simple and complex spikes "avoid" each other, or are antiphasic, in the rabbit flocculus[12], as is true when these spikes

are produced by labyrinthine stimuli in cats[10,11]). It is also well known that the flocculus is not the only cerebellar region influencing eye movements via the vestibular nuclei, or receiving visual and/or vestibular inputs (facts seldom mentioned by investigators of the flocculus). Nonetheless, in the author's opinion it will be difficult to explain the phenomena here in a radically different way without a certain amount of equally unexpected data.

A.3 Suggestions for Further Experiment

Despite their seeming simplicity, the VOR and optokinetic mechanisms could be used to examine all manner of neurophysiological hypotheses. The primary interest here, however, is to decide if these systems are suitable for testing the remaining features of climbing fiber axioms (a) and (b) that were stated in section A.1. Discussion below will thus consider experiments on possible "remote" effects of climbing fibers (corresponding to the postulated suppression of corticonuclear compartments neighboring active Oscarsson strips), and on the persistence of cerebellar reactions to climbing fiber volleys. In view of current interest in plasticity associated with climbing fibers, the author cannot resist a brief exploration of that topic, too.

A.3.1 Climbing Fiber Activity and the "Structure" of the VOR

In section 3.1.2 of the preceding report, it was shown theoretically that climbing fiber activity within anterior lobe Oscarsson strips facilitates changes in the structure of locomotor muscle usage--that is, in the amounts of activity present in certain muscles (e.g.,

proximal) relative to that in others (e.g., distal). Such structural alterations come about as a consequence of the rearrangement of excitation among different descending pathways governed by the anterior lobe; and that rearrangement in turn owed itself to the compartmental organization of the anterior lobe corticonuclear projection combined with the compartmental effects of Oscarsson strip activity stated in axiom (a), section A.1.

Now nothing definitive is known about any "compartments" or "strips" in the flocculo-nodular lobe, although a compartmentalized distribution of radioactive deoxyglucose has apparently been observed in rats subjected to prolonged rotation in a drum (Sharpe, unpublished). Thus, a direct test of compartmental activity redistribution using VOR--or optokinetic--circuitry is impossible (which is no problem, since there are other methods of testing the theory in the anterior lobe[5]). However, what about the more general principle of structural alteration--can flocculo-nodular climbing fiber activity be associated with changes in, say, the "structure" of the VOR?

By analogy with the locomotor system, VOR "structure" can be defined as the relative distribution of activity among muscles of the eyes during the VOR task. This in turn can probably be equated in most instances with VOR gain as a function of the plane of head motion and the direction of movement in that plane (to allow for possible direction-specific, or asymmetric, reflexes). Thus, putting on prism glasses eventually changes VOR gain in the plane the prisms affect, which, if not mimicked by gain changes in other planes (see

below), represents an altering of the muscle structure for the VOR.

Based upon this conception of structure, experiments on its posited climbing fiber adjustment are easy to come by. An obvious starting point is the influence exerted by climbing fibers driven by visual targets in one plane upon the VOR in another. That is, might increasing, say, horizontal VOR gain lead to a change in the vertical VOR? This should not be particularly difficult to assess experimentally. Indeed, such effects might be expected on the basis that certain climbing fibers in the rabbit nodulus and uvula, as well as in the flocculus, respond to horizontally moving (postero-anterally) visual stimuli[28]. One or both of these other regions may have some influence upon vertical eye movements.

It might also be interesting to examine the possible impact of "static" labyrinthine (utricular) receptors upon flocculo-nodular climbing fibers. In theory, the VOR could be restructured to compensate for nonstandard positions of the head (to rewire the influences of the canals upon the eye muscles, as it were). Similar thinking suggests an experiment in which head movements in one plane are combined with visual "consequences" moving in another. Would VOR modification occur only with reference to the projection of the aberrent target into the head movement plane, or would the reflex gradually be expressed as eye movements in the visual movement plane? Still another vision/structure relationship might become apparent if visual targets were presented to only one eye, which affects only one olive (rabbits). The asymmetric VOR which could result is discussed in

section A.3.3 below.

It should be repeated that these experiments are primarily of philosophical interest vis à vis the possible connection of climbing fiber activity with the structuring of the musculature for some task. They would say nothing about whether any observed restructuring were a consequence of a compartmental anatomy in the flocculo-nodular lobe of the cerebellum (not to mention the possibility of lateral inhibition between compartments). Positive results might, however, motivate further investigations along these lines.

A.S.2 Persistence of Climbing Fiber Effects and the VOR "Integrator"

It was postulated in the body of this report that the cerebellar anterior lobe complex had inherent in it a short-term memory capacity by which to "store," temporarily, the compartmental activity patterns created by climbing fibers. Reciprocal excitation between cerebellar and reticular nuclei could, in theory, account for such storage[5]. This is because recurrent excitation, provided it is not unduly potent, has the general effect of prolonging the operational time constant of a neural network. It imparts the properties of an "integrator[9]."

Interestingly enough, there appears quite distinctly to be an "integrator" within the VOR circuitry, accounting for the translation of head velocity information, provided by the semicircular canals, into eye position[25,26]. The location (if there is a single location),

construction, and actual time constant of this integrator are a matter of some controversy. Cerebellar involvement in the integrator has been claimed on the basis of VOR anomalies in cerebellectomized (or cerebellar cooled) cats[7]. It is also suggested by the inability of cerebellectomized monkeys to hold deviated eye positions following saccades[30] (but this could very well be due to a loss of "visual" climbing fibers and their optokinetic influence; section A.2). However, the question here is to decide whether climbing fiber influences on the VOR are designed to be temporarily stored. So the experimental test which first comes to mind is to assess whether the apparent vestibular nuclear excitation released by the fibers (section A.2) has access to the VOR integrator, no matter where it is or how it works. This is readily done be activating, say, flocculus climbing fibers unilaterally in the rabbit (either by direct olivary stimulation; or by presenting moving visual targets or even mere light flashes [20,21,22] to only one eye, occluding the other), and observing whether the resulting eye deviations are retained actively for any period, or whether there is simply a rapid, passive return to neutral position. The experiment should be controlled by a prior demonstration that an eighth nerve (or canal) stimulus <u>is</u> integrated. Incidentally, a positive result in this study would suggest that the vestibular nuclei (which are supposedly selectively affected by climbing fibers) are in communication with--or even part of--the VOR integrator, despite the well known evidence that their activity reflects head velocity much more than eye (or head) position. After all, it is certainly

possible to build integrators of sorts using "differentiators" placed in feedback loops. Collewijn and Baarsma[2] found that a distinct phase advance was present in the rabbit VOR in darkness, indicating that the "integrator" was not functioning particularly well. Recall that the darkness condition is also characterized by low VOR gain, and probably by reduced vestibular nuclear outflow (section A.2).

If the flocculo-nodular climbing fiber system is considered as part of the optokinetic reflex mechanism (section A.2), then there is added impetus for studying the possible storage or integration of climbing fiber inputs. Since the fibers respond only to moving visual targets, without any significant position selectivity (in fact, whole-field stimuli are best[28]), they essentially provide only velocity (or higher derivative) information about the targets. In the optokinetic reflex, this information could be used "raw," either in a velocity servomechanism equating eye velocity to target velocity or as a feed-forward "speedup" for a position servo. On the other hand, it may itself be neurally integrated into a position signal (which, of course, does not exclude its use in the above alternatives). Or, conceivably, it could even play some part in what could be a double integration (acceleration to position) responsible for the very gradual velocity maching (eye to target) occurring during successive beats of optokinetic nystagmus.

Methods for testing the persistence of the climbing fiber impact on the anterior lobe have been presented elsewhere[19], so again, the above experiments are not the only means (and, for that matter,

not the best means) for examining that axiom. Nonetheless, the author's intuition is that there must be some commonality among the physiological processes associated with the climbing fiber system in all parts of the cerebellum. The problem is seeing the parallels--seeing, perhaps, the gains of the VOR in different planes as homologous to the structure of a locomotor act, or the latter's short-term memory phenomena disguised in the VOR "integrator."*

*Since this section was written, Barmack and Hess (personal communication) have investigated more closely the effects upon rabbits' eye movements of stimulating the "visual" olive (dorsal cap region, projecting to the flocculus and possibly to other cerebellar areas). The eye movements produced were as described in section A.2; but moreover, it was found that following stimulus cessation, the eyes continued to drift in the initial direction for periods of approximately 2-5 sec, while gradually decelerating. "Resetting" saccades in the opposite direction could be superimposed somewhat randomly on this basic drift. The phenomenon was most clear in the absence of visual inputs which would act to stabilize the drift through the olivocerebellar system. Interestingly enough, during the presentation of the initial olivary stimulus (30-50 μa pulse train, 30-50 hz for 500 msec), eye position appeared to the author to change as the square of the elapsed time--that is, according to a constant acceleration format. In other words, the climbing fiber signal (more precisely, the nuclear consequences of the signal) may be doubly integrated before emerging as eye position (cf. the above discussion of optokinetic nystagmus). One therefore gains the impression that there are two cascaded "integrators" in the VOR/optokinetic mechanism. One sums and stores the effects of climbing fiber inputs and transmits to a second which sums the cumulative climbing fiber contribution with canal inputs, and then integrates the result. Barmack and Hess have noted that the VOR and the eye movements evoked from the olive do appear qualitatively to summate. Both the posited integrating functions could depend upon the excitability of reticular regions, since anesthetic levels which reduce the VOR (and supposedly affect the reticular formation) seem also to extinguish the prolonged eye movements got by olivary stimulation. In any case, Barmack and Hess's elegant observations do much to place on a firmer footing both the concepts of climbing fiber "excitation" of the cerebellar (or vestibular) nuclei, and of the prolonged, dynamic action of climbing fibers on the cerebellar complex in creating "tonic" biasing of musculature employed in particular acts.

A.3.3 An Experiment on VOR Plasticity

Plasticity in the VOR as a consequence of visual cues was briefly discussed in section A.2. As was mentioned, such plasticity has often been ascribed to the Marr-Albus[1,4,23] theory of parallel fiber/Purkinje cell synapse conditioning by climbing fiber activity. Arguing in favor of the hypothesis, of course, is the presence of visual feedback on climbing fibers, and also the apparent multiplicative adjustment inherent in changes of VOR gain, which could come about through alterations in synaptic efficacies. On the other hand, there is no objective reason to localize plasticity only within the cerebellar cortex; Chan-Palay[8] found very little evidence of ostensibly plastic structural alterations (neuronal or axonal degeneration) in the cortex of normal rats, but saw considerable evidence of such processes in the dentate (lateral cerebellar) nucleus. And there is no reason to expect that the apparent "gain" of a neural system owes itself only to synaptic multiplication. Signals can be very effectively multiplied by recruitment nonlinearities, divergence-convergence projection schemes, etc., suggesting more esoteric manifestations of plasticity.

Some general ideas about plasticity and the forms motor learning may take are discussed at length elsewhere[6]. What will be proposed here is a simple experimental ploy for examining the nature of VOR plasticity. Briefly stated: It can be seen from figure A that visual information from each eye in the rabbit is transmitted to only the contralateral olive and ipsilateral flocculus. The question is,

therefore, can an asymmetry be engendered in the VOR by means of unilateral visual cues, such that the reflex has a certain gain going in one direction and a different gain going the other? If that were possible, one could then use the flocculus and VOR system for one side of an animal as a control for the other in a search for the location of plastic changes--i.e., by simultaneous recording from homologous sites. In conducting such a survey, one naturally would have to start at the inputs of each side (i.e., canals and retinae), since plasticity at any point in the flow of information will affect all downstream centers.

Asymmetric vestibular plasticity is already known through the well known phenomenon of Bechterew (compensation for the removal of one labyrinth, which can be disrupted by subsequent cerebellar lesions). Whether asymmetry can be produced visually is an open question, although so-called "flash-induced nystagmus" can be elicited in rabbits by unilateral flashes to one eye, conceivably via climbing fibers (Barmack, personal communication). If the experiment were to succeed, however, some very interesting phenomena surrounding plasticity might be accessible.

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