CIRCUITS IN THE CEREBELLAR CONTROL OF MOVEMENT

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Neuroanatomists have generally recognized that the cerebellum provides the greatest challenge in our initial efforts to discern functional meaning in neuronal patterns because there is a stereotyped and simple geometrical arrangement of its unique neuronal constituents. Presumably, it is for this reason that there is the most refined knowledge of microstructure that is available in the central nervous system. The pioneer investigations of Ramón y Cajal[1] have led in recent times to fascinating developments concerning microstructure, geometrical arrangements, and numerical assessment.[2]

As shown in Figure 1,[3] there are only two kinds of afferent fibers conveying information to the cerebellum, the climbing fibers (*cf*) and the mossy fibers (*mf*); and there is only one type of efferent fiber from the cerebellum, the axons of the Purkinje cells (*Pc*), which terminate in the cerebellar nuclei (*cn*) and otherwise largely in Deiters' nucleus. The climbing fiber is uniquely distributed to a single

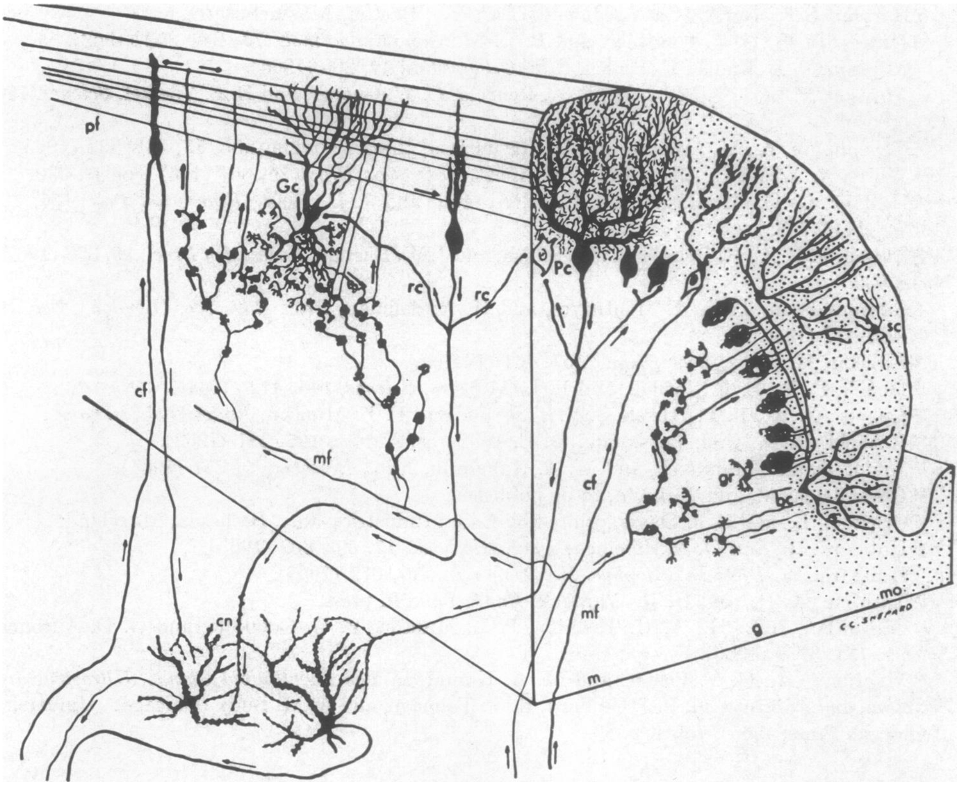

FIG. 1.—Perspective drawing by Fox[3] of a part of a folium of the cerebellar cortex. The principal components are shown in diagrammatic form, and are described in the text.

TABLE 1

PRINCIPAL MOSSY FIBER PATHWAYS IN CEREBELLAR CORTEX

Excitatory Pathway			Inhibitory Pathway		
	Divergence number	Convergence number		Divergence number	Convergence number
Mossy fibers			Mossy fibers		
↓	600	4	↓	600	4
Granule cells			Granule cells		
↓			Parallel fibers		
Parallel fibers			↓		
↓	300	100,000	Basket cells	$\sim$30	$\sim$10,000
Purkinje cells			Basket cell axons		
			↓		
			Purkinje cells	$\sim$50	20

Purkinje cell[1, 2, 4] on which it has a powerful excitatory action.[5] On the other hand, the mossy fiber input is characterized by enormous divergence and it has both excitatory and inhibitory actions on Purkinje cells. For our present purpose it is sufficient to outline the two major pathways. The excitatory pathway is by mossy fibers to granule cells (*gr*) which discharge impulses along their axons, the parallel fibers (*pf*) that give excitatory synapses to Purkinje cells, the approximate divergence and convergence numbers being given in Table 1.[2] The inhibitory pathway is by mossy fibers to granule cells to parallel fibers to basket cells (*bc*) that give a dense array of inhibitory synapses on the bodies of the Purkinje cells. The approximate divergence and convergence numbers are also given in Table 1 for the sequential neuronal links in this inhibitory pathway.[2]

The mossy fiber action is effected in the rectangular lattice that is determined principally by the parallel course of the parallel fibers for about 3 mm along a cerebellar folium and by the basket cell axons that spread for up to 1 mm orthogonally thereto. A sharply focussed mossy fiber input would give a "beam" of parallel fiber impulses that results in a 3-mm strip of excited Purkinje cells "on-beam," and, by action of the basket cells, a zone of inhibited Purkinje cells 1 mm off-beam on either side.[2, 6] It will be appreciated that this arrangement gives excellent opportunities for the integration of the inputs by the various mossy fibers that have overlapping excitatory and inhibitory actions, these arbitrary zones of potential interaction being limited to a few square millimeters (Fig. 2).

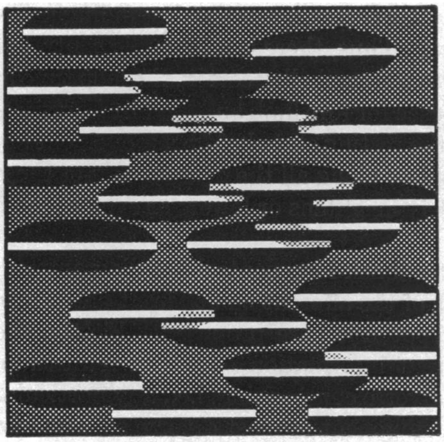

FIG. 2.—Diagram of a square centimeter of cerebellar cortex showing levels of Purkinje cell excitation or inhibition that result from many sharply focussed mossy fiber inputs, the bands of excited Purkinje cells being shown in white, the deeply inhibited cells on either side in black, while the grey toning symbolizes the Purkinje cells with background excitation or those with a conflict of evoked excitation and inhibition. It is assumed that in reality there would be much denser packing of the MF inputs and that the zones of excited and inhibited Purkinje cells would be much more diffuse and various in shape.

It can be assumed that there is no significant transfer of information from each small zone to another in the cerebellar cortex because the only association pathways would be by the Purkinje axon collaterals that are weakly inhibitory.[2] Impulses passing to some focus in the cerebellar cortex via mossy or climbing fibers influence at most only a few square millimeters of cerebellar cortex. The absence of excitatory association paths gives for any particular input an areal restriction that has never been considered in relation to the mode of operation of the cerebellum in the integration of information from diverse inputs.

The modality and the location of the receptors both contribute to the diversity of the inputs of information transmitted from a limb to the anterior lobe of the cerebellum. It has been found that disparate selections of this input are arranged in a mosaic-like manner to a large number of ill-defined patches.[7] This is illustrated diagrammatically in Figure 3*A*, where some movement, such as placing a foot on the ground, evokes the discharge of impulses from a wide variety of receptors, and these discharges via the diverse ascending pathways eventually act with various degrees of intensity on integrational patches in the cerebellar cortex. In Figure 3*A* no distinction is made between CF and MF inputs, which are shown diagrammatically in Figure 4 along with the efferent pathways from the cerebellar vermis to the spinal cord. Experimental investigation[7] on the mosaic distribution of subsets of information has been concentrated on the CF input, but it appears that the MF distribution is approximately congruent, though somewhat different concepts have been developed by Oscarsson.[8, 9]

It can now be asked: How are these numerous and diverse subsets of integration themselves integrated to give some coherent control of a movement? In answer, it is postulated that the integration actually occurs in the total movement process (Fig. 3*B*) that is evolving under control from the impulses discharged by motoneurones to the muscles, i.e., it is by the integrational mechanisms of the spinal cord, and more particularly in the play of muscular contraction which gives some movement of the limb that is, for better or for worse, a unity.

It can be asked: If the movement as so evolving under control by motoneurone discharges is "off-target," how is it corrected? The evolving movement will give a change in receptor activation and it is postulated that the input of this "revised" information into the cerebellar cortex (Fig. 3*B*) in turn gives "corrective" information in the efferent discharges from the cerebellar cortex down the descending pathways, and so changes the evolving movement. Thus, there is a dynamic control of an evolving movement by feedback loops up to the cerebellar cortex, the loop time in the cat being of the order of 20 msec and 30 msec for fore limb and hind limb, respectively. It is important to recognize that in the resting state before a movement begins, there is a background discharge of impulses along all the components of these loops,[2] and that the evolving movement merely heightens or lowers or even silences these discharges.

In Figure 4 the essential features of this feedback loop control are diagrammed, showing in more detail the neuronal elements of the afferent and efferent pathways.

There are three novel concepts in the hypothesis here proposed. Firstly, the integration in the cerebellar cortex of afferent information occurs in multitudes (probably thousands) of subsets of the most diverse composition, i.e., any particular afferent signal achieves representation as a component in most diverse subsets in a

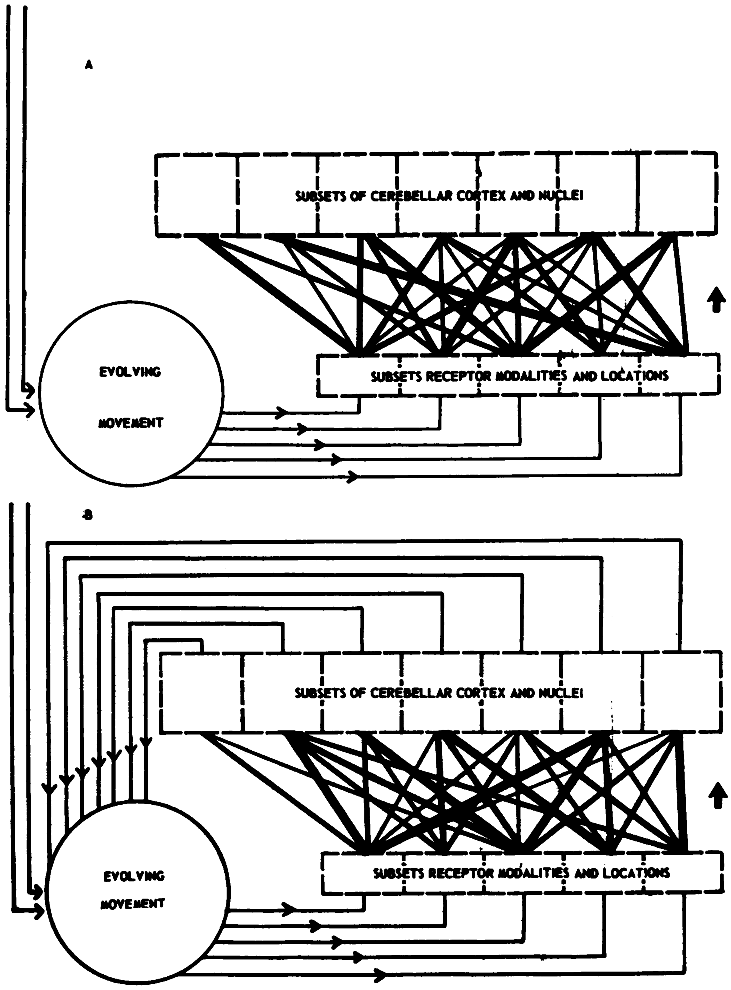

FIG. 3.—Diagrams of the circuits proposed for the flow of information from a hind limb to the vermis of the anterior lobe of the cerebellum and thence down the spinal cord to effect some modification of the evolving movement. (*A*) Onset of a movement in response to activity in some other descending pathway such as the pyramidal tract. This movement evokes the discharge of impulses in various receptors, as is signalled by the lower horizontal arrows, and in accord with observations, each class of receptor is shown with various intensities of input (symbolized by line thicknesses) on some integrational patches of the cerebellar cortex, but not on others. (*B*) This input of information into the cerebellum results in the discharge of impulses down the various cerebellospinal pathways, and so induces a change in the evolving movement and thus in the input of revised information (note line thicknesses) to the cerebellum via the sensory receptors of the limb, so completing the first sequence of the dynamic circuits of cerebellar control.

large number of integrational areas in the cerebellar cortex. Integration is done in what we may call a "piecemeal" manner, and in this integration each subset functions independently of all others. Secondly, the diverse assemblages of integration so achieved are not themselves integrated to any significant extent at higher levels, but at lower levels—provisionally in the neural machinery of the spinal cord, but ultimately in the movement itself, which by reason of the mechanical unity of a limb

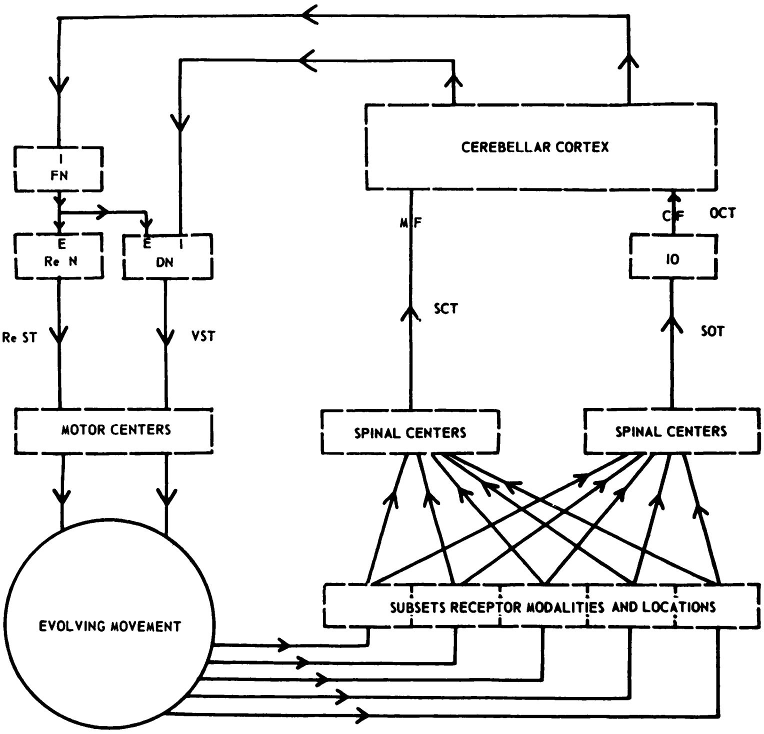

FIG. 4.—Diagram showing in more detail the pathways involved in the cerebellospinal circuits of Fig. 3. Spinoolivary tract, *SOT*, to inferior olive, *IO*, with climbing fibers, *CF*, in olivocerebellar tract, *OCT*; *MF*, mossy fibers of spinocerebellar tracts, *SCT*; *FN*, nucleus fastigeus; *Re N*, reticular nucleus with reticulospinal tract, *Re ST*; *DN*, Deiters' nucleus with vestibulospinal tract, *VST*.

in the bones and joints has itself a unity at any instant, no matter how bizarre. Thirdly, the evolving movement is brought into smooth and ordered performance by feedback loop operation as illustrated in Figures 3*B* and 4. It is important to realize that these feedback loops are operating even before the movement starts and are in continuous dynamic operation throughout all movements.

In general we can say that the MF input occurs via the cerebropontocerebellar pathway and that this has a wide origin from the cerebral cortex as shown by anatomic investigations and is distributed widely to the cerebellar hemisphere of the opposite side. However, it should be recognized that the physiological investigations of these pathways are still at a very early stage. More is known now about the CF input from the cerebrum, there being a monosynaptic activation of cells in the principal olive that in turn projects to the cerebellar hemisphere of the opposite side.[10] In Figure 5 the inputs to the pontine and inferior olivary nuclei are by collaterals of pyramidal tract fibers, and they are shown to have converging distribution of MF's and CF's to areas of the contralateral cerebellar hemisphere. It is postulated that integration likewise occurs there in subsets resembling those of Figure 3*A*. The output from the cerebellar hemisphere is solely by Purkinje cells that inhibit the neurones of the nucleus dentatus, which are excited by collaterals from the mossy fiber and climbing fiber pathways,[2] as indicated. From the nucleus dentatus the pathway leads via the ventrolateral (*VL*) nucleus of the thalamus back

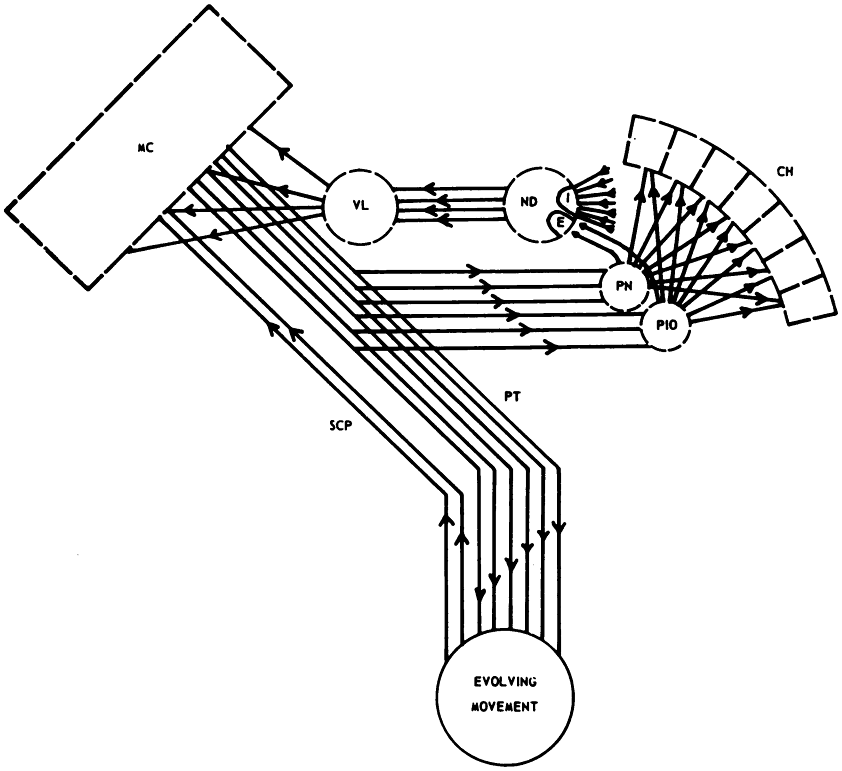

FIG. 5.—Diagram showing cerebrocerebellar pathways concerned in the operation of the cerebellar hemispheres, *CH*. *ND*, nucleus dentatus or lateralis; *VL*, ventrolateral nucleus of the thalamus; *PN*, pontine nuclei; *PIO*, principal inferior olive. *E* and *I* symbolize excitatory and inhibitory synapses. Note that the control of the evolving movement occurs only via the motor cortex, *MC*, and the pyramidal tract, *PT*. *SCP*, spinocortical pathways for information flow from movement to the cerebrum.

to the cortex. Meanwhile the pyramidal tract discharge will have changed the evolving movement and there will be revised input of information from the peripheral receptors up such pathways as the dorsal columns to medial lemniscus to thalamocortical fibers. The dynamic loop operation in control will later be considered in relation to Figure 7*A*.

As shown in Figure 6, the intermediate lobe of the cerebellum combines the operational pathways of Figures 4 and 5. The MF and CF inputs are both from the cerebrum as in Figure 5 and from the spinal afferents as in Figure 4. It has been shown that this spinal input is distributed to the intermediate zone in integrational subsets just as in Figure 3*A*.[7] The output resembles in part that for the cerebellar hemisphere (Fig. 5) in that it projects from the subcerebellar nucleus (the interpositus nucleus, *IP*) to the contralateral cerebral cortex via the VL thalamic nucleus, but, as shown in Figure 6, the axons from IP also innervate the neurones of the red nucleus, and so the output projects down the spinal cord in the rubrospinal tract to participate more directly in the evolving movement in addition to the more indirect path via the cerebral cortex and the pyramidal tract.

In Figure 7*A* and *B* a diagrammatic summary is given of the essential features of the circuits concerned in cerebrocerebellar control of movement. It is seen that in

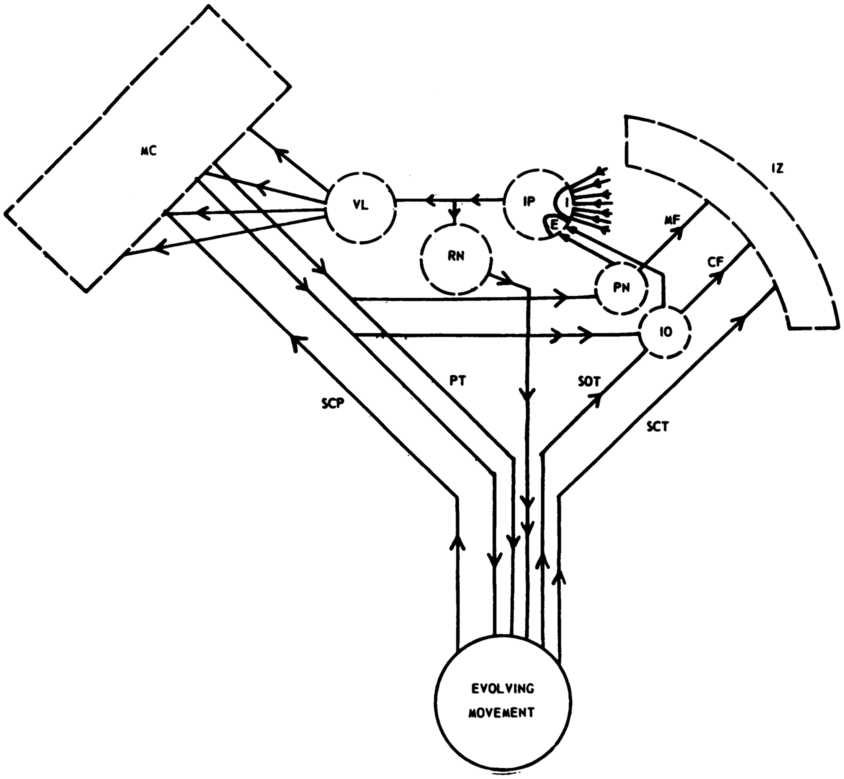

FIG. 6.—Diagrams of the complex pathways involved in the operational linkages of the intermediate zone, *IZ*, of the cerebellar cortex both to the motor cortex, *MC*, and to the spinal cord, and so to the evolving movement. *RN*, red nucleus; *IP*, nucleus interpositus; *IO*, inferior olive. Other symbols as in Figs. 4 and 5.

A (cf. Fig. 5) the cerebellar hemisphere does not receive information directly from the various spinocerebellar pathways.[2] The flow of information from the movement is represented as occurring via the cerebral cortex and is given in the modification of discharge from pyramidal cells. Thus the evolving movement can project sensory information to the cerebellar hemisphere by the following pathway: receptors to spinocerebral pathways to cerebrocerebellar paths through the pontine nuclei and the principal olive. The integration of the presumed diverse subsets of corticocerebellar information will occur in the evolving movement as in Figure 3*B*, but of course it will also occur in the immense and complex association paths in the cerebral hemispheres. Figure 7*B* shows diagrammatically the more complex circuitry that is postulated to operate in movement control by the intermediate zone of the anterior lobe in the cerebellum. It will be seen that there are three locations at which integration can occur in the cerebral and cerebellar contributions to the control of movement: in the cerebral cortex with expression in the pyramidal cell discharge; in the cerebellar cortex with expression in the Purkinje cell discharge; and in the spinal cord where the motoneuronal discharge finds expression in the evolving movement.

There are three components of this hypothesis of the operative circuits by which the cerebellum controls movement. Firstly, there is the input into a multitude of

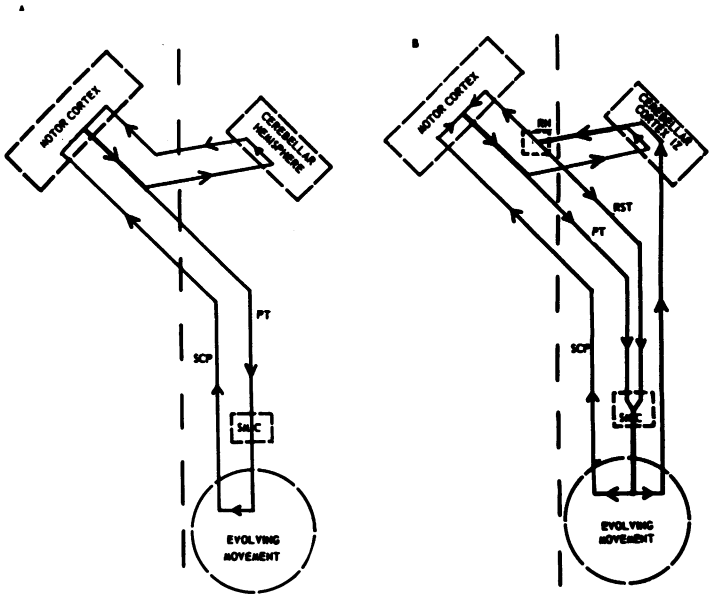

FIG. 7.—Simplified operational circuits of the situations shown in more detail in Figs. 5 and 6. The vertical broken line shows the midline, and hence the various decussations are revealed. Symbols are as in Figs. 4, 5, and 6. *SMC*, spinal motor centers; *RST*, rubrospinal tract.

independent integrating areas of the cerebellar cortex of very diverse subsets of information from the receptors activated by the movement and by the cortical controlling centers.[7] Secondly, the piecemeal integration so effected is transmitted in the cerebellar efferents both to the spinal cord and to the cerebral cortex and is unified provisionally in the neuronal mechanisms of the cerebral cortex and spinal cord, but finally in the changes produced in the evolving movement. Thirdly, the changes in the evolving movement are fed back by receptor organ discharges to the cerebellum and to the cerebral cortex, so completing the operational circuits, which are shown in the several diagrams. It is an essential part of the hypothesis that there is a continual feedback of information to the cerebellar integrating mechanisms. All integrations there are piecemeal and provisional. The coherence and smoothness of movements are achieved by the circuits that are continuously in operation not only during a movement but in all sequences of movement.

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