1951

Spasticity: a problem of disordered motor function

"The neurologist is placed in the unenviable position of being less sure about his knowledge of the motor system and less sure of his interpretation of motor defects than he formerly was. It is no longer possible for him to state with any degree of assurance that spasticity, hyper-reflexia and pathologic reflexes are certain evidences of pyramidal tract disease."

-- A. J. Lubin

SPASTICITY:

A Problem of Disordered Motor Function

Thesis, third year Medicine

H. L. Taylor BUSM III

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I. INTRODUCTION

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A. DEFINITION

Spastic paralysis is a syndrome which is seen in disruptions of the anatomic and physiologic integrity of the motor aspects of the central nervous system. It is manifest in such conditions as cerebral thrombosis, cerebral hemorrhage, brain tumor, amyotrophic lateral sclerosis, multiple sclerosis, cerebral diplegia and in cases of chronic bulbar palsy. In this paper it is proposed to discuss some of the work that has been done in various attempts to elucidate the origin of spasticity.

First however, what is spasticity. The American Illustrated Medical Dictionary (16) defines spasticity as a state or quality of marked hypertonus of muscles. Fulton (26) defines spasticity as augmented resistance to passive movements. Walshe (103) states that spasticity is increased muscle tone that can be readily detected by the passive stretching of the muscles whereupon a clearly increased resistance to the movement can be felt. According to Walshe this resistance has qualities which can be most easily elicited from involved knee extensors.

> "If the thigh rests upon the examiner's left forearm, placed under it as the patient lies in bed, and the right arm grasps the leg just above the ankle, on flexing the leg at the knee, a few degrees of movement are easily carried out without marked

> resistance, but once this range is passed an active resistance is felt to develop quickly in the quadriceps, and once more force is needed .... to continue the flexion. After another thirty degrees of flexion this resistance melts quickly, and the rest of the movement is relatively easily carried out. This .... has been spoken of as "clasp-knife" rigidity."

Kennard (48) defines spasticity as increased resistance to movement of the "clasp-knife" type together with increased tendon jerks. Denny-Brown and Botterell (14) agree with these, but for them spasticity also involves the acceptance of mild, barely discernible resistance to movement of the "clasp-knife" type without any other signs.

Spasticity may also include, in addition to the "clasp-knife" phenomenon and increased tendon reflexes, an increase in the reflexogenous area for these reflexes, a spread of activity to other muscles or muscle groups, and clonus or rhythmical repetition of the reflex movement involving the reiterative, metered contraction and relaxation of the involved muscles.

Combining these several definitions we see that all of them have in common the concept of hypertonus of muscle; to this is added the phenomenon of "clasp-knife" resistance to passive movement which may be readily apparent or barely discernible; and finally increased tendon reflexes and clonus

may be included.

> For the purposes of this paper the definition to be used will include as a common denominator the "clasp-knife" phenomenon which may or may not have added to it the factors of hyperactive reflexes and clonus.

It is easy to see that the term "spasticity"in any given instance may be used to mean one of several things, and if the term is not defined by a writer there are as a result difficulties in the interpretation of his findings concerning spasticity. At the risk of obscuring some of the factors involved, in the absence of a definition in any given instance this paper will utilize the broad definition of spasticity given above in the reporting of the data of various workers herein contained.

B. THE BASIS OF SPASTICITY

The lowest level mechanism upon which the spastic phenomenon is based is the stretch reflex, (14, 26, 75). The stretch reflex is the active resistance of a muscle to an extending force, whether it be an opposing muscle or an external force. The afferent neuron for this reflex arises within the muscle itself and is stimulated into activity by the tension receptors. Thus the stretch reflex is a proprioceptive reflex. The knee jerk is the classical example of the stretch reflex. The physiological significance of this

reflex manifests itself in the maintenance of posture. The weight of the body in most animals tends to flex the joints, and by so doing acts as a stretching force on the extensor tendons bridging these joints. The resulting reflex contraction of the extensor acts in the counteraction of gravity and thus serves in the maintenance of posture.

From this the relation of spasticity to the stretch reflex can be readily seen. In spasticity the animal of individual concerned is unable to inhibit this effect of stretch on a muscle voluntarily and so the increased resistance to passive movement comes about. There is however something which causes the muscle to relax at some point during the imposition of the stretch, which indicates that although the individual cannot voluntarily relax the stretched muscle, there yet remains some involuntary mechanism which prevents the muscle from maintaining tension against a too severely imposed stretch.

C. APPROACH TO BE USED

The approach in this paper is that of the clinician. In his examination of any problem he must first determine what is involved, and this implies that the anatomical structures concerned must be discovered. Having determined where the damage is, he must find what the function of those parts

is (physiology) and how that function has been altered by the insult (pathologic physiology). Therefore the data to be presented here will be divided under two general headings: structure and function. For we must know what is involved and in what way it is involved before it will be possible to achieve any concept of the genesis of spasticity as that phenomenon is seen in neurological disease.

Because of the difficulty in obtaining adequate controls in human subjects and because of the virtual impossibility of achieving discrete lesions in the human by which to attempt to demonstrate the functions of various centers and tracts, because of this the bulk of the material to be presented will be from animal experimentation. This is done with the full realization that the transfer of findings from animal to human subjects, or even from one animal to another, cannot be done with certainty of the applicability of the facts, and therefore can be utilized in the understanding of the human only as an approximation.

II. STRUCTURE

II. STRUCTURE

A. THE PRECENTRAL MOTOR CORTEX

1. Gross

The precentral motor cortex is that area of the cerebral mantle which is bounded posteriorly by the central fissure of Rolando, inferiorly by the Lateral or Sylvian fissure and which extends from these landmarks forward toward the frontal pole of the hemisphere. In addition to the part on the lateral surface of the hemisphere there is an extension onto the paracentral lobule on the medial surface of the brain (7). The section of the precentral cortex that is here under consideration is made up of those areas which are said to be the principle cortical areas involved in motor function, and so areas 44, 45 and 47 are not considered here. Although area 8 is important in motor function, it will not be considered here. A glance at the frontis will demonstrate adequately the boundaries of the precentral motor cortex on the dorso-lateral surface of the hemisphere.

The central sulcus demarcates the posterior border of area 4γ, and it should be noted that the border of this area extends to the depths of that sulcus (7), although according to Campbell (10) never reaches the deepest part of that fissure. Area 4s lies close to the superior and inferior precentral sulci (7). The anterior border of area 6 is not mark-

ed by any sulcus (7). The anterior border of area 44 seems to be marked by the diagonal sulcus of Eberstalter (7).

2. Histologic

It can be seen from the above that the demarcation of the motor area by gross anatomical features is indefinite. Indeed, considerable testimony to that fact is to be derived from the difficulties of the neurosurgeon in finding with certainty the large Rolandic fissure at operation (24). The major criteria for the anatomical definition of the motor areas are therefore histologic.

The precentral motor cortex has been defined histoanatomically by the methods of cytoarchitecture and by the delineation of sectors and sub-sectors derived from the regions to which the various thalamic nuclei project. According to the latter scheme the frontal lobe can be divided into three parts (5, 98).

1) The precentral motor sector which recieves its radiation from the ventrolateral nucleus and which is characterized by being mostly agranular.

2) The limbic sector which recieves its radiation from the anterior nucleus of the thalamus.

3) the frontal sector proper which recieves its radiation from the medial (dorsomedial) nucleus.

[illegible]

By this method it is not possible to delineate the borders of the several areas precisely, especially in the human brain, however these projections enable one to approximate roughly the three broad types of cortex which can be distinguished using the methods of cytoarchitecture. This discussion will confine itself to that type seen in the precentral motor cortex.

Cytoachitonics was probably the first method used to delineate anatomically what had been shown by others to be physiologically distinct. This was the avowed purpose of Campbell (10) who states:

> "This histological investigation I undertook with the object of ascertaining whether the cortex of the parts which responded to electrical excitation could be differentiated from the "silent" parts, by the possession of any distinctive histological structure."

The precentral cortex, with which we are here concerned is made of several histologically distinct areas. These were designated as 4, 6, and 44 by Brodmann (7). Campbell (10) referred to area 4 as the precentral area and areas 6 and 44 were considered together as the intermediate precentral. In the terminology of von Economo and Koskinas (23) area 4 is subdivided into FA and FAδ, the latter being the Betz cell bearing area, area 6 is termed FB and area 44, FCBm.

Area FA and FB are typical of what Brodmann referred to as the agranular heterotypical cortex (7). Cell preparations fail to show an inner granular layer, except for a very thin zone where layers iii and v appear to merge, manifesting an increase in cell density and a concomitant decrease in cell size (7). Fiber preparations of this area show at roughly coincident levels an outer stripe of Baillarger and a diffuse outer boundary within the third layer (7).

Throughout the agranular cortex there is a low cell density and a poor differentiation into laminae. Area 4 and area 6 differ from each other in the frequency of the giant cells of Betz in area 4 and their rarity in area 6. The columnar pattern of cells in layers iii and v of area 6 is clearer than in area 4 (7).

Between area 4 and area 6 lies an area which has been designated as 4s which is said to function in the suppressor circuits. Von Bonin (5) believes that this area can be distinguished from the bordering areas by an increase in size of the pyramidal cells in layer iiic (or upper iv). Economo and Koskinas (23) remarked on such large cells between their areas FA and FB, although they knew nothing of any possible physiologic difference ascribed to that strip

of cortex. On the basis of the frequency of the Betz cell in layer v they have further subdivided area FA into areas FA and FAδ.

Von Bonin (7) has summarized the histological characteristics of the areas under consideration using a terminology modified from that of Brodmann as follows:

1) Area 4δ: Agranular, contains giant pyramidal cells of Betz. Unistriate, well developed radii.
2) Area 4a: Agranular, no giant cells of Betz, but otherwise the same structure as 4δ.
3) Area 4s: Agranular. Presence of large cells in the upper substratum of the fourth layer and no giant cells of Betz in the fifth layer. Otherwise is similar in structure to areas 4 and 6.
4) Area 6: Agranular, but showing a columnar pattern in layers iii and v. Cells are slightly smaller and the second layer is somewhat better demarcated from the third layer than in area 4.
5) Area 44: Dysgranular. small cells intermingling with much larger ones in layer iv. The uppermost part of layer iv contains numerous very large pyramidal cells. Both layers iii and v can be subdivided. Layers ii and iii are well demarcated from each other. It is bistriate with the outer stripe of Baillarger lighter than the inner one.

The summarized description given above applies to man, but the histological characteristics are similar to homologous areas in other primates.

The most conspicuous element of the precentral cortex is the so called Betz cell, which is found in the fifth

layer (7). These cells have been ill-defined and just what cells may be considered Betz cells remains in doubt since there have been no adequate criteria, physiological or anatomical to define them. In his enumeration and measurements of the Betz cells in area 4γ Lassek (53) included all pyramidal cells in layer v ranging in area from 900 to 4100 square microns.

The outstanding characteristics of area 4γ which it shares with areas 4a, 4s and 6 are:

1) Absence of an inner granular layer in the cytoarchitectural sense.
2) Low cell density, but large average cell size.
3) Preponderance of pyramidal cells and a confluence of the inner and outer stripe of Baillarger.

B. SOME FIBER PROJECTIONS OF THE PARIETAL CORTEX

Peele (85) has discussed the fiber projections from the parietal cortex. He states that all areas of the parietal lobes send two groups of fibers to other areas within the cortex. The first group consists of association fibers to the adjacent cerebral lobes. The second general group of fibers are those from one parietal lobe to symmetrical areas by way of the corpus callosum, and a few fibers to non-symmetrical areas of the contralateral cortex.

His investigation of projections to subcortical areas was made by ablation of the parietal cortex with subsequent sacrifice of the animals and study of the sections of the brain and cord by the Marchi method. His findings as to subcortical parietal projections follow:

1) All of the areas, i.e. areas 3, 1, 2, 5 and 7 send fibers to the thalamic nuclei lateralis posterior, ventralis postero lateralis, and the ventralis postero medialis. He noted that fibers from the rostral part of the parietal cortex terminated in the rostral part of the thalamic nuclei concerned. There was homology in all cases between the corticothalamic projections and Walker's thalamocortical projections referred to above.
2) All parietal areas sent fibers to the ipsilateral pontine nuclei.
3) All parietal areas sent fibers through the medullary pyramid to the spinal cord where they accompanied the lateral corticospinal tract of either side (vide infra), but for the most part to the crossed tract. Areas 3-2-1 and to a lesser extent, area 5, projected to the contralateral lumbar levels. Area 7 sent fibers to the cervical segments only and area 3 sent a few fibers to the ipsilateral cord.
4) Areas 3 and 5 sent fibers to the ventral third of the lateral zone of the substantia nigra.
5) Areas 5 and 7 sent fibers to the pretectal region and area 7 sent a few fibers to the superior colliculus.

C. EXTRAPYRAMIDAL SYSTEMS

In this paper the term extrapyramidal systems means all tracts made up of non-pyramidal fibers subserving a motor or inhibitory function. These include all of the corticofugal fibers to the brain stem (which are non-pyramidal),

the various efferent fibers to the basal ganglia, the intra-ganglear fibers, and the fibers to the cord and motor cranial nerve nuclei that originate from these centers. The fibers interconnecting the above mentioned structures with the cerebellum are also to be considered extrapyramidal.

Verhaart and Kennard (96) utilizing the method of thermocoagulation have destroyed isolated portions of area 4, 4s and 6 and then with the Marchi method have traced the non-pyramidal fibers to the various centers of the brain stem. From this study tey reached the following conclusions:

> Fibers from areas 6, 4 and 4s were found to end chiefly in the basal pontine nuclei, the substantia nigra and the thalamus. They were unable to trace any fibers to the red nucleus and they categorically deny the possiblity of fibers coursing to the magnacellularis. They were unable to confirm the existance of cortico-caudate fibers as postulated by the method of physiological neuronography of Dusser de Barrene, however they feel that their work does not contradict his findings because of the inability of the Marchi method to determine myelinated axon terminations.

Glees (34) has been able to demonstrate that areas 2s, 3s and 8s in the cats' brain are connected to the caudate by collaterals from corticofugal fibers.

> Verhaart and Kennard in the same study found that fibers from all areas studied passed to these same nuclei, but to different areas of those nuclei. It is felt that the principle connections between the cortex and the basal ganglia are by way of the cortico-nigral system. (96)

Hines (40) states that the whole area frontalis agranularis shares corticofugal terminations in the subthalamus, substantia nigra, reticular formation and in the pontine nuclei. Areas 4s, 6 and 8 share appreciable projection systems in the substantia nigra and the reticular formation, but she states that those from 4s form a large bundle, while those fibers from area 6 and 8 are few and scattered.

Some interconnections of the basal ganglia have been given by Papez (84):

> The corpus striatum includes the caudate nucleus and the putamen. It is in relation to the subcallosal bundle and the external capsule. It gives origin to the striopallidal and strionigral fibers which synapse in these nuclear masses. The substantia nigra makes efferent connections to the tegmentum of the midbrain which in turn connects to the superior olive and thence to the cerebellar cortex. This pathway of striatal origin appears to exercise inhibitory effects on the musculàr apparatus.
> The pallidum consists of two segments. These recieve afferents from the medial nucleus and the medial ventral nucleus of the thalamus. Transthalamic connections from other thalamic nuclei to the medial nucleus are present. The pallidal efferents end in the prerubral field, the hypothalamus, the subthalamic nucleus and the ventral lateral nucleus of the thalamus. The prerubral field sends a short tract of fibers to the red nucleus. the red nucleus gives origin to the rubrospinal, rubro-occulomotor and, according to Papez, to the rubroreticulo-olivary tracts.

There is evidence of interconnections between the cortex and the cerebellum by way of the corticopontine and

corticonuclear connections. It is felt by Bailey (2) that the pontine nuclei (and their fibers to the cerebellar cortex which pass through the middle peduncle to the cerebellum, mostly to the contralateral hemisphere) have connections with at least the lobuli simplex, ansiformis and paramedianus.

The efferents from the cerebellum go to widespread foci. The efferent connections of the fastigeal nuclei are to the vestibular nuclei and are concerned chiefly with the maintenance of postural tonus (2). Magoun and McCulloch (74) have found fibers passing from the anterior lobe and paramedian lobule of the cerebellum to the fastigeal nucleus. Fibers originating in that locus were found to pass to the bulbar reticular formation. Cells of origin in the reticular formation send their axones through the angle of the pyramidal decussation and then by way of the ventrolateral fasiculus of the cord to segmental levels, predominantly ipsilaterally, but with some crossing in the cord.

The efferents from the globose, emboliform and the dentate nuclei pass into the brachium conjunctivum, cross in in the conjunctival decussation and enter the red nucleus. (2) Some fibers end on the cells of the red nucleus, some in

the central medial nucleus. The remainder of the conjunctival radiation passes forward to enter the ventrolateral nucleus of the thalamus. This region of the ventrolateral nucleus connects with the motor cortex, and the radiation so formed is one of those which has been mentioned as delineating the precentral motor subsector.

D. THE PYRAMIDAL TRACT

1. Origin

The work of Holmes and May (44) showed that the giant cells of Betz in area 4 contribute their fibers to the pyramidal tract. From this they inferred that the Betz cells was the sole cell of origin of the pyramidal tract. Lassek (52, 54, 55, 57) has shown that there are about 34,000 cells of Betz (using the criteria referred to in the section on the precentral motor cortex) in each hemisphere, but that there are about 1,000,000 fibers of varying size in each medullary pyramid. Assuming that each cell contributes only one efferent fiber, it is impossible to say that only Betz cells give origin to this tract. It is significant that the large (9-22 micron) fibers number about 30,000 in each pyramid (54, 57), which correlates well with the number of Betz cells in accordance with the rule that the largest cells give rise to the largest fibers. The same investigator (55)

also demonstrated that ablation of area 4 eliminated 2-3 % of the total that are large fibers, and reduced the total fiber count by from 27-40%, indicating that area 4 must contribute small as well as large fibers, presumably from the smaller cells within the areal cortex.

Levin and Bradford (64) have shown that section of the pyramidal tract in the monkey at the cervical level produces in addition to dell damage in area 4, also the dropping out of cells in areas 3, 1, 2 and 5 of the parietal lobe. Peele (85) finds that parietospinal fibers arising in these parietal areas cross in the pyramidal decussation and enter the lateral corticospinal tracts exclusively. Those arising from the cortex just posterior to the central fissure (area 3) could be traced to the lumbar levels, those from area 7 to cervical levels only. He postulates from his own work and that of Levin and Bradford that the cells of origin of these fibers are in the internal and external of layer v of the parietal cortex.

At present areas 4, 3, 1, 2, 5 and 7 have been shown to contribute fibers to the pyramidal tract of the monkey. Hoff (42) has shown that there is a direct corticospinal path from area 6 to all levels of the cord. Some fibers pass superficially into area 4 an then are projected to the cord. Kennard (46) has also shown that ablation of area 6 causes the

degeneration of corticofugal fibers traveling in the corticospinal tract to the lower lumbar levels of the cord. Yet Lassek (55) found 50% of the pyramidal fibers intact in the monkey after a wide precentral-parietal ablation. The origin of a large proportion of the tract therefore remains in doubt. Tower (95) has shown by severing the pyramidal tract at the trapezoidal level that all of the fibers in the medullary pyramids degenerate, inferring from this that all the fibers in the pyramids are descending. The possibility of the subcortical origin of some pyramidal fibers should not be neglected. If chronic total decortication in several species of animals should leave a significant number of fibers in the medullary pyramids intact, it would of necessity indicate that there was such an origin. Peele (85) has suggested that all of the corticospinal fibers may not be motor in function in the strict sense, but as is possible with corticothalamic fibers, the fibers originating in the parietal cortex may function as a sensitizing mechanisms for cord sensory neurons.

2. Course

The fibers descending from the cerebral cortex are diluted by other fibers in the internal capsule, basis pedunculi; and only when they reach the level of the pons do they become at all concentrated (95). In the descent of the

pyramidal tract it is thought that collaterals are given off to such structures as the corpus striatum, the substantia nigra, the reticular formation of the upper brain stem and to the pontine nuclei (95). Corticobulbar fibers to the cranial nerve nuclei leave the pyamidal bundles at these levels also.

In the medulla the pyramidal fibers destined for the cord are collected into a large and densely concentrated areas, the medullary pyramids, and then at the level of the pyramidal decussation break up into three separate descending tracts. Fulton and Sheehan (29) in confirmation of the work of Leyton and Sherrington (63) have shown following area 4 ablation that:

> "at the level of the pyramidal decussation the large majority of degenerating fibers can be seen to cross over..., a few remain ipsilateral, but pass dorsally in the (ipsilateral) lateral column of the cord."

By sectioning the cord at various levels these workers were able to show that in addition to the well known crossed fibers there were a lesser number of uncrossed fibers (about 1/10 of the total) that took up the lateral position ipsilaterally and continued at least down to the level of the first sacral segment. They noted that these fibers, though less dense took up the same comma shaped configura-

tion as did the crossed fibers. In addition to these fibers they were able to show that there is a direct ventral tract made up of a very few fibers which continues down to the same sacral level, but which is very sparse at that level.

3. Termination

The termination of the pyramidal fibers has been investigated extensively by Hoff and Hoff (43) who found by the method of bouton degeneration that the degenerating terminal are numerous not only on the cells of the intermediate grey zone and at the base of the dorsal horn, but also that there are a few boutons around the cells of the ventral horn. These endings were found for the most part on the side contralateral to the origin of the fibers, but also a few were ipsilateral to the ablation. These workers also suggested that the ipsilateral fibers seemed to be of ipsilateral origin.

III. FUNCTION

III. FUNCTION

A. THE CORTEX

1. Stimulation Studies

In 1901 and 1917 Leyton (Groenbaum) and Sherrington (35, 63) published two papers on the excitable cortex of the higher apes which have become classics and which are the basis of much of the work on the cortical control of movement that has been done since that time. In their work on this problem they investigated the motor phenomena elicitable from the cortex of the chimpanzee, orang-utan and gorilla by means of faradization and in addition they notes the deficits resulting from cortical ablations. They were able to delimit an areas of the cortex from which motor responses were obtainable by primary stimulation, as opposed to the remainder of the cortex from which such phenomena were not elicitable. In these three species of primates they found that the "motor" cortex included almost all of the free surface and a large proportion of the sulcal surfaces of the gyrus centralis anterior (precentral gyrus). In addition to this area they were able to elicit motor activity by stimulation of the cortex of the gyrus marginalis on the medial surface of the hemisphere for a distance extending about half way from the mesial border to the sulcus cingulus. They found in this study that about

one third of the excitable cortex was buried in the sulci of this area.

They were not able to elicit responses from other areas of the cortex by the same method of stimulation, but they found that by primary subliminal (faradic) stimulation of any point on the "motor" cortex (i.e. facilitating stimulus) they were able to elicit a motor response from a corresponding point on the postcentral gyrus by secondary (faradic) stimulation. They concluded from this that although primary cortical centers for motor activity were to be found in the precentral gyrus, there were postcentral areas which when facilitated in this manner yielded motor responses, perhaps by cortico-cortical connections.

These workers were unable to discover evidences of minute localization of motor response, but were able to elicit a broad localization of response of the main motor parts of the opposite half of the body. Stimulation of a point at one time would elicit one response and stimulation of the same point at another time would call forth one which was different. This property they termed "temporal instability". Neither were they able to find a point for point similarity of response between the cortices of different subjects. It was their feeling that this "instability" was largely an expression of mutual influences exerted transiently by the

physiological states, for the time being, of different points of the motor cortex and of the subcortical centers they connect with. They were able to differentiate three classes of variability of response which they termed:

1) deviation of response,

2) reversal of response and

3) facilitation phenomena.

> By deviation of response they meant that stimulation of a point on the motor cortex at one time might for example yield flexion of the contralateral elbow, with adduction of the shoulder and flexion of the wrist, and at the second stimulation temporally separated by a variable, but short, interval would yield only adduction of the shoulder or perhaps extension of the ipsilateral elbow.
>
> By reversal of response they meant that stimulation of a point might result in flexion of the contralateral elbow at one time and extension at another. The meaning of facilitation has been indicated.

Their ablation experiments showed that destruction of an area which caused movements in the contralateral arm for example, caused a paresis with eventual recovery of the ability to execute gross volitional movements and even to accomplish, although this recovered to a lesser extent, activities demanding fine muscular adjustment.

From this work they advanced the premise that the motor cortex could be thought of as a

> "synthetic organ for the compounding and recompounding in varied ways movements of var-

> ied kinds, from comparatively small, though in themselves well coordinate, fractional movements or postures."

They felt that the partial movements were provided by the bulbo-spinal mechanisms and that by forming these movements into wholes, the organism is able to perform motor acts of various sorts.

It is interesting to note that Hughlings Jackson (45) postulated a similar building of complex voluntary movements from simple movements represented at lower levels.

> "The lowest motor centers represent all the muscles of the body in a few different movements. The middle motor centers represent (re-represent) all the muscles in more numerous and more complex different movements. The highest motor centers represent (re-re-represent) all the muscles in the most different movements"
> "Increasing differentiation is a passage from the simple to the more complex, there arising, the higher the level, more numerous degrees of difference between the most different movements represented."

In a similar way Tower (92) conceives of four levels of increasing complexity from below upwards by which motor activity is coordinated. She considers the segmental levels as being at the same time the initial and final site of integration: namely in that here the reception of an impulse from the afferent nerves begins the process of stimulation of various levels of the neuronal system and finally because it is at the segmental level that the resultant complex of

impulses activates the structures which will accomplish the act. Her next level of integration is the brain stem motor mechanism which is the level for reintegration and for the addition of the factors of posture and movement. This level projects onto the segmental mechanism. The thalamic (or thalamostriatal) motor mechanism is conceived of as constituting a level for further integrations and for pattern formation. This (these) structures project to the lower brain stem mechanism. The cerebral cortex represents the highest level of integration and projects onto each of the lower levels.

If my interpretation of these concepts is correct, Tower does not consider Jackson's "highest level" in her formulation. Rather, her highest level constitutes Jackson's middle level, i.e. the "motor" cortex. Be that as it may, the basis of both concepts is the same and it places the most complex motor center in the cortex. It is interesting to note that in none of these is there much consideration devoted to the sensory side of the "arc" which is part of the mechanism of motor activity. It is not beyond the realm of possibility that some of the integrating processes involved occur in those parts of the neuraxis which are considered sensory.

So far it has been indicated that an area of the cortex is involved in motor activity and that the destruction of the area from which that activity can be elicited results in paresis with subsequent recovery of a good portion of total normal function. These movements are of various sorts, ranging from very isolated ones involving only one muscle or a part of a muscle to those movements of a complex synergistic type. That there is no such thing as isolated or discrete movement has been argued by Walshe (101), and he is probably correct in that it does not occur in normal "volitional" activity; however that isolated movement can occur under experimental conditions has been demonstrated convincingly by Chang, Ruch and Ward (13). They recorded the simultaneous responses of eight muscles acting upon the ankle joint of the macaque electromyographically. By systematically exploring the dorsolateral surface of the precentral gyrus and recording isometrically the relative threshold, latency and tension ratio of these muscles, they found that when the stimulating current was near threshold value, a focus could be found for all muscles acting on or over the ankle joint except for the peroneus longus (the focus for this muscle was later found on the medial surface of the hemisphere). The foci of representation for any two of the eight muscles attached to the myograph were never found at

exactly the same point, although the fringes around contiguous foci for different muscles overlapped to a variable extent. No variation of current applied to these fringes was able to produce a solitary response, and in addition there were silent areas for the muscles attached to the myograph. The points of shortest latency were clustered about the restricted foci, while the points showing the longest latency between stimulation and musclular response were to be found on the fringe. When several muscles responded to stimulation near a focus, it was found that the muscle which had the greatest tension ratio was the one which also exhibited the shortest latency and the lowest threshold for that point.

The temporal consistency of response from the same focus as found in this series of experiments is contrary to the absence of this consistency in the work of Leyton and Sherrington. I am unable to account for this discrepancy with certainty, but it is felt that this is, at least in part due to the use of different anesthesia (Dial in this instance and chloroform in the earlier work) and to the fact that in the later study a sine wave stimulator was used, while in the work of Leyton and Sherrington a faradic current was use, the intensity of which is said to be more difficult to control.

Complex movements are also elicitable from the cortex and these comprise those which are observable on stimulation using the usual gross methods of observation. Hines (40) found that electrical stimulation of area 6 proper as well as its anterior and posterior borders elicited flexor synergies with grasping, increase in flexor tone and relaxation of the grasp. Electrical stimulation of the anterior border of area 4 as well as of the posterior border of area 6 evoked extensor synergies which were frequently bilateral, diagonally organized movements, an increase in extensor tone and inhibition of standing tone. Denny-Brown and Botterell (14) found that they were able to elicit complex bilateral synergic movement from the forward zone of area 4. They found that fragments of a response were the most common result of any stimulation. As an example of complex movement (not their context) the following is presented:

> "We learned to recognize extension of the contralateral elbow with associated flexion of the ipsilateral elbow as the frequent representative of a movement which in full development also included protraction of the contralateral shoulder, retraction of the ipsilateral shoulder, flexion of the contralateral hip and knee, and extension of the ipsilateral hip and knee."

This sequence of movement appears, teleologically, to be at least a fragment of purposive movement, in this case a movement of progression. If it be assumed to be such it can be stated that in addition to the discrete innervation of one

muscle or muscle group, the cortex is also able to build up complex, apparently purposive, movements. However the conditions are highly artificial and the natural modes of integration more complex than is indicated by this premise. It can be said however, probably with assurance, that some phase of neural integration necessary for voluntary movement does take place in the motor cortex, and it is probable that the cortex is the "site" of one of the final stages in the integrating process that finally results in purposive movement.

Since the work of Leyton and Sherrington it had been thought that only motor activity could be initiated from the "motor" cortex. However Dusser de Barrene and McCulloch (22) found that stimulation of area 4s could cause inhibition of activity induced by the stimulation of area 4. This finding was the result of Dusser de Barrene's own earlier work on the suppressor circuits as well as work done by Hines (38). Their findings will be discussed in more detail in another section.

2. Ablation studies

In addition to electrical stimulation the other most used method of investigating the functions of the cerebral cortex is by ablating portions of the cortex and then ana-

lyzing the residual function. This sounds as if it were a straight forward and uncomplicated method, but it has certain serious pitfalls which must be considered in any analysis of results so obtained.

It seems to me from reading the literature that the most serious of these is one that is not considered seriously enough by many workers. Namely that when ablations of the cortex are performed, to know precisely what has been ablated. There are two methods of accomplishing this: one by stimulation of the appropriate areas both before and after ablation, and the second is careful histological study of the ablated area when this is possible and in all cases the examination of the remaining cortex by histological methods after the subject has died or been sacrificed. In every instance these two methods should be correlated with each other. Walshe (100) makes the following comment which is illustrative of the reasons for the difficulties that may beset even the best efforts to control ablation experiments.

> "A cortical area is largely a convention, it is certainly not a structure; it is no more than a two dimensional representation that seeks to sum the conflicting claims of six independently varying cortical layers. Within a cortical area, one cortical lamina may undergo considerable change, while another may extend unchanged into another area. Therefore the correlation of cortical function with cortical structure must be a correlation with cells, fibers and their arrange-

ments in the relevant lamina or laminae, and in the particular case of the motor cortex it is a correlation with the large pyramidal cells that lie in layer v of areas 4 and 6."

Another mistake which has been made by some workers is the controlling of lesion of area 4 by observation of destruction of corticospinal fibers in the cord. Since, as reported in the section on anatomy, it is now well known that the pyramidal tract arises from other cortical areas, some of which are immediately adjacent to area 4, this method offers no proof that area 4 alone is ablated. Even if the most rigid controls have been undertaken, the concept of areal functional units is a philosophical one which has not as yet been proven or been disproven.

In spite of these drawbacks ablation is an important method for the study and investigation of cortical function and one which has been much used. The difficulty, as will be seen lies in the interpretation of the results obtained, and also in experiments which are apparently very nearly identical there are discrepancies in the results themselves or least in the observed results.

It has been mentioned that the work of Leyton and Sherrington early in this century, ablations of portions of the excitable cortex were carried out which caused a contalateral paresis from which the animals made a gradual

recovery. Many studies of the results of ablation in various animals including man have been made since that time. Fulton and Keller (21) in a study of the genesis and evolution of the Babinski response did a series of ablations in various primates. He found that the motor deficit from a cortical lesion is progressively more severe as the evolutionary scale is ascended.

> In the monkey removal of the leg area resulted in complete contralateral monoplegia, generally flaccid in character which lasted for about twenty-four hours. After that time voluntary movement appeared at the hip and gradually extended to the more distal joints over a period of six to seven days. Progression movements in the monkey showed little or no deficit three weeks after the ablation of the foot area. As the scale was ascended utilizing the baboon, gibbon and chimpanzee, the initial monoplegia was increasingly more enduring, the period of recovery more prolonged and the final deficit more disabling. In the latter two animals it was found that a Babinski response developed after the ablation of the leg or foot area. When these animals were subjected to hemidecortication, the ensuing train of events was initial flaccidity with paralysis followed by the development of enduring spasticity and the Babinski sign. In the one gibbon that was used in this work, Fulton and Keller extirpated the motor area bilaterally in two stages. The first operation was followed by flaccid paralysis of the contralateral extremities. The ablation of the second side was succeeded by spasticity for five days which then diminished. As will be indicated later, it is probable that encroachment on area 4s was responsible for the immediate spasticity following the second ablation.

Flaccidity has been the commonly accepted result of the extirpation of area 4 and parts thereof in the experimental

literature. Denny-Brown and Botterell (14) at Fulton's laboratory did extensive ablation experiments. They concluded from their observations that the result of ablation of the Betz cells cortex is a depression of motor function affecting all motor activities of the opposite side, the distal joints being more affected and for a longer time than the proximal. It is of interest that these workers were impressed by th fact that in strongly motivated activity (fear, anger etc.) the animals would use previously paretic limbs in a strong and efficient fashion. Hands which these animals were usually unable to use with strength and dexterity and which gave little resistance to passive movement would reach out in real and simulated falling to grasp the bars of the cage strongly. In other instances the animal would be seen to use its usually paretic leg in an apparently normal fashion. Because of this phenomenon these workers believe that movements are not lost as such by area 4 lesions, but that the mechanisms for these movements are depressed, noting however that this depression could be overcome under certain circumstances. They also found that if any of area 4 was left intact, the limb concerned progressed through all the stages which followed a complete extirpation at an accelerated rate as did also those limbs for the motor representation in area 4 had been destroyed,

though the acceleration was less marked with these limbs. These writers felt that this was a demonstration of some property of the motor cortex which counteracts paralytic depression. Further discussion of this concept will be deferred until the observations of other workers are presented.

Welch and Kennard (105) and Hines (37) have found in their studies of ablation that lesion of area 4 produces a flaccid paralysis, or as Hines prefers to the it, a hypotonic paresis. Ades and Raab (1) found that unilateral removal of area 4 produced a flaccidity with recovery over a period of time (three to four months). Subsequent removal of the contralateral area 4 caused little or no accession of paralysis of the limbs on either side of the body. They also found that if this procedure was complicated by section of the corpus callosum between the two ablations, there was no significant change in the results. If areas 3, 1, 2 and 4 were removed bilaterally in two stages they found that paresis succeeded upon the second operation as well as the first. In these experiments the ablations were controlled by stimulation studies, but there is no record of histological controls. These results conflict (as regards area 4 lesion) with the findings of others (14) and is the only

record of such a sequence of events that I have been able to find, and having observed no experimental work myself, I am able to offer no other comment as to the validity of the findings.

It has been shown by Richter and Hines (87) that ablation of area 6 (of Brodmann) will consistently result in the production of the grasp reflex in monkeys. The condition is transient when the lesion is unilateral and permanent when bilateral.

Hines (36) presented a paper which has stimulated much investigation of the functions which are associated with the precentral cortex. Her report is of sufficient importance to be quoted in full.

> "A strip of cortical tissue about 3 mm. in width passing through the center of the superior precentral sulcus, duplicating the curvature of the central fissure, ending on the lateral surface in the vicinity of the inferior precentral fissure, and extending on the medial surface of the sulcus callosus marginalis, was removed unilaterally and bilaterally in seven monkeys. Examination of serial sections fixed and stained, proved the cortex ablated was taken from area 4 of Brodmann.
>
> "Study of the surviving animals showed unmistakably, contralateral to the lesion, signs of partial motor impairment, which rapidly regressed, but also brisk spreading tendon reflexes, increased resistance to passive movement (particularly in the extensors) and clonus--all the classical signs of spasticity. And

these persisted. Contractures also developed if this lesion was extended posteriorly to include a larger portion of the motor field. These spastic animals never showed forced grasping.

"On the other hand bilateral removal of the area originally delimited by Richter and Hines for the production of forced grasping (Brodmann's area 6) did not produce either motor impairment nor any evidence of spasticity. However the subsequent extension of this lesion to include the anterior border of area 4 added to the condition of forced grasping, the signs of spasticity ennumerated.

"Clearly therefore, forced grasping and spasticity result from the interferance with the activity of the cortex in two regions, anatomically discrete and cytoarchitecturally distinct. The nervous tissue whose ablation produces forced grasping is concentrated in Brodmann's area 6; and that whose removal results in spastic phenomena is most strongly represented in the anterior part of Brodmann's area 4, the area giganto-pyramidalis of Economo and Koskinas.

"Consequently, forced grasping and spasticity are not integral parts of one syndrome of the premotor area. Rather these two conditions represent a loss of inhibitory functions having independent origin within the larger motor area of the cortex cerebri."

Denny-Brown and Botterell cited above have confirmed this finding in their study. They found that spasticity following lesion of the most forward part of area 4 to be productive of these striking findings. It is to be noted that these workers have defined spasticity as a mild (or by inference any greater degree) but consistent and accrescent resistance to passive stretch of muscle, which as they de-

scribe it is of the clasp-knife variety in its fullest development as opposed to the steady resistance of plastic rigidity. They found however that the spasticity was not lessened as such as lesions were placed within area 4 posterior to the strip area of Hines. Their study showed that such placement changed the accentuation of its distribution and altered its development in time. As a lesion was restricted to the caudal part of area 4, the spasticity was greater in the muscles of the hand and wrist and/or in the knee and ankle, and the later its development in time. As the lesion is restricted to the forward section of area 4 the spasticity developed earlier in the elbow and knee. Here it is of interest to note that the distribution of the severity of the paralysis as observed in the same study had an identical relationship to partial lesions of area 4. They also found that as the presence of a group of Betz cells accelerates recovery of the part represented, so also by the same fact is the speed of appearance and severity of the spasticity accelerated.

Denny-Brown and Botterell describe the sequence of events in the recovery of function in some detail. They compare the immediate flaccidity of the parts involved to spinal shock and suggest that the reaction be termed "pyramidal shock". They note that after the abatement of this flaccid

paralysis, the state may be reobtained by the administration of anesthetics, barbiturates or may reoccur due to stupor originating from illness or some other cause. In their series, this "pyramidal shock" had less effect on the proximal appendicular and axial musculature than it had on the distal appendicular muscles.

In recovery they found that postural activity was among the first to recover from depression, being followed by the tendon reflexes which sometimes became hyperactive. Variably there might be a period when the spasticity which developed might become unstable and postural reactions might be greater than normal; while the tendon reflexes in the same muscles might yet be depressed.

Based on their findings Denny-Brown and Botterell offer an interesting hypothesis in regard to the strip area of Hines. They state that the delay in the appearance of spasticity in all muscles in total area 4 lesions (i.e. when that condition which they describe as pyramidal shock is the greatest) might be due to the supression of spasticity, which like tendon reflexes and other motor phenomena, is also liable to "pyramidal shock". By this I believe that they mean that all motor activity is supressed and as such the connections in the circuits which produce spasticity

are also repressed (increased synaptic resistance?). They feel that the earlier appearance of spasticity in lesions with some Betz cell cortex remaining is due to the protection against "pyramidal shock" thus obtained. So, they believe, could the early spasticity in the ablation of the strip area of Hines be explained. However the results of other method of study of 4s, notably by electrical stimulation and the physiological heuronography of Dusser de Barrene and his pupils (vide infra) lead one to feel that in this forward border of area 4 there is at least a concentration of a class of cortical element which is involved in a special function. This is not to say that such elements do not exist in other areas of the cortex, but rather in those areas in which they may exist they are minute, scattered and beyond the methods of study that have been used in the investigation of the strip. Perhaps such scattered units would account for the diversity of findings, for as Fulton remarked in his closing discussion of the paper of Denny-Brown and Botterell, Denny-Brown has observed his animals longer and described them more carefully than any other investigator. These workers may have found conditions which may have been overlooked by other observers.

Hines (40) has described three types of resistance to passive stretching of muscle.

> The first of these is hypertonus so great as to constitute rigidity. This type is the result of bilateral frontal lobectomy, the distribution of this rigidity being of the same degree in all the muscles of the extremities, but confined to the ventral musculature of the trunk. The second type of resistance that she noted was of the clasp-knife variety and was confined to the middle 30 to 40 degrees of the arc of stretching. This type was caused by area 4 ablation either in its entirety or of the anterior division alone, or by the removal of area 6 and the posterior division of area 4. The distribution of the former resembled that characteristic of man's spastic paralysis, the elbow being held in flexion and the knee in extension. The distribution of spastic paralysis following the latter was the reverse in the contralateral elbow and knee. The third type of hypertonus resulted from the removal of area 6 and the anterior border of area 4 and was distributed alike between the flexors and the extensors of the contrlateral knee and elbow, thus resembling the plastic rigidity found by Denny-Brown and Botterell (14) following the ablation of area 6 alone.

There is obviously a difficulty at this point and I can think of two possible explanations. One is that the criteria for the designation of plastic rigidity are different. This I think to be unlikely. The other, which seems the more probable, is that there is a difference in the histological criteria used for the delimitation of these areas of the cortex. This is not difficult to conceive of when one realizes that the "borders" between areas are ones of gradual change of characterisitics. To the inexperienced eye even sections of cortex from what is definitely area 4 or area 6 present many difficulties in differentiation

utilizing the criteria of the characteristics of cell distibution, size and shape.

Removal of area 6 alone according to Hines (40) causes the appearance of the grasp reflex. Kennard and Fulton (50) find that forced grasping and spasticity exist for a longer period after bilateral lesion of area 6 than succeeding upon unilateral lesions (there is here probably encroachment on the anterior division of area 4). They found that in every instance the removal of a second motor or premotor area there was evidence of bilateral somatic innervation, namely that following each extirpation of a contralateral area there was an accession of the grasping phenomenon in the ipsilateral extremities. When they made a complete bilateral extirpation of areas 4 and 6 there resulted a permanent and complete loss of voluntary power. Forced grasping and spasticity were extreme and it was easy to demonstrate the postural and righting reflexes of Magnus and de Kleyn. It was their impression that the bodily reflex status of their experimental subjects was identical with that of the thalamic preparation. (Denny-Brown (15) believes that what these workers term the grasp reflex in the thalamic preparation is actually a shoulder righting reflex.)

Kennard (47) found that the monkey deprived of motor

and premotor tissue in infancy is capable of highly developed and coordinated motor performance. She believes that this is due to the integration from other cortical areas, namely the frontal association areas and the postcentral regions. In this connection Denny-Brown and Botterell (14) believe that movements are not returned because of vicarious function of any other center or centers, but rather by some circumstance that counteracts the depression (vide supra). Kennard found that the motor deficit under these conditions of ablation consists of the loss of finer movements as exemplified by prehension in such activities as the grooming act. Infantile patterns of behavior such as reflex grasping as shown by the tendency to climb and cling were brought out by such total ablations of the motor areas and these persisted indefinitely. It should be noted that in this study voluntary purposeful activity was also observed. Kennard noted that with specific lesions there was the appearance of characteristic postures. With bilateral extirpation of motor and premotor areas, hyperextension and progression on a broad base were noted. With the addition of postcentral ablation to this lesion, scissors gait appeared. (This was probably due to an increase in proprioceptive deficit.)

In her study of the development of nervous activity in the monkey Hines (39) concluded that the tonic innervation of flexors and related muscle groups was related to the immaturity of cortical areas 4 and 6. Spasticity and the inhibition of spontaneous movements in the infant macaque she felt to be due to the partial development of the pyramidal tract and the incomplete development of area 4 (4s) and its projections.

Fulton and Kennard (28) have found that there is bilateral representation of the musculature in both the motor and premotor areas, but especially in the latter. In extirpation of the premotor area there was better recovery after ablation of the first premotor area than from the more profound and permanent depression of function and increase in spasticity that was seen bilaterally following destruction of the contralateral area. The spasticity was seen in its most profound form when all four areas were destroyed, this also being noted in their later paper abstracted above (50).

Kennard and Kessler (51) and Peele (86) have studied the motor performance of monkeys after the ablation of the parietal cortex. The former (and earlier) workers found that this procedure caused a motor deficit which was not as severe as that which followed ablation of area 4 or 6. They

also noted that emotion is able to improve fine motor performance. (In this connection it is worthwhile to recall that earlier in this presentation it has been stated that Denny-Brown and Botterell found this same improvement of function by emotion to obtain in their ablation studies involving precentral cortex). In this study Kennard and Kessler also investigated placing and hopping reactions following this type of ablation. A tactile deficit appeared following unilateral or partial ablations of either areas 3-1-2, 1-2 or 5-7. They found proprioception to be much less affected by these lesions than tactile responses. However when bilateral ablations were undertaken, there was permanent abolition of the hopping and of the tactile and proprioceptive placing reactions. Muscle tonus and tendon reflexes also were affected by these lesions, the results being absent or decreased knee jerks accompanied by decreased resistance to passive manipulation, these conditions having become operative immediately after all parietal ablations. Later they found that with the passage of time, the knee jerks might become hyperactive, but the resistance to passive manipulation never became increased.

Peele (86) confirmed these results except that he felt that there was no real motor deficit, but rather what he termed as a "loathness to move". He added to the findings

of Kennard and Kessler that the proximal musculature was more hypotonic than the distal. He believed that the hypotonia was due to the interruption of the parietospinal fibers to the pyramidal tract because the distribution of the hypotonia follows that described by Tower (93) following her pyramidal section in the monkey. In another place Peele (85) suggests that the thalamic and cord projections of the parietal cortex function as a sensitizing mechanism that could function in the facilitation of carrying out skillful and useful movement patterns, or for the accommodation of sensory cells in order that they might be aided in recieving incoming impulses.

Welch and Kennard (105) have written on the relation of the cerebral cortex to spasticity and flaccidity (by spasticity they include also the rigidities). They have made the following summary from certain types of differential ablations which they have made.

1) Removal of areas 6 and 4s causes the production of moderate paresis which is spastic in nature.
2) Removal of area 4 alone leads to paresis without spasticity.
3) Removal of the postcentral gyrus produces a transient flaccidity with some paresis which is more marked in the chimpanzee than in the monkey.
4) Ablation of areas 4, 4s and 6 together or seriatim causes immediate spastic paralysis.
5) Addition of postcentral ablation to the ablation of any motor or premotor area leading to

spasticity, results in increased spasticity. In the chimpanzee definite spasticity appears only after an initial flaccid paralysis.
6) Combined postcentral and area 4 lesions produce spasticity.
7) Addition of a contralateral motor area lesion to a lesion which resulted in spasticity, increases that spasticity.
8) Removal of an entire hemisphere secondary to the ablation of areas 4 and 6 increase the spasticity to a greater degree than does secondary ablation of the postcentral gyrus.

It is appropriate to pause at this point and summarize that findings that have been discussed as being resultant from cortical ablation.

A) General motor ablation
   1) Leyton and Sherrington (63) found that the ablation of a motor area caused a paresis in the contralateral extremity with eventual recovery of volitional movement which enable the animal to accomplish apparantly normal activity.
   2) Fulton and Keller (27) removed the leg areas of monkeys with resultant flaccid paralysis with recovery beginning in 24-48 hours. The same procedure in higher anthropoids yielded similar results, but recovery was at a reduced rate and with more residual paralysis. In one gibbon there resulted spasticity for 5 days. (Probable encroachment on area 4s.)
   3) Denny-Brown and Botterell (14) found similar results (though they noted the late development of spasticity) and added that the paretic limbs could be used efficiently under the stimulus of emotion.
B) Differential motor ablation
   1) Area 4
      a) Denny-Brown and Botterell (14). Flaccid paralysis succeeded by the development of spasticity distributed to the

proximal musculature with anterior division ablation and to the distal musculature with posterior division ablation. The rate of development of this spasticity depended on the presence of residual Betz cells, being hastened by their presence. This was interpreted to mean that their presence lessened "pyramidal shock".

b) Hines (37). Flaccid paralysis. See Hines (40) below.

c) Welch and Kennard (105). Paresis without spasticity.

2) Area 4s

a) Hines (38). The production of spasticity as manifested by increased resistance to passive movement, increased tendon reflexes, clonus. With this there was a moderate degree of transient paresis.

b) Hines (40). Clasp-knife type of passive resistance.

3) Area 6

a) Richter and Hines (87). There resulted the consistent production of the grasp reflex.

4) Areas 4 and 6 (It is probable that 4s is included)

a) Kennard and Fulton (50) found that bilateral extirpation of these areas resulted in a permanent and complete loss of voluntary power, extreme forced grasping and spasticity.

b) Hines (40) found that ablation of area 6 and the posterior division of area 4 caused the production of spastic paralysis, while area 6 and the anterior division of area 4 resulted in plastic rigidity.

5) Parietal ablation

a) Kennard and Kessler (51) and Peele (86) found that this resulted in moderate paresis (or as Peele interprets the state: loathness to move) and hypotonia. There was a tactile deficit and a lesser degree of proprioceptive deficit in unilateral ablation. With bilateral ablation there was the permanent loss

of both tactile and proprioceptive hopping and placing reactions.
b) Welch and Kennard (105) Removal of postcentral gyrus produces a transient flaccidity.

6) Various combined ablations. Welch and Kennard (105).
a) Removal of 6 and 4s causes moderate spastic paresis.
b) Ablation of 4, 4s and 6 causes immediate spastic paralysis.
c) Addition of postcentral ablation to that of a premotor or motor ablation leading to spasticity causes increased paresis and the persistance of the spasticity.
d) Addition of contralateral ablation to areal ablation yielding spasticity increases that spasticity.
e) Removal of an entire hemisphere secondary to removals of areas 4 and 6 increases the spasticity to a greater degree than does secondary ablation of the postcentral gyrus.

B. CORTICO-SUBCORTICAL CONNECTIONS AND EXTRAPYRAMIDAL SYSTEMS.

Dusser de Barrene and his co-workers have established the usefulness of strychninization of the cortex as a method of indicating functional inter-connections. This method has been termed "physiological neuronography" (71). This group has shown that strychnine applied locally to any region of the cortex causes the appearance of changes in the usual action potentials that are recordable from an area with which there are functional connections. These changes were designated by them as strychnine spikes (19).

This method has been particularly use in the demonstration of cortical-subcortical connections as they derive from the "suppressor strips" as exemplified by area 4s. The other suppressor areas which these workers have demonstrated on the lateral surface of the brain, 2s, 8s, and 19s, are shown on the frontispiece of this paper.

Dusser de Barrene and McCulloch (20) have shown that there is suppression of electrical activity in the arm and leg areas of area 4 as the result of local stryninization of the arm and leg areas of area 4s. That this involves connections with the nucleus caudatus and thalamus opticus has been indicated in the same paper. The nucleus caudatus is "fired" (i.e. develops "strychnine spikes") by the local strychninization of 4s, but not by that of areas 6 or 4. Further they report that local strychninization of the nucleus caudatus causes a typical suppression of electrical activity in the thalamus and in area 4 (by "typical" they mean like that achieved by stryninization of area 4s). From this they conclude that the normal electrical activity of the sensori-motor cortex (this term being used in the sense of the Jacksonian concept that sensory and motor activity are not separated discretely in the cortex) depends upon the influx of thalamo-cortical impulses and that this activity can be suppressed by strychninization of area 4s.

By laminar coagulation the same workers (22) have shown that in the cortex only the presence of layers v and vi are necessary for the occurance of this phenomenon.

Leão (59, 60, 61) and Leão and Morison (62) have elicited a type of cortical depression which apparently due to cortico-cortical connections, or perhaps to polarization-depolarization characteristics of membranes. The application of a current having low intensity to the cortex for a period of four to six minutes is accompanied by a spreading depression of activity in the cerebral cortex of the rabbit. Each cortical region first becomes negative with respect to an extracortical reference electrode for one to two minutes. This negativity reaches a maximum of eight to fifteen millevolts in one half to one minute and then decreases more rapidly. This is succeeded by a wave of positivity of lower amplitude for three to five minutes. This phenomenon is independent of sub-cortical connections and at least the deepest three cortical laminae. Sudden cortical anemia abolishes spontaneous electrical activity and prolongs the period of negativity of the slow voltage variation, and if the anemia alone is prolonged for two and one half to five minutes, it by itself produces the slow voltage variation for the duration of the anemia.

That this is to be contrasted with the phenomena elicited by Dusser de Barrene and his pupils is indicated by Leâo (recall that this phenomenon is unaffected by the removal of the lower three layers of the cortex). That this is not the same phenomenon is further indicated by the work of Sperry (89) who has shown that dicing of the sensori-motor cortex down to the superficial white matter fails to affect spontaneous activity more than transiently and no alteration in the usual excitability of the cortex is to be noted.

In a study stemming from the work on suppressor circuits, Dusser de Barrene, Garol and McCulloch (17) have found that with the exception of areas 2s and 4s, electrical stimulation of all of the sensory cortex (i.e. that cortex, stychninization of which causes evidences of somatic sensory excitement) elicits the contraction of skeletal muscles. Stimulation of area 4s and 2s causes suppression of motor response due to preceding and simultaneously continuing stimulation of cortical area 4. There is also suppression of motor after-discharge which normally follows cortical stimulation, and the succeeding relaxation of skeletal musculature on cessation of that stimulation. This does not occur with stimulation of the parietal cortex unless there has been primary facilitation from the motor

cortex and there is the presence of existing musclular tension (see also Leyton and Sherrington (63) referred to above). This study indicates that stimulation of the cortex probably utilizes the same connections to the lower (and other cortical) centers as does electrical stimulation.

Other cortico-subcortical connections as demonstrated by physiological neuronography have been reported by Garol and McCulloch (17, 31).

1) From areas 8s, 4s and 2s to the nucleus caudatus.
2) From areas 6, 4, and 1 to the putamen.
3) From area 6 to the external segment of the globus pallidus.
4) Possibly from areas 4 and 5 to the internal segment of the globus pallidus.
5) From the Rolandic arm area (arm subdivision of areas 4, 3-1-2) to the corresponding portion of the lateral thalamic nucleus.

Except for 4s they submit no physiological significance (as noted above) for these connections.

In addition to the above, Magoun (73) has found evidence by the same technique of connections between area 6 and the midbrain tegmentum, and also to that area from the lateral associational, limbic, sensori-motor and auditory cortical areas.

Garol and Bucy (30) have investigated the cortical suppression of motor response in man. Upon stimulation of what they think to be the "s" areas in man they have found sup-

pression of motor function following lesions in the caudate, putamen, globus pallidus, substantia nigra or following removal of the cerebellum. In the same paper they state that stimulation of the suppressor areas in the monkey and chimpanzee causes:

1) The lessening of existing muscular tension throughout the body, but more especially on the contralateral side.
2) A rise in the threshold to stimulation of area 4.
3) The failure to produce, in the absence of summation or recruitment, a motor response.
4) A return to normal electrical excitability of the cortex upon cessation of stimulation of the cortical cuppressor areas.

They note that all of these phenomena were abolished by undercutting the suppressor area.

In addition to these cortico-basal ganglear and possible corticospinal suppressor circuits, McCulloch, Graf and Magoun (72) have utilized the method of physiological neuronography to indicate possible connection between 4s and the bulbar reticular formation. They applied strychnine to 4s and were able to record strychnine spikes from the ipsilateral reticular formation (note the strychnine impulses will not be recordable past a synapse). This circuit is interrupted by section of the basis pedunculi, but not by section of the medullary pyramid. Using the Marchi method Verhaart and Kennard (96) have traced such a pathway

to the pons, while Hines (40) was able to trace such fibers to the reticular formation of the bulb.

Hines (40) reports that the inhibitory action obtained from the cortical surfaces of areas 4s, 6 and 8 with the pyramids severed is non-topical and bilateral. As stated earlier she has indicated that these regions share appreciable projection systems to the substantia nigra and the reticular formation. Also the cortico-tegmental fibers from 4s ending in the midbrain form a large bundle, while those from 6, 8 and posterior 4 consist of a few scattered bundles. She suggests that those from 4s carry impulses inhibiting the standing tone that is exaggerated subsequent to ablation of 4s.

In an interesting study Bodian (5) has produced poliomyelitis in rhesus monkeys and then sacrificed them while they were still in the preparalytic spastic phase of the disease. In the cord he found only minimal lesions which were confined to the last cervical and first thoracic segments. The severest lesions were found in areas 4 and 6, the dorsal thalamus, the fields of Forel, the substantia nigra, the superior colliculi, the midbrain tegmentum, the reticular formation of the midbrain, the vestibular nuclei and the basal cerebellar nuclei. Of these severe lesions,

the most severe were found in the reticular formation and in the vestibular nuclei. These findings in a spastic type of paralysis in the light of the proposed cortic-bulbo-reticular pathway from 4s that has been presented above gains importance from and adds emphasis to the indications of an inhibitory mechanism in the bulbar reticular formation demonstrated by Magoun and Rhines (75, 76). These workers found that electrical stimulation of the bulbar area caused an inhibition of motor activity whether initiated reflexly, in decerebrate rigidity or by stimulation of the "motor" cortex. This excitable region was found to be distributed in the bulbar reticular formation chiefly in the ventromedial part, but with a long antero-posterior distribution of some of the excitable points. They suggest that this is the starting point of the second neuron of a 4s-reticulospinal (or cranial motor nerve) inhibitory system.

Niemer and Magoun (83) have found reticulospinal tracts which facilitate motor activity arising from each level of the brain stem, while the inhibitory tracts referred to above restrict their origin to the bulbar segment. The influence of these connections from each side of the brain stem is held by these workers to be exerted upon both sides of the cord. Both brain stem and spinal crossings were found for those tracts whose stimulation is followed by inhibition of

activity. They found these reticulospinal connections to be widely distributed in the lateral and ventral funiculi of the cord. It was noted that those fibers subserving facilitation occupied and area which overlapped the area which carried inhibitory fibers, but these were respectively relatively concentrated dorsally and ventrally within the spinal white matter. Magoun (73) reports that the inhibitory effect produced by the stimulation of these fibers as they lie in the brain stem can be evoked by brief shocks and that the fibers are possessed of a low threshold.

Cannon, Magoun and Windle (12) found that the interruption of the basis pedunculi in the monkey gives rise to a paralysis which is characterized by being intermediate in quality between flaccidity and spasticity. These characteristics are described as hypotonicity of all muscle groups except for the extensors of the digits, hyperactive tendon reflexes and the absence of clonus. They hypothesize from these findings that inhibitory pathways descending from the cerebral cortex do not course entirely within the basis pedunculi, thus they believe that the fibers whose interruption is responsible for the phenomenon of hypertonicity and clonus have deviated in part from the corticospinal projection prior to reaching the cerebral peduncles. Comparing their findings with those of Tower (to be discussed in the section

on the pyramidal tract), they conclude that these fibers whose interruption in the basis pedunculi is followed by hyper-reflexia, deviate from the pyramidal fibers before the level of the pyramids is reached.

In a similar way Whittier and Mettler (107) found that in fulgerated lesions directed at the subthalamus, there was the development of spasticity in six instances, four of the monkeys exhibiting lesions in the medial part of the peduncle; however in three cases with similar lesions no spasticity was present. They found also that the appearance of paresis was associated with the destruction of the pallidum or its efferent pathways when such lesions were accompanied by destruction within the internal capsule of the peduncle.

Mettler, Ades, Lipman and Coller (80) studied the effects resulting from the stimulation of various of the basal ganglia. They found that stimulation of the caudate, putamen or claustrum inhibits the execution of movements induced by cortical stimulation, this effect being most marked on those movements which were initiated from the ipsilateral cortex. Stimulation of the globus pallidus in this study exerted a "holding" effect on cortically induced movement. Subsequent to the cessation of the cortical o-

cortical and pallidal stimulation the time required for relaxation of the part was prolonged. This effect as well as the inhibitory effect referred to above was most marked ipsilaterally. In the same work stimulation of the substantia nigra caused the production of increased extensor tone, principally in the contralateral part of the body and imparted a factor of tremor to cortically induced movements. Stimulation of the subthalamic body or the region of the red nucleus produced contraction of the contralateral dorsal midline musculature.

In the placing of lesions in the basal ganglia of the cat, Liddell and Phillips (65) found that there resulted the development of a slight but persistant contralateral extensor hypertonia. They noted that there was no clasp-knife phenomenon seen in this extensor rigidity.

Mettler and Mettler (81) undertook a study of the effects of striatal injury. They found that ablation of the caudate and putamen causes the development of hyperkinesia which can be quieted by the reduction of proprioceptive and especially tactile stimuli from the extremities. Here it is again noted by Mettler that he is unable to produce anything but inhibition of activity by stimulation of the striatum.

As the spastic hemiplegia from cortical lesions is less than that following lesions of the internal capsule and contiguous structures, Mettler (78) has found that there is less spasticity (as measured by resistance to passive movement, lowering of reflex threshold, hyperactivity of reflexes, enlargement of reflexogenous zones and the spread of reflexes or clonus) following hemidecortication alone than following ablation of cortex, putamen and caudate. When the subthalamus is destroyed, there results a sustained resistance to passive movement.

In an electromyographic study of spasticity following injury to "suppressor systems" in the cats brain Lindsley et al (67) have found that the most characteristic feature was the exageration of stretch reflexes, most marked in the antigravity muscles. The threshold of the stretch reflexes was low, the response to the stimulus was excessive and its prolongation after the cessation of the stretch was frequent. There was, following these lesions, a hyperactivity of reflexes, these reflexes being repetitive, commonly inducing clonus. After the spasticity following lesions of the cerebral or cerebellar (vide infra) cortex had subsided, injury to the caudate nucleus caused the reappearance of spasticity. They noted that the most severe spasticity resulted from combined lesions of the cerebral and

cerebellar systems. Schreiner et al (88) found that in cats with pre-existing spasticity, lesions of the basal ganglia or upper brain stem did not significantly decrease the spastic state in any instance, but was frequently followed by and increase in spasticity.

Kennard and Fulton (50) have found various dysrhythmias appearing after large lesions of the putamen and globus pallidus, or following smaller combined lesions of the cortex, nucleus caudatus and the putamen. The tremor following such lesions is found only during complex movements or postural adjustments. Such tremors may be present following the abatement of paresis resulting from the included area 4 and area 6 lesions, but it is not present during the peak of that paresis. With lesion of the globus pallidus, the area 4 lesion which is made in the approach to the pallidum, confuses the source of the resulting increased resistance to passive movement and hyperactive reflexes.

The relation between pyramidal and extrapyramidal function has been investigated by Mettler (77) who states:

> "The pyramidal and extrapyramidal systems constitute a closely organized and integrated functional unit. Not only the final motor neuron, but also the cortex forms a common ground for these two so-called systems. In this arrangement, the striatum occupies the position of an inhibitory mechanism. Stimulation of it produces inhibition and removal of it engenders evidences

> of motor release. It stands...between the cortex and the final common path as a part of the route through which the cortex may exert an inhibitory effect.... The pallidum is contrasted with the striatum as a positive motor mechanism through which associated movements involving the larger muscle masses (chiefly those of axial and proximal portions of the appendicular skeleton) are involved in motor discharge."

In a later paper, Mettler (81) investigated the effect of brain stem lesions on the patellar and plantar reflexes. changes in these may be produced (in the absence of evidence of paralysis) by damage to the lentiform (the effect being contrlateral), to the mesencephalic tegmentum (the effect being usually ipsilateral) or damage to the area occupied by the rubrospinal system in the pons and medulla (usually producing a homolateral effect). In each of these the plantar reflex is abduction and/or extension of the hallux with or without extension of the toes. (In the monkey, the form on which this study was made, this has been considered as the equivalent of the Babinski in man by Fulton and Keller (27).) In no instance was Mettler able to produce these altered reflexes by damage to the reticulospinal or vestibulospinal systems.

Magoun and McCulloch (74) have found in cats and monkeys that excitation of: 1) the tactile projection areas of the cerebellar cortex (which is that cortex near the vermian

vein of the anterior lobe and the anterior folia of the paramedian lobule); of 2) the fastigeal nucleus; of 3) the bulbar reticular formation; or of 4) its descending fibers in the angle of the pyramidal decussation all result in the suppression of the motor response to cortical stimulation, diminished tendon reflexes and relaxed decorticate or decerebrate rigidity. With the electrical recording of impulses initiated in the cerebellar cortex they found that three milleseconds elapsed before the impulse reached the bulbar reticular formation, while only one millesecond elapsed when the impulse was initiated from the fastigeal nucleus. By destruction of the above structures together or separately there was the enhancement of tonus and deep reflexes. In this system the effects were unilateral for the most part. Sprague et al (90) found that the stretch reflexes of decerebrate cats were decreased by stimulation of the reticular formation or by stimulation of the cerebello-bulbo-reticular fibers.

Schreiner et al (88) found that the stretch hyperreflexia of spasticity was decreased by section of the pontobulbar tegmentum and abolished by the destruction of the vestibular nuclei. They concluded that spasticity is maintained by a facilitory influx to the cord conducted by the bulbar facilitory fibers in part, and in part by the vestibulospinal tracts. This system is, as deduced from this

brain stem transection, supplemented by flow of impulses from higher centers "for the production of spasticity".

In the literature surveyed in this section on extrapyramidal systems there have been indications of at least two pathways by which there can be inhibition of movement.

> The first of these is that presented by Dusser de Barrene and others (17, 20, 30, 80). The structures involved in this pathway include at least 2s and 4s in the cortex, the caudate, the thalamus and possibly the putamen and the claustrum (80). It has been shown that stimulation of 2s and 4s causes the suppression of motor response (17). It has also been shown that stimulation of 4s inhibits the spontaneous activity of area 4 and of the thalamus as does stimulation of the caudate as well (20). Stimulation of the caudate, putamen and claustrum inhibits cortically induced movements, while stimulation of the globus pallidus causes a holding effect on existing motion and a prolongation of relaxation time after muscle contraction (80). From these phenomena, the pathway most convincingly suggested is from 4s to the caudate to the thalamus and from the thalamus to area 4. When 4s has been stimulated there is a cessation of activity within the thalamus and consequently within area 4. The findings from the ablation of the basal ganglia indicate that there is the development of resistance to imposed movement. "Basal ganglear" lesions (65) produce a slight, persistant, non-clasp-knife type of hypertonia. Hemidecortication plus destruction of the caudate and putamen produce greater spasticity than does hemidecortication alone (78). Partial injury to area 4 and destruction of the globus pallidus causes increased resistance to passive movement and hyperreflexia (50). Just what part of the phenomena is due to the lesion of the pallidum, and what part to lesion of area 4 cannot be evaluated.
>
> That there is a second pathway for the inhibition of motor function is indicated since the stimulation of the cortex causes the suppression of motor response following lesions

> of the caudate, putamen, globus pallidus or substantia nigra (30). The pathway from 4s to the reticular formation (72) is such a route, and it has been given support by the indication of suitable fiber tracts by means of the Marchi method (40, 96). Stimulation of either 4s or the reticular formation causes the inhibition of motor activity (17, 73, 75, 76, 83). Indications from lesions of this pathway as one method by which spasticity can be produced have been given in the case of the lesions of pre-paralytic (spastic) poliomyelitis (5). It has also been noted that this reticular system is influenced by connections from the cerebellum by way of the fastigeal nucleus (67, 74, 88, 90).

Here then are two paths which apparantly carry inhibitory impulses, one acting at the cerebral level and one acting on the cord via the reticular formation, and perhaps the basal ganglia. Lesions involving these circuits produce spasticity or spastic-like states. However as far as discrete lesions are concerned, only damage to 4s has produced spasticity of a degree approximating that observed clinically.

C. THE PYRAMIDAL TRACT

That the signs of release seen in spastic paralysis are not entirely due to injury of the pyramidal tract was clearly indicated for the first time by Tower in her experiments involving the unilateral section of the pyramidal tract in the cat.(91). Foerster (25) found that deafferen-

tation of spastic muscles abolishes the spastic phenomenon. It was his theory that the pyramidal tract exercises both excitatory and inhibitory functions. The latter consisted of the "imbibing or sucking up" of the excess afferent impulses which reach the ventral horn cell.

> "If this inhibition fails, the unimpeded sensory afflux charges more and more the anterior horn cell, increases its excitability and produces a permanent motor stream from the ganglion cells to the muscle, that is to say, the spastic contracture."

The concept that both spasticity and paralysis was due to injury of the pyramidal tract has has much influence on the thinking of clinicians and research workers. Before Tower's experiments on the section of the pyramidal tract in the cat (91) and in the monkey (93) there were indications that the explanation of these phenomena was not entirely true. Some of these will be mentioned in the next section of this paper.

In the cat Tower (91) found that after unilateral section of the pyramidal tract at the level of the trapezoid body, there supervened a paresis of the contralateral extremities in which they were held in extension. If the animal were placed in the supine position, the legs on both the normal and affected sides would be held in extension. Shortly, however, the unaffected legs would begin to flex and thereupon would resist extension imposed by the obser-

ver, but would aid flexion so imposed. The affected legs were not considered to be held stiffly in extension, but were "almost neutral, neither flexion or extension being much resisted, and passive flexion imposed was commonly retained". She interpreted the extension of the affected limbs as a normal extension abnormally prolonged because of a deficiency in flexor activity. In the affected limbs she noted also an absence of clonus and clasp knife phenomena and other signs of spasticity except moderate resistance opposed to passive movement. This picture, she felt, was sufficient demonstration that severing the pyramid does not increase the excitability of the spinal extensor center as does the hemiplegic lesion of man. She postulated that the excitatory and inhibitory effects of cortical activity were dissociated to a large extent at some pre-spinal level. (N.B. From evidence presented above (11) this dissociation may occur between the level of the basis pedunculi and that of the medullary pyramid.) The excitatory component was considered as passing to the spinal cord as the corticospinal tract. In this paper she states (91):

> "The pyramidal section, by destroying the... excitor component which is largely flexor produced the manifold deficit...one aspect of which was uninterrupted extension. Yet by preserving virtually intact the second inhibitory component, the syndrome was kept free of evidence of subcortical release, as rigidity and spasticity."

Another expression of this concept is Hines' statement (37):

> "We would allocate paralysis to the interruption of the corticospinal tract, and spasticity to that of the extrapyramidal systems closely associated in cortical space."

Liddell and Phillips (66) repeated the procedure utilized by Tower because they felt that from the sections presented in her paper that she had damaged the medial fillet as well as the pyramidal tract. They found that division of a single pyramid is followed by increased tone in the extensor muscles of the contralateral limbs, especially the hind limbs. The increase in tone is permanent and the resistance in them to forced flexion was of the same order as the body weight of the animal. They found that bilateral division of the pyramids reduplicates the findings. They note that the performance of many muscular acts is unimpaired, especially those acts which they characterized as being of a semi-automatic character, i.e. progression. This description follows more closely the classical description of the symptomatology of pyramidal lesion, with tonus greater in the extensor muscles than in the flexor muscles, but the absence of clasp-knife phenomena is noteworthy. It should be remarked that although Tower's inferences from her findings state that there is no increased extensor rig-

idity, the description of her cats is remarkably like that of Liddell and Phillips. It is possible that the increase in the tonus of the extensor muscles is equivocal.

Perhaps the most important lesion of the pyramidal tract of which a complete report has appeared in the literature at this writing is that accomplished by Tower in the monkey (93). She was able to accomplish this by severing the pyramidal tract both unilaterally and bilaterally with minimal involvement of other structures. She presents an analysis of her histological studies of these lesions.

> "Reconsidering this anatomical material, two facts are outstanding. First, damage to the cranial nerves of their nuclei excepted, the lesion may considerably transgress the limits of the medullary pyramids, without introducing variations into the symptom complex. Most significantly, damage to the medial lemniscus has ranged from nil to quite grave without this being appreciated. With unilateral lesion, slight damage to the remaining pyramid has also been without consequence except for the tongue. Although the medially lieing fibers, which are the ones so damaged, are many of them corticobulbar, they are probably not all so, and the limits set on minuteness of examination by the uncooperative monkey, must mask slight degrees of paresis, degree that would, perhaps, be demonstrable in the human. Only destruction penetrating deep into the tegmentum has produced additional symptomatology within the scope of this analysis. It is noteworthy that except when the deep tegmentum is damaged, there are no degenerating fibers within the inferior olive, eliminating that source of possible confusion.
>
> "Second and basic to the argument that section of the medullary pyramids interrupts [illegible]

> corticospinal action and that alone, is the fact that retrograde degeneration stops short almost immediately above the lesion. This means that the nerve cells fiving rise to the corticospinal fibers, together with their axones down to the pons have survived amputation of their longest terminal. It is reasonable to assume therefore that these cells and their prepyramidal terminal, of which the last would be the pontine collaterals, are intact and functioning. If this be true, that except for the corticobulbar involvement, severing the medullary pyramids has produced the desired interruption of corticospinal function, and that alone."

The state that she describes as resulting from unilateral lesion is hypotonic paresis which affects all somatic function and some visceral function. The features of this paresis are diminished muscle tone, reduced cutaneous reflexes, slow, full, pendular tendon reflexes, defective initiation and depression of all motor performance, the disappearance of all "non-stereotyped" behavior and the elimination of all discrete usage of the digits. (It should be noted that Walshe (101) and Denny-Brown (15) dispute the use of the term "discrete" as applied to the use of the digits, in that no digital movement is accomplished in a discrete way. I feel that this argument is largely a semantic one, since she defines her use of the word discrete as the accurate approximation of the thumb and index finger, or of the thumb and all of the fingers as in the "grooming act" or in the picking up of small objects, the former

which she found to be absent and the latter grossly impaired.)

The striking phenomenon within the orientation of this paper is the hypotonia which Tower found following this lesion. In her unilateral sections the hypotonia was to be seen and felt at all times that the animals were awake. There was diminished resistance to passive movement in all joints and in all directions through which the joints could be moved consistent with anatomic continuity. The distribution of this hypotonia was not equal. The lower extremity was more hypotonic than the upper and both were more so than the trunk. In the extremities the proximal musculature was more hypotonic than the distal. Also the tone was affected by posture. Sitting in a chair all the muscles of the shoulder were about equally and gravely affected, but from the shoulder to the digits the extensors were more hypotonic than the flexors and the finger abductors more so than the adductors. In the leg, flexors and extensors of the knee were about equally slack, but the dorsiflexors of the foot and the plantarflexors and adductors of the digits were more affected than their antagonists. When standing and to a lesser extent when supported prone, she found the tone to be increased in the antigravity muscles so that the previously weaker plantar flexors of the toes and the extensors of the knee to be greater than that of their antagonists, though

still more slack than the corresponding muscles of the normal side. She was unable to elicit tonic neck or labyrinthine reflexes, nor were clonus or the clasp-knife phenomena elicitable. In bilateral lesions the deficits were changed only in that the methods of compensation for motor deficits were achieved with more difficulty and in that the animal became exceedingly fatigued by all activity. There was in these lesions no evidence of spasticity.

Denny-Brown (15) states in a footnote that he has accomplished pyramidal section in the monkey with resulting plastic type of resistance to passive movement. As he has not as yet published a full report, no further information as to his results, either physiological or anatomical are obtainable.

In an analysis of her findings in regard to pyramidal section in the monkey, Tower states (93):

> "The deep reflexes are unattended by adaptive reflexes or by active rebound or afterdischarge of any sort....Movement is sweeping and sometimes grossly tremulous, poorly gauged to the objective, and suggestive, in the hypermetria, of the phenomenon of past pointing. In this connection, the very slackness of the muscles themselves must constitute a condition in which the volume of incoming sensory stimulation per unit of displacement through space is materially reduced contributing further to delay and weakened reactions of proprioceptive origin in the extremity responding."

Utilizing the concept that one of the functions of the pyramidal tract is to permit more delicate actions of muscles, which seems accurate from the nature of the deficit following relatively pure pyramidal lesions, I interpret this deficit to mean that the afferent limb of the motor mechanism is functioning properly and that the proper integrations take place at the higher centers, but that one of the executive members of that system is destroyed and so the proper combination of impulses is prevented from reaching the anterior horm cells and the integrative mechanisms of the cord. Thus the movements which are possible must be those which can operate with those connections making up the extrapyramidal systems (such as the reticulospinal facilitory system of Magoun (73, 83). Thus it would seem that considering the flail-like movements that Tower states are the result of pyramidal lesion, proprioception, at least, is intimately involved in normal pyramidal function. Some of these proprioceptive impulses and their "meanings" in the higher centers of integration are lost to the lower centers by the destruction of the pyramidal tract. Tower feels that performances may be eliminated by pyramidal lesion, either because they are specific functions of the pyramidal tract in the sense that no other system is able to create the pattern of performance or, because they

they are dependent upon this tract not for organization, but for a reinforcement that brings them to threshold.

In a later study Tower (94) undertook the placement of pyramidal lesions in the pons with resultant incomplete bilateral damage, and complete and incomplete unilateral interruption in several monkeys. She states:

> "The results of the pons lesions, as distinguished from...the results of corticospinal lesions were simple, consistent, and unexpected. Outstanding was spasticity, producing in all parts of the body exaggerated postural and tendon reflexes, excessive tone of "clasp-knife" quality, and readily elicitable clonus. These effects were most marked in parts showing no evidence of pyramidal lesion, but when superimposed upon the effects of such a lesion they modified the familiar hypotonic paresis in the direction of spasticity."

Cannon, Beaton and Ranson (11) have interrupted the lateral corticospinal tract of monkeys producing a paresis, more predominant in the lower than in the upper extremities when the lesion was placed at the level of the fourth cervical segment, the weakness being more prominant in the distal than in the proximal musculature. The paresis so produced is characterized by hypotonicity, hypoactive reflexes and absence of clonus, indicating that there is in this tract no pathway whose interruption produces spasticity.

The three experiments summarized here show that there

seems to be a difference in the results when the lesion is placed in the medullary pyramids, in the lateral corticospinal tract or in the pons. Actually from her summary of pontine lesions, we do not have any indication of the exact extent of the lesions except that damage was found in the pyramidal fibers. Other experimenters, notably Magoun, as has been mentioned above, have found tracts in the same region interruption of which is followed by spasticity and whose stimulation causes inhibition of activity, and have related these findings to a cortico-reticulospinal system. This may have been the system damaged with the resultant spasticity observed by Tower in the pontine lesions. On the other hand possibly only pyramidal fibers were interrupted. If this be the case another hypothesis can be entertained, if it be assumed that at the level of the interruption some, at least, of the bulbar collaterals have not left the pyramidal fibers, and that the interruption above this branching interrupts fibers to structures the innervation of which must be interrupted for the production of spasticity. I have been unable to find data for either of these possibilities nor have others been suggested in the literature. Of the two the former seems to be the more likely in the light of available evidence. All of this however is based on the assumption, one made in the absence of definite evidence to the contrary, that Tower's observations of med-

ullary pyramidal section in the monkey were accurate. The finding of Denny-Brown, as yet undocumented in the literature, and the discrepancy between the findings and analyses of Tower as over against those of Liddell and Phillips should make one hold some reservations of the subject.

Lloyd (69) has stimulated the proximal ends of the dissociated segement of the severed isolated medullary pyramids producing effects which were all excitatory and none of which were inhibitory. As mentioned in the section on anatomy, the endings of the tract are in the intermediate grey matter of the cord, and it is Lloyd's interpretation that they are thus in a position to influence both the motor neuron and the sensory fibers entering over the dorsal root.

Lassek (56) made a study of the histories and autopsy records of individuals with tumors of the brain producing paralysis. In the cases of tumor with a unilateral motor deficit, he found that one or more of the classical pyramidal tract signs might appear with little or no loss of axones in the pyramidal tract. He found that in 6.7% of 119 cases presenting the appropriate history, destruction of the pyramidal tract was complete; in 7.6% of the cases the destruction was partial. Thus in cases presenting the

classical pyramidal symtoms only 14.3% of the cases showed any demonstrable pyramidal tract damage. He concluded that tumors located in any part of the cerebrum may produce motor difficulties without signs of damage to the pyramidal tract. He also reported that 88 out of 102 cases presenting the Babinski sign there was no demonstrable pyramidal lesion. It should be noted that this was an anatomical study and as such gives no information as to the functional state of the pyramidal tract. Also it gives no evidence as to other tracts involved. As such it gives only partial negative evidence as to the production of symptoms of the so-called upper motor neuron lesion. In the presence of the evidence as to pyramidal tract function, it is not lesion of the pyramidal tract per se that is operative in the production of spasticity.

IV. COMMENTARY

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Among the earliest thinkers to consider mechanisms to account for the appearance of phenomena such as spasticity, rigidity and other accompaniments of central nervous system injury was the brilliant theorist and clinician, John Hughlings Jackson. In the course of his thinking he developed two general concepts in the attempt to account for these findings. These are presented in a collection of his writings (45). The earlier of these, involved what could be termed "release" and the second "influx". Of release he stated:

> "The symptomatology of all nervous disease is a duplex;...in every case there is a negative and...there is a positive element.... The doctrine of evolution implies...that there is an 'adding on' of new organizations. But this 'adding on' is at the same time a 'keeping down'. The highest nervous arrangements evolved out of the lower, keep down those lower.... If this be the process of evolution, than the reverse process, of dissolution, is not only a 'taking off' of the higher, but is at the same time a 'letting go' of the lower.... The higher nervous arrangements inhibit (or control) the lower, and thus when the higher are suddenly rendered functionless, the lower rise in activity"

By this statement he meant that as evolution proceeds the functions of older, more primitive structures are taken over and superceded by newer more highly developed ones. When these developmentally later and more integrative structures are damaged or destroyed by insult of one sort or an-

other, those lower are released to function unimpeded and there results rigidity, hyperactive reflexes, clonus, spasticity and/or contractures.

However, Jackson did not seem to be satisfied with this concept, for he developed the theory of "influx" at a later time as an alternate explanation of the appearance of spasticity etc. Of "influx" he wrote:

> "this hypothesis starts with the assumption that the spinal centers recieve impulses from both the cerebrum and the cerebellum" which normally oppose each other. "In accordance with this hypothesis the rigidity of the common cerebral paralysis, hemiplegia, results because cerebral influence upon these centers is no longer antagonized; there is then unimpeded and, therefore, greater cerebellar 'influx' into the lowest motor centers and hence rigidity of the muscles."

Of these two concepts, that of influx seems to be the one which most closely corresponds to the facts elicited since then by experimental investigation, and it is the concept most widely held today, although many writers refer to the phenomena involved as "release" phenomena. In discussion of "release" phenomena however, they are spoken of as being the result of the lack of opposition of systems which are "amicably antagonistic", resulting in the findings of spasticity etc.

In reviewing literature which has accumulated since the presentation of Hughlings Jackson's theory, two general

concepts of the genesis of spasticity have become apparent. These will be presented and evaluated separately.

One of these stems from Foerster's idea that the pyramidal tract is both excitatory and inhibitory in function. If this is the case than destruction of, and damage to the tract would result in both spasticity and paralysis. In the section on the function of the pyramidal tract the vast bulk of data presented indicates that it is facilitory in function. Section of the pyramidal tract has resulted in hypotonic paresis in the hands of Tower. Lloyd and others have found that stimulation of the central ends of severed pyramidal fibers produces no inhibition of activity, but results in motor activity. There is here indication that the impulses carried by pyramidal fibers at, and distal to, the level of the medullary pyramids are facilitory in function. Doubt is cast upon this by the finding of Denny-Brown (15) from his section of the pyramidal tract as noted above; the findings of Liddell and Phillips in the cat (60); and the questioned validity of the analysis by Tower of her findings in the cat (91). The possibility exists that the pyramidal tract is not of a single functional nature, but is mixed, containing both inhibitory and facililitory fibers. Elucidation of this awaits further experimental study.

The second concept as to the genesis of spasticity is based on the notion that the pyramidal tract is solely excitatory in function while the extrapyramidal system includes both excitatory tracts and inhibitory tracts. Lesion of the excitatory tracts in the extrapyramidal system or in the pyramidal system leads to the development of paresis or paralysis, while injury to the inhibitory tracts causes the "release" of the phenomena of spasticity etc. Or to put it in another way, the activity of the excitatory system is now unopposed by the modifying influences of the inhibitory systems and as such causes unimpeded facilitation in the lowest motor centers.

The remainder of this presentation will be devoted to a discussion of what these inhibitory and excitatory systems, both pyramidal and extrapyramidal seem to consist and how they could function integratively.

We have seen that Hines (36) has been able to produce spasticity which developed early in the post-operative phase by the ablation of a narrow strip of cortex which has since been designated as area 4s. This spasticity was accompanied by clasp-knife phenomena, hyperactive reflexes and clonus. After ablation of area 4 other than the strip area, she observed only hypotonic paresis. Denny-Brown and

Botterell (14) were able to confirm the production of spasticity after anterior area 4 lesion. That Dusser de Barrene and others have been able to elicit an inhibitory action from 4s and not from adjacent areas 4 and 6 indicates that there is probably in 4s a concentration of elements, which when stimulated results in the inhibition of motor activity, and when destroyed is followed by the development of spasticity.

However a difficulty arises from the observations of Denny-Brown and Botterell, who in addition to confirming the work of Hines as regards the anterior portion of area 4, found that ablation of posterior area 4 also resulted in the production of spasticity rather than the flaccidity found by Hines. The spasticity which they found in posterior area 4 lesion was somewhat different in distribution, later in development and quantitatively less severe. A possible explanation of these contradictory findings may be deduced from the findings of Hines and Boynton (41). They have studied the development of the electrical excitability of the motor cortices of the foetal and infant macaque. They found that in the early development of the nervous system, the types of movement elicitable by electrical stimulation of the cortex were of what they termed a "non-pyramidal"

or "holokinetic" type, e.g. the defecation pattern, the clutching pattern and movements of progression. In the same area were found points whose stimulation resulted in chalasis or the inhibition of movement. Later in development there appeared a new type of activity resultant from electrical stimulation of the same area of the cortex. These were movements termed the pyramidal or "idiokinetic" type which consisted of activity of individual muscles or muscle groups. As these idiokinetic points appeared they were surrounded by holokinetic points and points the stimulation of which resulted in chalasis (relaxation or inhibition of contracted muscles). As the areas for idiokinesis became larger, the areas for holokinesis and chalasis were to be found only rostrally. But rather than being replaced by idiokinetic points, the formerly holokinetic and chalatic points were overlayed. By manipulation of the stimulating current applied to an area which usually produced idiokinesis, holokinetic movements and chalasis could be produced.

We can see from this paper that there are suggestions of two general types of cortical elements. These termed idiokinetic or pyramidal are considered to be concentrated in area 4, and those termed holokinetic and chalatic (together, extrapyramidal) are found in both the motor and pre-

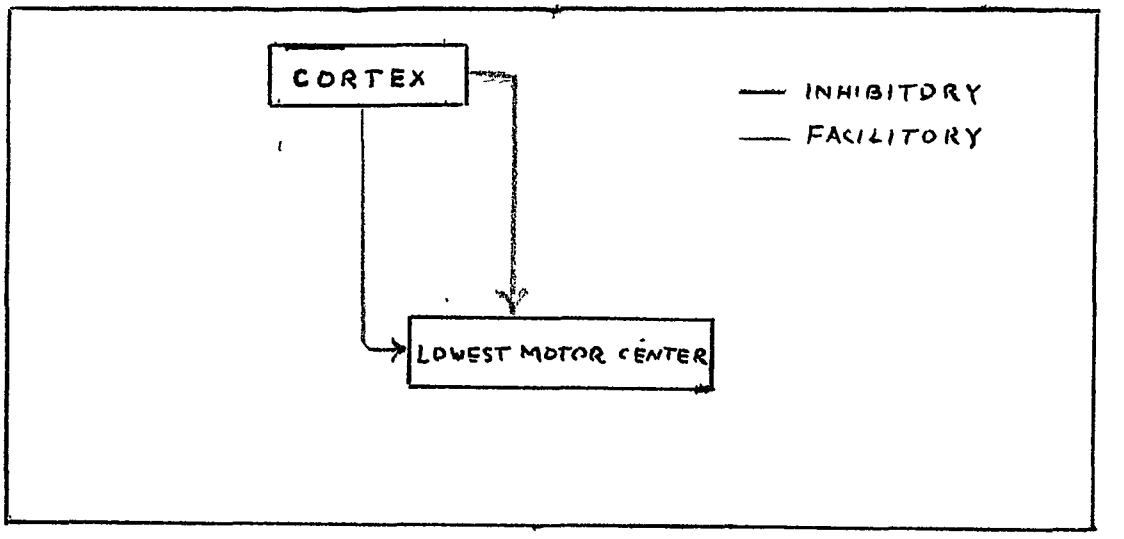
motor cortex, but seem to be the most concentrated in the latter. If we assume that the concentration of these elements is as follows, it is possible to understand the discrepancy between the findings of Hines and those of Denny-Brown and Botterell. In area 4 there is a high concentration of pyramidal element and a lesser concentration of extrapyramidal (holokinetic and chalatic) elements. Ablation of this area would result in paralysis (due to many pyramidal elements) and less marked spasticity (fewer inhibitory elements). This spasticity is due to the fact that facilitation of the lower motor centers is not lost, but persists from other areas. On the other hand ablation of 4s which contains many inhibitory elements and few of the pyramidal results in minimal paralysis and a high degree of spasticity.

Although the above paragraph is extrapolation, some supportive evidence has been presented in earlier sections of this paper.

1) We have seen that a high proportion of the pyramidal tract has its origin from area 4 (55).
2) Hines and Boynton (41) have found that the appearance of idiokinetic movement correlated with the functional maturation of the pyramidal fibers.
3) Data from the work of Verhaart and Kennard (96) indicates that non-pyramidal fibers have origin from area 4. And finally,
4) fibers have been shown to arise from area 4s by Hines (40) which appear to have an inhibitory function.

I feel then that the possibility is not remote that the observations of Denny-Brown and Botterell as well as those of Hines and others are not mutually exclusive, but rather that the conditions of observation and the criteria for spasticity were different, the former workers eliciting more subtle signs of spasticity. The essential conclusions that both inhibitory and facilitory fibers arise from the cortex is indicated by the findings of both workers. If the above hypothesis by which the attempt is made to harmonize the divergent findings is true, differential lesions of relative concentrations of these elements could produce a condition which is primarily spastic or predominantly paretic.

In the figure below a composite schematic representation is begun of facilitory and inhibitory tracts from the cortex (and other centers) the the lowest motor centers.



It is of interest to note that in 1919 Walshe (99) made the suggestion that there was evidence that cerebral lesion underlying a typical spastic hemiplegia might consist, in addition to a destructive lesion of the cortico-spinal path, in the interruption as well of another descending pathway. He quotes Bergmark (4) as saying that:

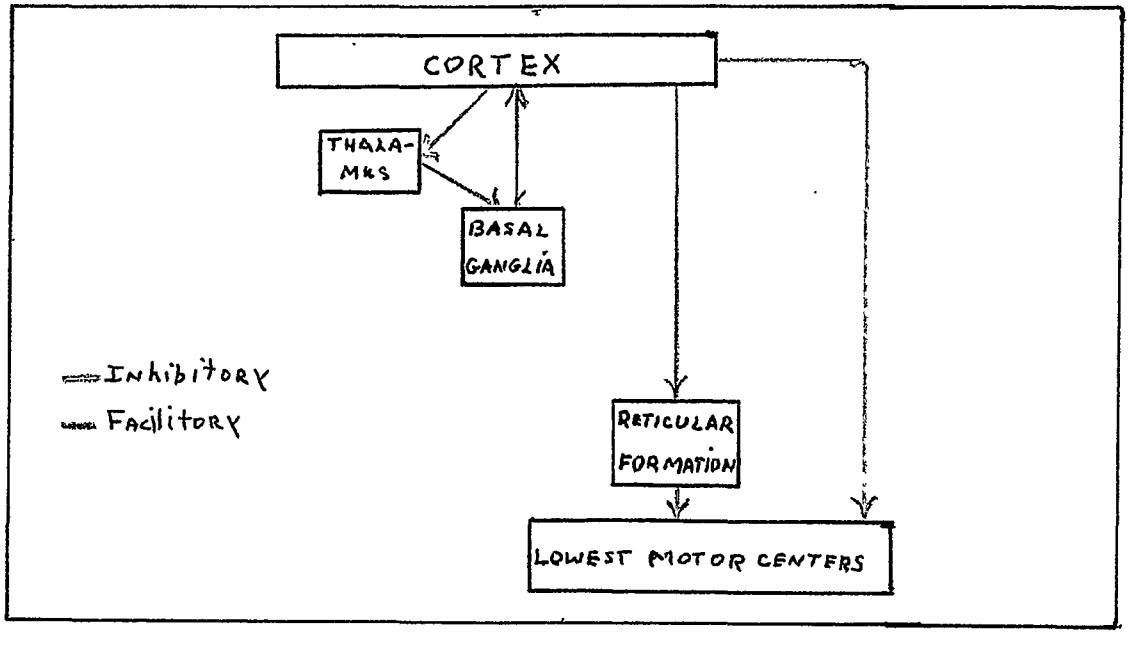
> "Cortical lesions do not produce definite increase of the reflexes or the typical late contracture found in hemiplegia of capsular origin."

Walshe further states that Weed (104) believed that the inhibitory influences arises in the cortex and is tracable to a spot in the mesial anterior portion of the internal capsule, stimulation of which caused the inhibition of the rigidity of the decerebrate animal. Weed was able to trace this area down to the medial one fifth of the crus. This area was occupied not by pyramidal fibers but by fronto-pontine fibers which Campbell (10) had been able to show as originating in the (his) intermediate precentral area. (Note that by this region he may have meant either anterior area 4, area 6 or part of both.)

That there are two broad pathways from 4s for the inhibition of activity has been indicated, one lieing entirely within the hemispheres involving area 4s, the caudate, thalamus and area 4, and the other descending to act upon cells in the bulbar reticular formation (31, 40, 41, 72, 75).

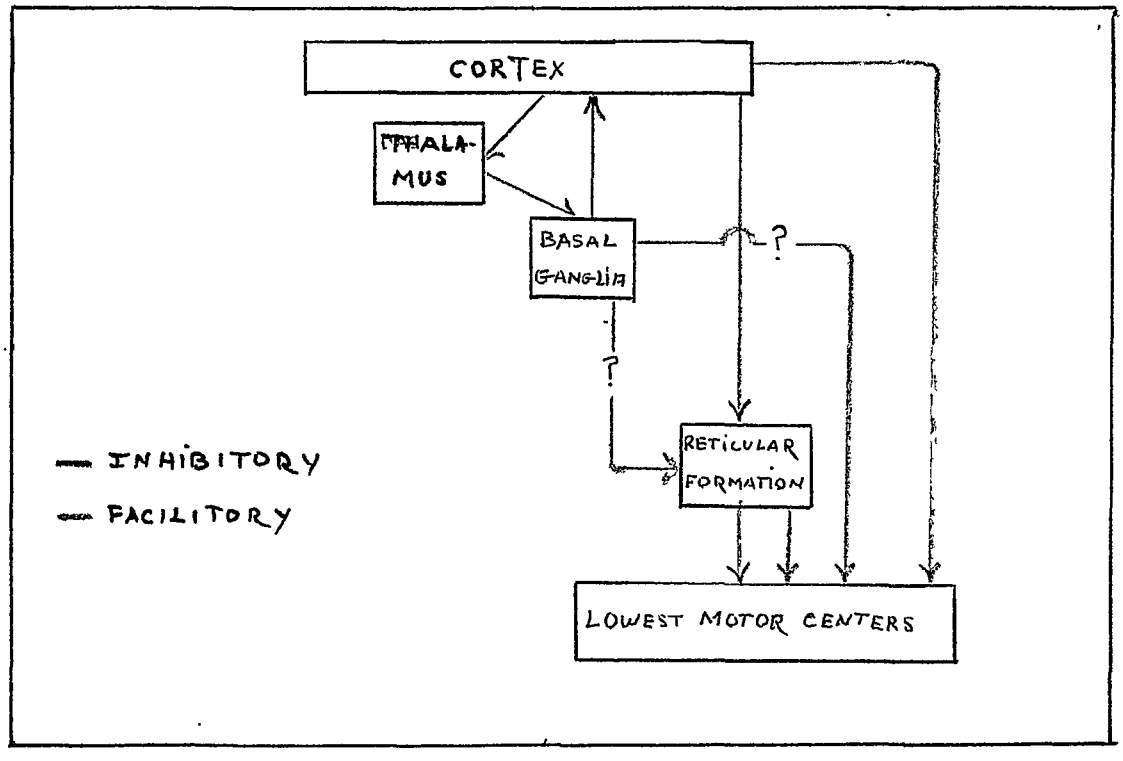
It appears that the reticular formation is the lowest of the centers which upon stimulation results in inhibition of movement. Denny-Brown and Botterell (14) state that damage to the corticospinal neurons leads to the depression of the lowest motor centers which in turn leads to the development of paralysis. On the other hand they feel that disorders of intimately associated neurons passing to the mesencephalic and bulbar mechanisms lead to the production of the most characteristic features of the hemiplegic type of spasticity. In this connection Hines (37) feels that by differential lesions of area 4 it is possible to separate from the total phenomenon of spastic paralysis the parts of which it is composed. She feels that the characteristics of spasticity are produced by lesion of 4s. By adding to this a lesion of 4γ and possibly of 4a she feels that it is possible to complicate the spastic phenomenon with the impairment of voluntary activity and the development of contractures. Finally she feels that by cutting the pyramids it is possible to produce paralysis without the signs of spasticity. In considering lesion of 4s we might state that there has been destroyed a concentration of fibers which project to the mesencephalic and bulbar mechanisms (as well as to the thalamus and the caudate) for the inhibition of activity, and applying Jackson's concept of influx we have

left unopposed the facilitory impulses of the motor systems. In lesions of the motor area facilitory fibers are destroyed and in addition to this it seems probable that inhibitory fibers are destroyed also. Thus there is reduction of function and the production of a degree of spasticity. By lesion of the pyramidal tract that major facilitory tract is destroyed producing hypotonia and paresis. These inhibitory tracts are added to the schema below.



That the pyramidal tract is not the only facilitory pathway is indicated by the fact that motor function is not entirely lost with pyramidal lesion. In an earlier section of this paper evidence of other facilitory pathways has been given, namely such pathways as that from the reticular formation (75, 76) and possible pathways from the globus pallidus,

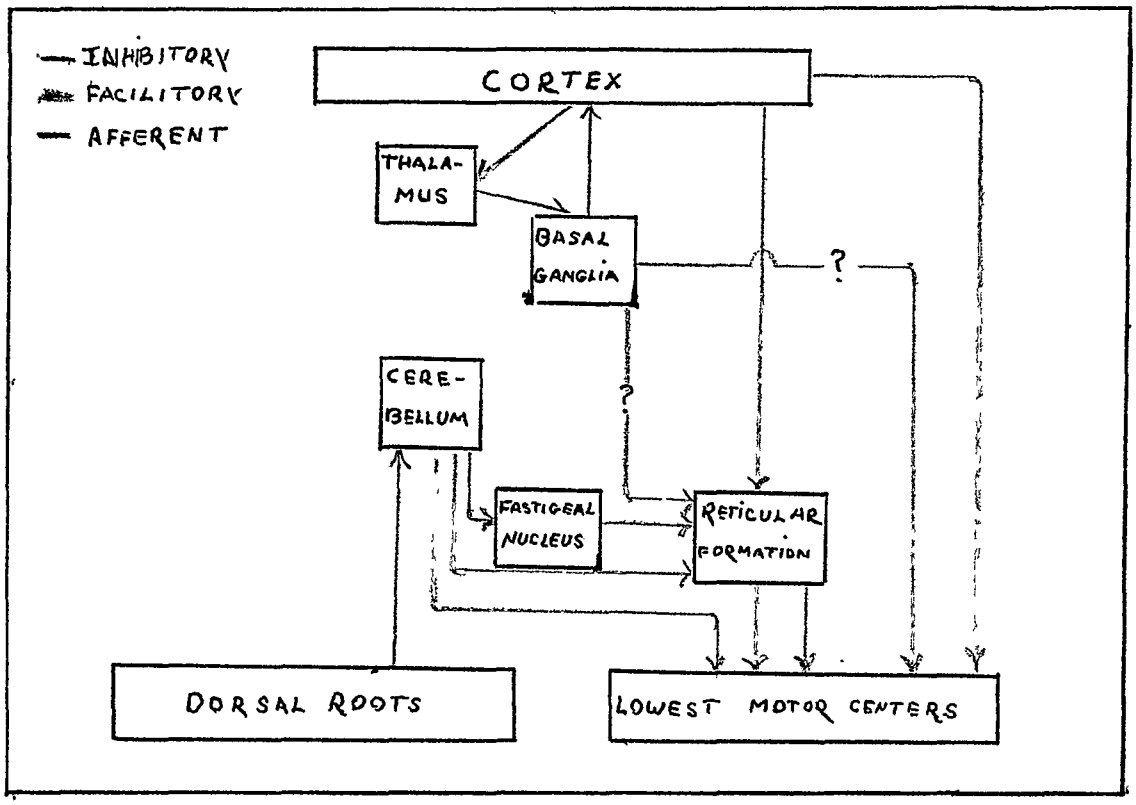
substantia nigra, subthalamic nucleus and the region of the red nucleus (79, 80, 81). How many of these pathways actually exist and subserve such a function is not adequately demonstrated, nor is their precise function more than hypothesis. These possible tracts are placed in the continuation of the schema which follows.



In addition to this there is evidence of facilitation and inhibition of lower centers involving the afferents to the cerebellum and the efferents from the tactile area of the cerebellar cortex to the fastigeal nucleus and finally to the reticulo-bulbar inhibitory center (74), and from the cerebellum to the red nucleus to the rubrospinal tract which is said to be facilitory in function (84). It is

known that decerebrate rigidity can be produced by transection of the brain stem as far caudally as the level of the vestibular nuclei, but destruction of those structures or of the vestibulospinal tracts will abolish this extreme degree of extensor rigidity, a lesser degree of which is seen in spasticity (26). Moruzzi (82) studied cerebellar function by recording electromyograms from ankle extensors of cats during decerebrate rigidity and the myotactic reflexes in cats the brain stem of which was sectioned at the intercollicular and postcollicular levels. He found that there was inhibition of decerebrate rigidity and myotactic reflexes when the hindlimb area of the anterior cerebellar lobe was stimulated at a frequency of 50 to 300 pulses per second, whereas facilitation resulted from rates of from 2 to 30 pulses per second. Intermediate responses were found to occur when frequencies from 30 to 50 per second were used. Both thypes of response were cortico-cerebellar in origin, but the facilitory effects were less resistant to conditions causing the depression of electrical activity of the cerebellar cortex. He found that the facilitory after discharge following low frequency stimulation was related to the post-inhibitory rebound following higher rates of stimulation. As gradually increasing frequencies of stimuli were applied to the same area of the same preparation (in the absence of changing voltage) there was a change from facilitation to

prolonged facilitory afterdischarge and eventually to inhibition. It is to be noted that inhibition was still elicitable after histologically complete ablation of the midbrain indicating that midbrain relays and the crossed cerebello-bulbar tracts were said by this worker not to be required for the outflow of inhibitory impulses. Adding these findings to the schema we find:



That hypotonia and paresis are present upon ablation of the postcentral gyrus has been indicated by several studies which have been discussed (51, 85, 86, 105). At that point it was stated that with unilateral ablation of the postcentral gyrus there is a deficit of tactile reactions and a less marked deficit of proprioceptive reactions.

With bilateral ablation of postcentral cortex there is a permanent loss of these tactile and proprioceptive hopping and placing reactions. It was also stated that the addition of postcentral ablations to that of a motor area which had resulted in spasticity and paresis, caused the degree of paresis to be increased, but had no noticable effect on the spasticity. It is known from the work of Peele and others referred to above (64, 85) that there is a pyramidal projection from the postcentral gyrus, but that this is not sufficient in quantity to account for the loss of function succeeding upon the destruction of the somatosensory cortex.

Gay and Gellhorn (32) found that proprioceptive influences which were elicited in the following ways all were followed by excitation within the cortical areas.

1) Passive flexion or extension of an extremity.
2) The stimulation of the peripheral end of a ventral spinal root.
3) The stimulation of the central end of a muscle nerve.

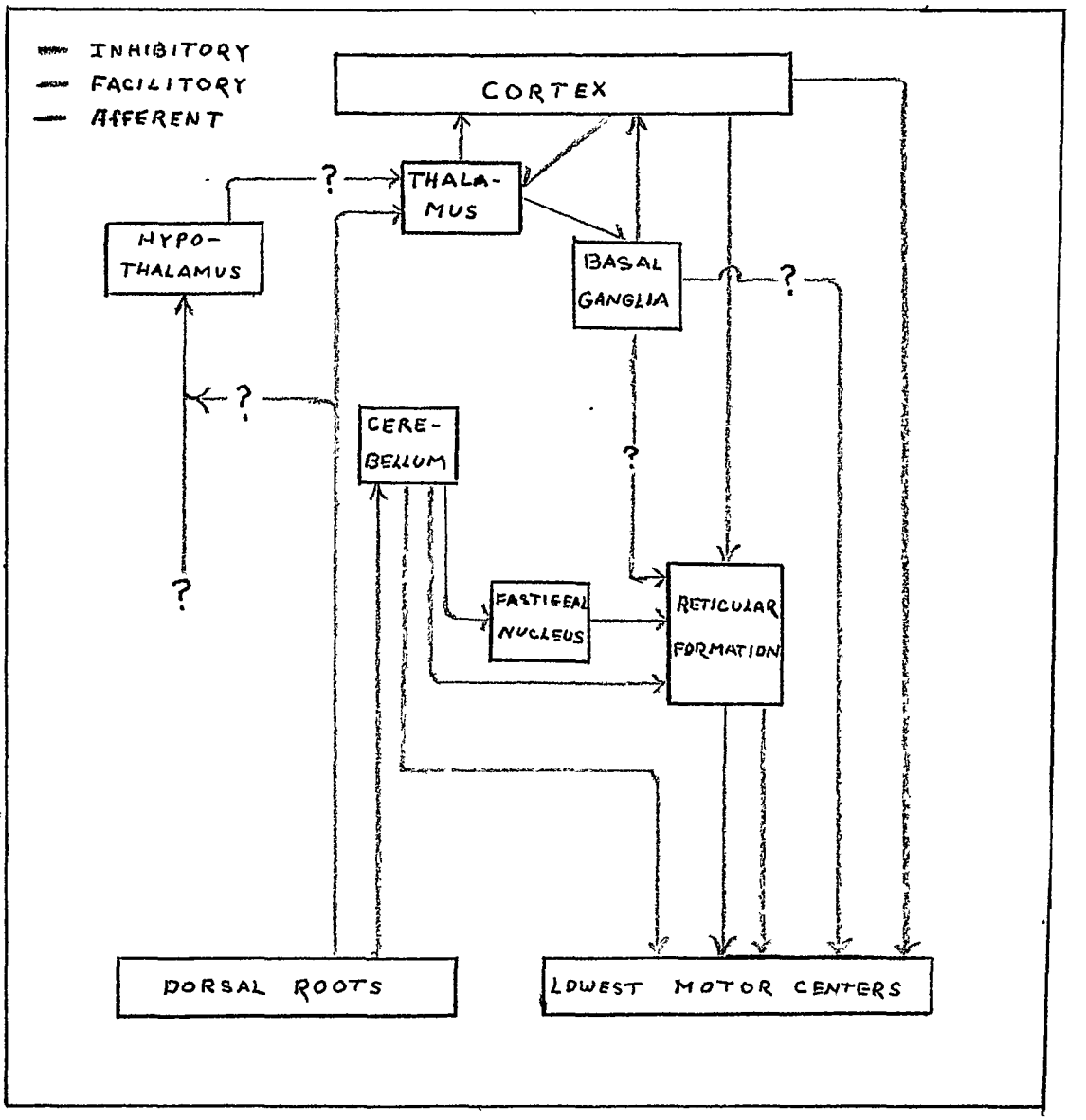
This activity was indicated by the disappearance of "Dial" potentials and/or an increase in the amplitude and frequency of background potentials. That tension receptors were primarily involved in the setting up of these afferent impulses was indicated by the fact that on stimulation of the first sacral nerve with a strength of current insufficient to

produce cortical activity of itself, became effective in producing such activity if the muscles were caused to contract isometrically or under a load. In the cat the principle area of the cortex so excited was the total sensoimotor area and in the monkey the areas involved were the precentral cortex (areas 4 and 6) and to a lesser extent the adjacent part of the postcentral sensory cortex. In a continuation of the same study Gellhorn(33) found that fixation of a muscle at increased length increased the response to stimulation of the appropriate cortical focus while the muscle is building up tension isometrically. These proprioceptive impulses also enhance the response of other specificly functionally associated muscles e.g. biceps and extensor carpi. These effects seem to be based on the interaction of proprioceptive impulses with those from cortical stimulation increasing the number of discharging motor units. Proprioceptive reinforcement of cortical stimulation by muscle activity is accompanied by the inhibition of antagonistic muscle complexes, and coinnervation results from increased cortical stimulation and also from weak cortical stimulation plus strong proprioceptive impulses. In an earlier paper Barker and Gellhorn (3) found that electrical stimulation of the frontal, parietal or occipital suppressor areas of the cat yielded not only diminution of cortical activity but also the lessening of the

cortical effects produced by somatic afferent impulses.

There is some evidence to indicate that these are not the only afferents influencing cortical activity. Lindsley et al (68) have found that destruction of what they have termed the ascending reticular activating mechanism, at the level of the basal diencephalon was followed by chronic somnolence and typical sleep activity in the EEG. These EEG findings were not present when the lesions were placed in the periaqueductal grey or in the midbrain tegmentum wherein the long sensory paths travel. They found that it was possible to activate the synchronized EEG by somatic and auditory stimulation when either the long sensory paths or the ascending reticular activating systems were destroyed by lesions placed just behind the thalamus. The reticular activating system recieves collateral sensory excitation from the long afferents in the lower brain stem, and the afferent impulses so carried and the direct arrival of impulses carried by the long afferents at some site above the midbrain result in EEG activation. However only the excitation of the former indirect system is able to result in prolonged wakefulness. These worker suggest that the poverty of behavior after lesions of the reticular activating system may mean that its influence may be directed both cephalically activating the EEG and caudally facilitating motor

activity. We may now add these afferent systems to our schema.



These papers present evidence of the influence of afferent impulses on the motor cortex, so that cortical activity is increases by the increase stimulation of extero- and interoceptors. Denny-Brown (15) in a section entitled

"The Meaning of Spasticity" states:

> "Our studies of spinal animals...have convinced me that experimental spasticity in all but extreme degrees is a variable process influenced not only by transient inhibitions accompanying painful stimulation, but augmented by a variety of specific proprioceptive stimulation. There are a number of different extraneous factors which influence it, even at the spinal level. The basic response is certainly the stretch reflex of the muscle concerned, but the increased susceptibility to the proprioceptive stimuli arising in other muscles is an essential part of the process which makes the difference between a normal stretch reflex and spasticity. Some specific tactile responses augment the reaction...some condition it...some inhibit it. ...In decerebrate rigidity all but painful stimuli augment the reaction, in a manner which suggests that all proprioceptive reactions had recieved a substantial subsidy of excitation. The inclusion of the midbrain in the surviving neuraxis allows a variety of stimulation to the body surface...to modify the proprioceptive reflexes in a manner...we call the righting reflexes....It can therefore be stated that at the level of the pons and midbrain the proprioceptive mechanism as a whole is coordinated by a general facilitating effect which is balanced against a series of modifying stimuli from labyrinth, neck and body surface. The balance is however not perfect, and a residual soft plastic rigidity remains. In time, an overaction of some proprioceptive reactions which we call spasticity is seen following lesions at higher levels....
>
> "After partial (italics in the original) damage to area 4 an [illegible] initial mild spasticity of the whole limb rapidly lessens as movements of the promimal joints are regained....Spasticity vanishes when contact placing and instinctive grasping return. Spasticity is certainly not a normal function. It is an exageration of proprioceptive function due to the absence of some

> normal factor which conditions such function. (There are indications) that the factors whose absence consistently correlates with the appearance of spasticity are tactile reactions and to less degree some visual control of movement....Spasticity following lesions of the cerebrum is therefore a condition resulting from the disturbance of balance of normal reflex effects, particularly as between tactile and proprioceptive reactions."

Of interest in this connection are two studies of the modification of spastic paralysis in man. Browder (9) found that excision of the parietal cortex in three case of spastic hemiplegia in man caused a reduction in spasticity. Wilder and Penfield (106) made large removals of sensorimotor cortes in three patients who had been hemiplegic since infancy. Each of these patients showed an objective lesion of the Rolandic cortex. In each case the cortex was electrically excitable in that movements of the paretic extremities were produced by stimulation of the sensorimotor cortex at higher than usual threshold. Following ablations no increased deficit in posture or movement could be found. In none of the cases was the spasticity increased, and in two it was decreased.

In this discussion we have had evidences of a "driving mechanism" of motor function. Evidence that the "inhibitory" and "facilitory" efferent systems are influenced by stimuli

arriving over afferent systems. There is here indication that in the normal animal the arrival of these impulses are integrated at various levels to produce coordinated and useful activity. In lesions producing spasticity this coordination is not present. The "driving" impulses still arrive but only facilitory systems remain functionally relatively intact to make up the efferent part of the "arc" and thus the stretch reflex which ordinarily balanced in an efficient way recieves unmodified (or abnormally modified) impulses with resultant spasticity.

V. SUMMARY AND CONCLUSION

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A. SUMMARY

1. A survey of literature devoted to the elucidation of motor function, with special reference to the problem of spasticity is presented.

2. A survey of the anatomy of the structures involved in spasticity is presented.
   a. A description of gross and histologic structure of precentral motor cortex is included.
   b. Fiber projections from the parietal cortex are indicated.
   c. Extrapyramidal systems are defined and briefly described.
   d. The origin, course and distribution of the pyramidal tract is described.

3. A discussion of the relation of motor function to spasticity is presented.
   a. The cortex.
      1) Stimulation studies are discussed.
      2) Ablation studies are discussed and experimental results are summarized on pages 46 through 48.
   b. Cortico-subcortical connections and extrapyramidal function are discussed, with a summary of data on pages 63 and 64.
   c. Physiological studies of the pyramidal tract are presented.

4. A discussion of the relation of motor function to spasticity is presented.

B. CONCLUSION

The problem of spasticity is not solved. Its solution awaits the completion of many more clinical and experimental observations. There are, however indications that workers in the field have abandoned the concept that there is any one tract which, when disrupted, will produce spasticity.

Rather, the evidence indicates that spasticity is the result of disordered total integrative somatic (skeletal) activity---- the afferent systems are involved as are the efferents, both facilitory and inhibitory. The proper and accurate conclusion concerning the genesis of spasticity is to be reached by meticulous, painstaking anatomico-physiological experimental studies. Any conclusions so reached must be correlated with findings in man. The studies as pursued in man must be careful, long term observations of patients exhibiting motor deficits and spasticity; the validity of these observations must be established by correlation with the post-mortem study of the brains and spinal cords of such patients. Only when these have been completed will the problem of spasticity be solved.

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