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The Evolution of Our Knowledge of the Brain During the Last Sixty Years

ILLUSTRATED WITH A SERIES OF PERSONAL OBSERVATIONS

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THE EVOLUTION OF OUR KNOWLEDGE OF THE BRAIN DURING THE LAST SIXTY YEARS

ILLUSTRATED WITH A SERIES OF PERSONAL OBSERVATIONS *

CHARLES K. MILLS, M.D.

This paper is intended to be largely autobiographic. One of its chief designs is to show that any large subdivision of the brain cannot be understood without taking its anatomic and physiologic relations to other parts of the same great organ into consideration. I entered on my neurologic experiences with some handicaps and some advantages. I did not have a master to guide and counsel me when I started on my neurologic career, nor did I have, like some of our distinguished colleagues of this Society, the advantages of foreign study. On the other hand, I had command of abundant clinical and pathologic material, at an early date, as the result of my connection with the neurologic services of the University of Pennsylvania and the wards for patients with nervous diseases of the Philadelphia Hospital. I shall try to show how my personal development, as illustrated by the cases described and authorities referred to, was largely that of the evolution of neurology during the last sixty years.

At the last meeting of this Society a somewhat acrid debate was precipitated regarding the prefrontal lobes as anatomically and physiologically a higher, or the highest, psychic subdivision of the brain. Some of the speakers seemed to think that to recognize a higher or highest psychic area in the brain was equivalent to locating the mind in this situation. This is a serious, but not uncommon, mistake. One part of the brain may be the organ of the mind or of mentation, if this term is preferred, but the anatomic boundaries of the mind itself are much larger and may, in fact, take in the entire nervous system, or, as some have suggested, the entire body. Evolution enters into the decision of such a question.

According to Hughlings Jackson—and I do not know of any one better for a neurologist to follow—the nervous system is divided into at least three levels, possibly more. The lowest, first and best organized is that of the spinal cord; the second or middle level evolves from the first and includes the motor and sensory areas of the cerebrum; the highest level, which represents the final evolution of the nervous system, has its abiding place in the most anterior, that is, the prefrontal, portion of the brain (*J. Ment. Sc.* **33**:25 [April] 1887).

The question of centers comes into a discussion of this sort. Most would-be critics have a false idea of what a localizationist means when he speaks of brain centers. Here again, I believe, Hughlings Jackson's definition is the best, and it is the one to which I have always adhered. A center, according to Jackson, is simply a spot or location in the brain in which a particular movement or impression is represented in greater measure than anywhere else. Every such center is associated in some way with other parts of the brain, as all parts are connected or related anatomically and functionally (Evolution and Dissolution of the Nervous System, London, John Bale and Son, 1888, p. 1).

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* Abstract of paper read at the regular meeting of the Philadelphia Neurological Society, March 25, 1927.

In the process of evolution the highest psychic prefrontal region, as it evolves more and more, becomes more strongly organized, and eventually is nearly independent of the lower levels from which it has been developed. In apparent contradiction to the general law that the last organized is the least organized, this highest evolutional level, taken as a whole, is the most organized. Within this highest level however internal evolution is constantly taking place or tending to take place, and, speaking only of this level, the last organized becomes the most evanescent or the least organized.

It is within this region that such higher qualities of the mind as will, memory, reason and emotion are represented; they are not represented by limited and separated units or centers, but by the working together of the highest and the most complex nervous machinery here represented. This region is an area of what Jackson terms re-re-representation, in which the nervous levels below for both sensation and emotion are triply represented (*J. Ment. Sc.* **1** [April] 1887).

It happens that some of my first published neurologic experiences were related to the prefrontal lobe. One of the first cases of tumor of the brain which came to necropsy, which I observed and reported, involved the first and second frontal, the convolution of the callosum and the callosum itself of the right side of the brain. I published this case in detail (*Philadelphia M. Times* **9**:184 [Jan. 18] 1879). The mental symptoms, briefly told, were: slowness of comprehension, lack of attention, explosive speech, loss of memory and lack of reasoning faculties, such as comparison and judgment, and emotional manifestations, including weeping.

Since recording this case I have had somewhat numerous midfrontal and prefrontal cases under my observation, accounts of some of which have been published, like that reported by Dr. Weisenburg and myself (*J. A. M. A.* **46**:337 [Feb. 3] 1906). The symptoms, although differing in minor respects, were all examples of tract impairment or loss of the higher attributes of mentality.

In my experience, cases in which the lesions in the brain were on the right side, were particularly noticeable for emotional manifestations. Emotion and emotional expression take the same place in extent of representation in the right cerebral hemisphere that language does in the left.

This is as good a place as any to recall my contributions on the subject of emotion and emotional expression. I first became interested in these questions from observing patients in the wards for nervous diseases at the Philadelphia Hospital who exhibited a variety of emotional manifestations which were not under control of their wills. Sometimes these manifestations were apparently of a distressing sort, as weeping with or without lacrimation; sometimes they were agreeable in appearance, as involuntary laughing, smiling or grinning. In the course of time I had the opportunity to make necropsies in cases of this sort which I had studied during life. I found lesions variously distributed, as for instance in the cortex, in the lenticular, in the caudatum, in the geniculate bundles of the internal capsule, in the corticobulbar tracts, in the nucleus ruber, in the pons oblongata, in the cerebellar prepeduncle or in the thalamus. I thoroughly discussed the subject of the cerebral mechanism of emotional expression in two papers, one presented at a meeting of the College of Physicians in 1911 (*Tr. Coll. Phys.*, Phila. **34**:147, 1912), and the other at the meeting of the American Medico-Psychological Association, May 28-31, 1912 (*Tr. Am. Medico-Psycho.* **19**:297, 1912). The paper presented to the College of Physicians was afterward published in a memorial volume to Bianchi.

I will present, in condensed form, a few of the most important facts and hypotheses included in these papers. I held that emotion and emotional expression were separately represented in the cerebral mantle, the former in the prefrontal region, where, as Bianchi (A Textbook of Psychiatry for Physicians and Students, New York, William Wood & Company, 1906) and others have maintained, the final syntheses occur which result in the higher psychic processes including emotion, while emotional expression is more especially represented in the midfrontal region, in a zone closely contiguous to that concerned with emotion itself. I had shown that an emotive zone representative of emotional expression was probably located in the midfrontal and posterior part of the prefrontal region, that zone being entirely cephalad of the motor zone as usually regarded, that is, forward of the precentral convolution. This zone also included an anterior projection of the second and upper portion of the third frontal convolution, and it was more highly developed in the right hemicerebrum than in the left.

The views maintained by me were derived partly from the results of faradic excitation of the human cortex during operations by Dr. Frazier (*Univ. Penn. M. Bull.*, Phila., **18**:134 [July and Aug.] 1905), and partly from a general study of the literature on the subject, psychologic and neurologic. Among the movements demonstrated as having their representation in the midfrontal zone for emotional expression were those for closing and opening the eyes, for opening the mouth, both by movements of the jaw and of the lips, for bending the head forward, backward or to one side, and for the movements of Darwin's (The Expressions of the Emotions in Man and Animals, London, John Murray, 1872) so-called muscles of grief. These muscles, especially in the upper part of the face, are for the movements of the corrugator supercilii, the frontalis, the pyramidalis nasi and the muscles of the eyelids (*Tr. Coll. Phys.*, Phila., **34**:147, 1912).

Hughlings Jackson, broadly generalizing, applies the evolutional theories of Herbert Spencer, Laycock, Bain and others to the explanation of increasingly complex reflexes as we pass from the lowest to the middle and from the middle to the highest levels of the brain. He lays down the proposition that the frontal half of the cerebrum is motor and the posterior half is sensory. I appreciated this fact early, and in 1888 I indicated my conviction that the sensory region was not only separate, but was situated posteriorly to the rolandic fissure (*Tr. Cong. Am. Phys. & Surg.*, 1888, vol. 1; *Brain* **12**:233 [July] 1889; ibid. **2**:258 [Oct.] 1889).

One object of this paper has been to show that the evolution of our knowledge of the brain, and especially of localized centers in the encephalon, during the last sixty years, has been illustrated by my own clinical and pathologic experiences. I have recorded cases authenticated by operations and necropsies occupying almost every particular functionally limited districts of the brain—cases of prefrontal, midfrontal, postfrontal, postcentral, postparietal superior and inferior, occipital, third frontal, insular, retro-insular, supratemporal, midtemporal, thalamic, subthalamic, superior, inferior and posterior cerebellar and spinal. An excellent opportunity of rounding out my experience in cerebral localization by the report of an actual case was afforded and put on record in a paper by me, "The Cerebral Centers for Taste and Smell and the Uncinate Group of Fits" (*J. A. M. A.* **51**:879 [Sept. 12] 1905).

This paper recorded a case in which a tumor, arising in the uncinate convolution, spread to other regions of the brain. I had notes of this case extending back to 1899 and 1900. I can only briefly give its main features.

The patient became subject to epileptic seizures differing from one another in some details but having as marked features distinct auras of smell and taste with smacking of the lips and champing of the jaws; he died at the close of a serious seizure. Necropsy showed a tumor which evidently had begun in the uncinate region and had extended backward and inward.

My personal views on inhibition differ somewhat from those usually held. It is well known to all that, in cases of incomplete transverse lesion of the spinal cord, reflexes in the parts supplied below the lesion are exaggerated, sometimes grossly so, as evidenced by such phenomena as patellar clonus, ankle clonus and the toe reflexes of Sinkler (The Toe Reflex, *Med. News* **53**:611 [Dec. 1] 1888), and other defensive reflexes. Usually these cases are explained on the theory of withdrawal of cerebral inhibition, but I doubt the correctness of this explanation.

In a paper presented to the Philadelphia County Medical Society, in 1915 (*Penn. M. J.* **18**:496 [March] 1915), I cited Bastian's (*Medico Chirurgical Trans.* **73**:151, 1890) well known case of complete transverse lesion of the cervical cord, and referred to another case of my own of equally complete transverse lesion of the thoracic cord. Certainly all cerebral inhibition must have been withdrawn in these cases; yet in both cases and in others which I have studied, there was complete atonic paralysis with lost reflexes in the lower limbs.

My view is that there is a special peripherospinal and cerebral tonectic apparatus (*Neurol. Centralbl.* **33**:1266 [Dec. 16] 1914). Sensory stimuli maintain a standard tonectic state in the normal person or a uniform condition of tonic innervation. When the corticotonectic stimuli are rhythmically delivered, they maintain the motor system in the state of normal muscle tonicity. Complete withdrawal may occur either through lesion of the sensory pathway or through more or less complete lesion of the pyramidal tract. If there is a partial block, the result is an overcharge of tonic innervation. The hypertonia is expended in a forcible and irregular way on the lower spinal neurons and gives rise to the resulting hypertonicity and increased reflexes.

It is at least doubtful whether the Nissl second type of small cells is set aside for inhibition. My own studies, of the cerebral cortex, of the striatum and of the cerebellar deep nuclei, point to these small cells as associating in function. In fact, to me it does not seem necessary to assume two types of cells, one for excitation and one for inhibition. The large motor cell types may exert inhibitory influence in particular cases, as can be shown by numerous examples. Inhibition is a function of much importance in the central nervous system, but it does not follow that it requires a distinct type of cells for its performance, as in the vegetative system.

In 1917, a paper by Dr. George Riddoch (*Brain* **40**:265 [Nov.] 1917) appeared on "The Reflex Functions of the Completely Divided Spinal Cord in Man, Compared with Those Associated with Less Severe Lesions." In 1920, a paper by Head and Riddoch also appeared (Studies in Neurology, London, Oxford University Press, vol. 2, 1920, p. 467). The work by Riddoch was conducted largely under the direction of Head. Both of these articles have great significance in connection with the discussion of inhibition.

Riddoch's paper at first seemed to oppose Bastian's views, founded on his cases of complete division of the spinal cord in the cervical region, and also my views founded on cases of cervical and of thoracic complete transection. Careful reading of the paper, especially of the cases reported by Riddoch, indicates that Riddoch's observations and conclusions are not entirely opposed to those of Dr. Bastian and myself.

The question of the origin of cerebral tone must first be borne in mind. Tone, like every other function in the human nervous system, has its origin in the outside or inside periphery. Impressions or stimuli in the periphery outside the body are received by exteroceptors, namely cutaneous and mucous membrane receptors. Impressions or stimuli from within the body—from muscles, joints, bones and labyrinth—received by propioceptors are conveyed with the cutaneous sensory impressions to the thalamus and thence to the sensory tonectomotor cortex and lastly to the highest or psychic prefrontal regions.

The peripheral impressions or stimuli are received and transformed in the cerebral tonectic zone and these transformed impulses are conveyed by efferent tracts, pyramidal and extrapyramidal, to the centers in the oblongata and spinal cord.

The cerebellum is, in one sense, a combination of the lowest spinal level and the middle level. It is subordinate to the cerebral level of which it is a sort of appendage or appanage. Tone derived from the periphery is primarily a cerebral function. Tone, however, may be aroused directly in the spinal cord or in the spinocerebellar portion of the cerebrospinal apparatus.

Inhibition is an active process. When all the levels of the nervous system are intact, tone impulses or stimuli are conveyed to all parts of the motor nervous system and keep all movements in a state of normal balance. If the spinal cord is severed in the cervical or thoracic region, tonic innervation is no longer conveyed from above to the spinal centers below the site of the section; hence atony results, and the muscles, tendons, etc., become flaccid, and the reflexes disappear or are greatly lowered. In the first place, this is the result of the shock of an operation or injury completely severing the cord. When the shock passes off, reflex activity begins to return through the influences or stimuli received directly from the periphery. In this way we have the phenomena of the reflex activity described by Head and Riddoch. These reflexes, however, never attain the normal perfection of reflexes which are present when the spinal cord is intact.

In cases of partial lesion, cases in which the cord is incompletely divided, tonectic impulses force their way through the imperfect block and overcharge the centers below the site of the lesion.

The discussion of the reflex activities of the bladder and the phenomena of sweating after complete spinal transection are particularly instructive. Head and Riddoch quote largely in defense of their position from Sherrington (The Integrative Action of the Nervous System, London, 1906) and also from Jackson.

Note.—This paper, as first presented to the Society, included a somewhat elaborate discussion of the cerebellum and also of sensation and its cortical representation. The cerebellar material has since been included in a paper presented at the annual meeting of the American Neurological Association in May, 1927, and the notes on sensation have been expanded into a "Discussion of Sensory Disorder in Organic Disease of the Nervous System" for the combined meeting of the Neurological Section of the Royal Society of Medicine and the American Neurological Association held in London, July 26, 27 and 28, 1927. These remarks on sensation will appear in the transactions of this combined meeting to be published in *Brain*.

DISCUSSION

Dr. J. H. Lloyd: Dr. Mills has taken the pains to go over practically the long period of his work as a neurologist, for which I believe we all feel grateful. In discussing the paper, I find the field so large that it is necessary for me to limit myself, and I have picked out merely one or two points to which to refer.

Dr. Mills wisely avoided discussion of the so-called faculties of the mind, and has substituted the term mentation. This is a good enough term for our purpose. The present day school of psychologists is opposed to the old-fashioned terms. They do not like the term, mental faculties. One of them would even abolish the term consciousness. They use new terms instead, such as mental complexes, mental mechanisms, behavior patterns, correlations and integrations. What do they mean? Dr. Mills has avoided all that, and has substituted one comprehensive term—mentation.

Dr. Mills holds that the higher mental functions are located practically in the prefrontal region. He has entertained that idea for a long time and has described a syndrome caused by lesions of the prefrontal region, consisting of retarded cerebration and explosive speech. I saw a man with a fracture of the skull recently, and the roentgen ray showed that the fracture extended down into the frontal bone; the man had the exact condition Dr. Mills has described. On operation, a blood clot was found over the prefrontal region. I have seen many such cases, and the syndrome, if I may call it that, is unmistakable; but I must say that I hesitate to limit the higher mental functions to the prefrontal area.

To illustrate what I mean, I may speak of the evolution of the cortex of the brain. Herrick, in his recent book, shows that there is no cortex of the brain in fishes, and what is called the pallium is nothing but an epithelial membrane. It has no nerve elements in it except possibly three limited areas in the higher forms of fish where there may be a beginning of the cortex of the brain. One is over the big olfactory structures and becomes the hippocampus, and the next is over the corpus striatum. These two constitute the first development, the archipallium. Then there is another extending a little forward called the neopallium, from which is evolved the cortex of the higher forms of life. As we ascend the vertebrate scale, through the reptiles, birds and lower mammals, this cortex grows larger and larger in the neopallium, and the fair inference is that the function called mentation grows with it. Especially in those regions of the cortex which are the centers for the great cranial nerves it is likely that this function develops; in other words, the higher mental faculties are probably very active in these centers. For instance, many of our ideas depend on our use of language; it has even been debated whether we could form abstract ideas and engage in abstract thinking without the use of language. Now this center is in the temporal lobe (largely), in the auditory centers, the primary center for speech. Hence I infer that some of the higher mental functions may be active here.

The same may be said of the visual centers in the occipital cortex, for many of our higher and more complex mental processes are connected with the sense of sight; and also of the superior parietal lobule, where is located the stereognostic sense, by which we have many of our goemetric ideas.

From all this I should infer that the higher functions of mentation are not limited to one region of the cortex. Nevertheless, I think, with Dr. Mills, that they manifest themselves in a peculiarly active and dominant way in the prefrontal areas.

In discussing the cerebellum, I refer again to comparative anatomy. The cerebellum in the reptile is exceedingly small, according to Edinger, but in the birds it has undergone an enormous evolution. It is almost as big as the forebrain. A bird is endowed with an important function—the function of flight—which requires the finest adjustment, the finest balancing. It does seem, therefore, that the cerebellum in birds has something to do with flight. All we know about the human cerebellum we have derived from the study of its pathology. That is not the best way to study a thing, but we are forced to do it. I have seen a number of cases of lesions of the cerebellum. I saw a man who had a tumor of the cerebellum involving the middle cerebellar peduncle. He had forced movements of the head to one side, and when he sat up his body was forced to one side. It was not a hemiplegic condition or loss of power on one side, but it was an excess of power on one side. I think that tends to confirm the idea that the cerebellum has to do with balancing movements. The same can be implied from the disease known as Friedreich's ataxia. The movements are not the same as those of tabes. They suggest a cerebellar lesion. I presented a case here a few years ago in which careful studies were made. The boy died of an acute disease, and we had the cord in the full bloom of the disease. The cells in Clarke's column at many levels of the cord were destroyed, and the direct cerebellar tracts were sclerosed. The inference was that there was interference with the cerebellar function.

Some of the cases which Dr. Mills refers to are those of the pons and associated pontile and cerebellar disease. The trouble with these lesions, it seems to me, is that they are often too destructive. No two cases are alike. One pontile lesion destroys one part and another lesion another; hence the necessity for careful interpretation, such as he gives. For instance, Dr. Mills has referred to the subject of paralysis of conjugate movements of the eyes. Some years ago I had a case of a young man who had pseudobulbar palsy. Autopsy showed lesions in the corpus striatum. That man had complete paralysis of the conjugate upward movements of the eyes, and paralysis of convergence. If I had been guided by that symptom, I should have been misled, for instead of a true ophthalmoplegia it was what some German writer has called a pseudo-ophthalmoplegia. The lesions in the corpus striatum cut off the tracts from the motor centers in the forebrain to the nuclei of the third nerve in the midbrain.

Dr. Mills has properly called attention to the necessity of differentiating between astereognosis, caused by a lesion in the parietal lobe, and cerebellar ataxia. It is also necessary to distinguish between labyrinthine vertigo and cerebellar ataxia. They are distinct; labyrinthine vertigo is subjective; there is no motor disturbance, such as ataxia or forced movements.

To me the great value of Dr. Mill's paper is its suggestiveness. It gives many hints and indications, based on a long and extensive experience, which should point the way to further fruitful study. It is the work of a pioneer and leader.

Dr. Francis X. Dercum: During the fifty years that I have known Dr. Mills, I have listened to many of his papers. Dr. Mills has not kept pace with the evolution of our knowledge of cerebral localization, he has led it. Indeed, he has been the world's greatest leader in this field. While some of our friends on the other side of the water might dispute this statement, we on this side have no hesitation in acclaiming it.

I have also listened to Dr. Lloyd's remarks, which have been delivered with his usual clearness and impressiveness. I fully share his views regarding the "behaviorists." There is only one psychology, and that is the physiology of the brain. Dr. Lloyd has approached the subject from the biologic point of view, and this also inspires my sympathy. In my early days, the nervous system of man seemed to me to be hopelessly complicated, and I turned to the fishes in which the fundamental problems of vertebrate structures are presented in a much simpler form. In the fish, the motor organ of the brain is represented by the striatum; indeed, by a structure corresponding to our own globus pallidus. Because of its primitive and relatively simple character, it is spoken of as the paleostriatum. Immediately back of this motor organ is a sensory structure, the primitive thalamus or paleothalamus. It is made up of nuclear aggregations, corresponding to those in our own epithalamus (habenula), of nuclear aggregations in the hypothalamus (eminences back of the optic decussation and the mammillary bodies) and in nuclear aggregations for smell, for taste, for the viscera and for the body generally.

There are also numerous receptors grouped about the head and spread over the body which receive the impacts from the outside world. The first impacts are the chemical impacts which are received by receptors for smell and taste and are transmitted to a large brain mass, the "nose brain" as Herrick terms it, and to the contiguous area for taste. In a similar manner, the light impacts are received by special receptors which transmit impressions to the "eye brain"; next are receptors which transmit impulses to the "ear brain"; other receptors transmit impulses to the "visceral brain"; others still, diffused over the body, transmit impulses to a "skin brain." To this primitive arrangement, Edinger applied the term paleo-encephalon. It corresponds in mammals to the brain stem, which is made up of the medulla, the quadrigeminal bodies and crura, the thalamus and the striatum. The brain stem is also spoken of as the segmental brain, because, like the spinal cord, it is capable of a segmental interpretation.

The impacts which are received by the various receptors of the fish are transmitted through the striatum to the motor neurons of the spinal segments. The fibers descending from the striatum constitute the first or primitive motor pathway. It is the only motor pathway in the fish and practically the only motor pathway in amphibians, reptiles and birds. Its fibers correspond to the pallido-rubrospinal tract in ourselves (von Monakow's bundle).

It is interesting to note that in the fish the impacts received by the receptors result in alternate contractions of the muscles of the two halves of the body; the two halves contract in sequence, and this results in the act of swimming. It is important, further, to emphasize the fact that the synaptic relations of the motor neurons of one side of the striatum of the fish are in synaptic relations with the motor neurons of the opposite side; that is, the motor pathways decussate. Here is the first instance of the occurrence of decussation and also of an explanation of the decussation; for if the motor pathway did not decussate, the contraction of the muscle would be on the same side as the impulses which leave the striatum, and forward motion of the animal would be impossible. I will return in a moment to the fact of the contraction of the two halves of the muscle masses in sequence. It is the first instance—if the action of the mandibles and fins is omitted—of coordinated movement.

This primitive nervous system of the fish answers every purpose so long as the organism remains a fish and so long as it is limited to an aquatic habitat. Changes, however, become necessary when the animal becomes terrestrial and is forced to make new adaptations, adaptations necessitating new and more complex movements. It is exceedingly probable that the neuron associations in the primitive brain are fixed; that is, they permit little or no variation or adaptation in their responses. Especially is this true of fishes and doubtless also of amphibians. In reptiles there is possibly a slight variation in responses and possibly a little more in birds. It is not unlikely that the striatum, increasing a little as the organism advanced in the vertebrate scale, primitively had a little power of changing the associations among its neurons. However, when terrestrial life was definitely established, an increase in the number of neurons took place. This increase was brought about by the proliferation, the heaping up, of intercalary neurons at the distal extremity of the neural tube. This new formation, barely noticeable, if present, in fishes, slightly more noticeable in amphibians, a little more evident in reptiles and still more evident in birds, is spoken of as the pallium; it constitutes the end-brain and in mammals becomes the cerebral cortex. The intercalary neurons of which it is composed present no fixed relationships with each other; therefore variability and an increased power of adaptation to the responses received from without become possible. These intercalary neurons gradually increase in number and promote to an immeasurable degree the possibilities of the adaptations of the organism to the demands of a new and changing environment. Their number increases rapidly as one advances in the vertebrate scale until in man the enormous number of approximately 10,000 million is reached.

The cortex is a great usurper. With its establishment, the striatum undergoes a reduction in importance. In mammals the striatum is no longer, if indeed it has ever been, the seat of any variable or adaptable neuron combinations; but now it becomes definitely the seat merely of fixed neuron associations. It should be borne in mind, however, that the striatum increases greatly in size as the vertebrate scale is ascended; not only is the putamen added, but also the caudatum; together these structures are often spoken of as the neostriatum. The addition of the putamen and caudatum increases both the number and the complexity of the possible neuron associations. This increase corresponds to and keeps pace with the constantly increasing size and complexity of the cortex.

With the continued growth and development of the telencephalon or cortex, a new motor pathway develops, the cortical or pyramidal motor pathway, which enters into direct relations with the motor neurons of the segmental brain and of the spinal segments. There is, therefore, a double innervation in the muscles; first, the primitive innervation from the striatum through the pallidorubrospinal tract, and secondly, another innervation from the cortex through the pyramidal tract. This is entirely in accord with the interpretation which Dr. Mills has advanced of a double innervation from the upper and lower levels of the brain.

I shall now consider the most interesting feature of the entire problem. Many years ago, I became interested in the lateral line system of fishes, which consists of tubular formations containing at intervals structures which are morphologically and practically identical with the maculae acousticae of the semicircular canals.[7] These lateral lines are distributed over the head and along the sides of the body. The interesting point is that the nerves that arise from the maculae which they contain terminate in the same area in the medulla as the nerves from the receptors in the ampullae of the semicircular canals; i. e., the auditory nerve and the lateral nerves terminate in an acousticolateral area on the posterior aspect of the medulla. Now, just as the telencephalon, the cortex, is produced by a proliferation of cells at the distal end of the primitive neural tube, so is the cerebellum produced by a proliferation of cells from this acousticolateral area. The heaping up of these cells forms the primitive cerebellum; the cells first develop structures corresponding to the nucleus dentatus and the other nuclear masses of the cerebellum. This acousticolateral area receives the proprioceptive impacts from the muscles and joints, the exteroceptive impacts from the semicircular canals, and, in fishes, also from the lateral lines. As a result of the constant inpouring of these impulses there is a constant outpouring of impulses, a continuous stream, which finds its exit from the cerebellum through the red nucleus and thence by the rubrospinal pathway to the cord and to the muscles. As a result of this outpouring of impulses, every muscle of the body is constantly kept tense like a violin string. Sometimes the pitch, the intensity of the muscle tone is raised, sometimes it is lowered, but it never ceases except in disease. In addition, therefore, to the muscle tone, due, first, to the pallidorubral innervation and secondly, to the pyramidal innervation, there is a third tonic innervation derived from the cerebellum.

Further, it is a significant fact that the cerebellum develops in proportion to the development of the telencephalon; the more the telencephalon grows, the more the cerebellum grows. Birds offer an apparent exception to this statement, because of the relatively large size of the cerebellum, but in birds, while the pallium is small and the cerebellum large, the striatum is exceedingly large and still discharges some of the functions which are discharged in the mammalia by the usurping telencephalon.

What is the physiologic interpretation of the interaction of these three intoning processes? Impacts from the outside world received through the various exteroceptors reach the thalamus; thence they are transmitted to the cortex. Transmission through the cortex then takes place and in due course a motor exit is reached, and a "voluntary" movement is initiated. At this instant, however, there is immediate cooperation by the striatum—associated movements as in the arms and legs in walking—and also most important modifications in the cerebellar intoning, in accordance with which the tone of the muscles concerned in a given movement rises or falls.

The action of the cerebellum can be readily illustrated by simple flexion and extension of the arm. The muscles concerned both in flexion and extension are, through the influence of the cerebellum, constantly maintained in a state of tone, i. e., in a state of moderate contraction. Like the strings of a violin, both flexors and extensors are attuned to a certain pitch. When impulses are sent down from the motor area of the cortex to the extensor muscles, these muscles contract and the arm is extended, but the flexor muscles do not suddenly relax; they yield gradually like a band of tense rubber, and the extension of the limb is accomplished smoothly and evenly, not jerkily and suddenly. This applies to the extension, the unfolding of the various segments of the arm in their entirety; the extension of the upper part of the arm on the shoulder, the extension of the forearm on the arm, of the wrist on the forearm, of the hand on the wrist and of the fingers on the hand. These movements occur in an associated sequence. The separate and incoordinate extension of the segments of a limb means asynergia and is a symptom of cerebellar disease. The simultaneous and combined action of flexors and extensors, it may be added, have been termed by Tilney cocontraction.

The rôle of the semicircular canals, as Dr. Mills has stated, is most important in relation to posture and equilibration. The lateral line organs of fishes, of which I made a personal study which was published in the proceedings of the Academy of Natural Sciences in 1879, are sensory structures for the perception of succussions and coarse waves in the water, and also for the environmental relations of the fish as to depth and position in the water. In the same year I made a study of the morphology of the semicircular canals, which was published in the *American Naturalist*. In addition to the lateral lines, the fish also presents well developed semicircular canals which add to the perceptions derived from the lateral lines, those of spatial relations. It is exceedingly probable, that the semicircular canals have their origin in the lateral line organs of primitive fishes. Time will not permit a full discussion of this subject, but it is certain that the semicircular canals with their peculiar relations to each other in the three dimensions of space did not originate spontaneously. In some of the primitive and lowly organized fishes, the myxines for instance, there is only one semicircular canal; in the lamprey eel, again there are only two. It would seem that in the myxines and lamprey eels and other lowly organized fishes now no longer extant, some of the lateral line elements became deepseated and were taken in at the base of the skull of the organism by a process of involution of the surface tissues. This is the more probable as the petrosal bone in which the semicircular canals are embedded is not a part of the mammalian endoskeleton but is really an ectoskeletal structure. However this may be, the facts of the relation of the wonderful receptors in the maculae acousticae in the ampullae of the semicircular canals are of the utmost interest The impacts received from the hair cells are transmitted to the bipolar neurons in the vestibular ganglion. Thence they are transmitted by the vestibular nerve to the group of closely related vestibular nuclei in the medulla. These vestibular nuclei in turn have most important and significant connections; namely, with the dentate and other nuclei of the cerebellum, with the various segments of the spinal cord, with the nuclei of the abducens, pathetic, trigeminal and oculomotor nuclei, with the thalamus and with the cortex. That impulses from the maculae of the semicircular canals should greatly influence posturage and equilibration, can readily be understood, while the relations to abnormalities of movements of the eyeballs, such as nystagmus, are of course well known clinically and have of late years been abundantly studied by the Bárány method.

In regard to the question which has been raised as to the function of the frontal lobes, all impulses, exteroceptive, interoceptive and proprioceptive enter the thalamus. From the thalamus they enter the cortex. Here the various sensations and feelings received from the thalamus are synthesized, and analyzed in the manner which I have described in my book on the "Physiology of Mind," and the details of which I have not the time to go into now. Suffice it to say that discrimination is the result of the purely physical processes of synthesis and analysis. Necessarily, in the posterior or sensory portions of the cortex, i. e., the portions posterior to the fissure of Rolando, thinking is concrete; one deals here with actual sensory impressions and feelings. All conceptions are concrete.

In the parts anterior to the fissure of Rolando, synthesis, analysis and discrimination are carried on to a far higher degree. Here synthesis and analysis deal with symbols, and the concrete thinking of the posterior association areas now gives way to abstract thinking. This I believe to be the function of the frontal lobes.

I wish to speak in regard to one other point only, and that is in regard to the increase of the tendon reactions in incomplete lesions of the cord and the entire loss of these reactions in complete lesions of the cord. In incomplete lesions of the cord some fibers of the pallidorubrospinal tract or of the pyramidal tract must have escaped. If the fibers of the pyramidal tract or of the pallidorubral tract have escaped, an increase of tendon reactions necessarily follows. If the cord is severed completely, all intoning influences are cut off and all tendon reactions are necessarily lost.

Dr. Mills' paper has been a great stimulant. I need hardly add that—as my remarks have shown—I am substantially in agreement with the interpretations he has given.

Dr. W. G. Spiller: Dr. Mills' paper embraces many subjects relating to the anatomy, physiology and pathology of the entire central nervous system, and he has given us gleanings from his experience covering a period of sixty years. It is difficult to know where to begin in the discussion of such a variety of topics.

He early accepted the division of the motor and sensory cortex into two separate parts, and he has seen this view gradually gain ground until now it is practically accepted by every investigator of note. Foerster believes that sensation as well as motion has a somatotopic representation in the cortex, the one corresponding in level to the other. He believes there is some representation of sensation in the precentral convolution, but this opinion seems to be based entirely on investigations carried on in the ape's brain. Dusser de Barenne has determined the extent of the sensory zone by placing strychnine on the cortex of the ape, and has found that this zone extends into the precentral area and even into the frontal lobe. The recognition of the irritation is by means of hyperalgesia in the periphery of the body, and it is bilateral from unilateral strychnine irritation, but more intense in the contralateral limb. This method has not been used on the human brain. Foerster has used electric irritation extensively on the human cortex under local anesthesia and has never produced paresthesia from any part other than the postcentral and upper parietal areas. Strychnine is a more delicate test for sensation.

There has been doubt as to the amount of pain representation in the cerebral cortex. Foerster believes pain is so represented, but the impairment of pain disappears more quickly than does other sensory disturbance, and pain sensation usually is the least affected.

There is considerable evidence that higher psychic function is represented in the frontal lobes, but the whole brain is necessary for mental development. Two cases of tumor of the parietal or occipitoparietal lobe under my observation may be used in elucidation of this subject. These tumors, by their weight or circulatory disturbances, probably produced symptoms from the first left temporal convolution. It was possible for each patient to read words, letters and figures correctly; they made no mistakes. They found that they did not grasp fully the meaning of what they read or of what they heard. One man especially was carefully studied. He found it necessary to speak slowly and to consider the words he intended to use. This was the first evidence of a slight word deafness. He had difficulty in recalling the words he wanted, he made no mistakes, but his acoustic word center had lost some of its rapidity of action. Later he probably would have been unable to recall the word he wanted, and would have used a wrong word, and still later would have failed to understand the spoken word. A similar condition existed regarding reading. These were defects of intellect, and there was probably a mental deficit. One cannot believe that the frontal lobes can be separated from the rest of the brain and perform their function. They are connected with the entire brain by numerous tracts, the cingulum, the superior longitudinal fasciculus, the uncinate fasciculus and the fronto-occipital tract of Forel and Onufrowicz. Such extensive connection shows the importance of all parts of the brain in the proper performance of the function of the frontal lobes.

Dr. Mills has abundant proof of the effect of extensive degeneration of one cerebral hemisphere on the opposite cerebellar hemisphere. I have reported such a case, as have others.

The localization in the cerebellar cortex has been done especially by Bolk, Rijnbark and Rothmann, but there is comparatively little evidence of localization in the human cerebellar cortex. The best recent evidence of this is to be found in the work of Ingvar. With regard to the effects of complete transverse lesion of the spinal cord, I would like to direct the attention of Dr. Mills to the investigations of Head and Riddoch and others.

Dr. C. W. Burr: I could quarrel with Dr. Mills about several things. I could quarrel with him on the so-called higher psychic centers, and I would enjoy it very much. I think the cause of our quarrel would be that we are using different words to describe the same thing. That is the cause of a great number of quarrels.

Now I am in a dilemma. I cannot conceive of thought except as a chemical process, and I cannot conceive of a chemical process unless there is a place in which it occurs. On the other hand, I find it absolutely impossible to conceive what chemical process is back of wisdom, judgment and clear reasoning.

Dr. Mills: I think that those who have discussed my paper have on the whole sustained my position, even with regard to what Jackson calls the highest level of the nervous system. In this prefrontal region, nervous phenomena are triply represented—there is a region of representation in the spinal cord, of re-representation in the sensory motor middle level and of re-re-representation in the highest level. Jackson definitely speaks of the highest psychic level as concerned with memory, will, reasoning and emotion. The difficulty is that we do not all have the brain of a Jackson, a Laycock, a Bain or a Ferrier. I am certain that I do not have it; yet I understand this theory of highest triple representation.

About the question of mentation, I would like to refer to what I have written about the concrete memory field. Conceptual mentation is a sort of mentation that in one sense requires the use of higher elements of the mind. Dr. Spiller and Dr. Lloyd refer to mental loss from lesion of the temporal or parietal lobe. Number blindness, letter blindness or word blindness may occur from a focal lesion in one of these lobes. This is a form of impairment of mentation, but it is not the highest mentation or even as high as it may appear to some.

Dr. Spiller, in calling attention to the views of Bastian and myself, with regard to the persistence of atonia after complete transverse lesion of the spinal cord in the cervical or thoracic region, refers to the investigations of Head and Riddoch, with which I am not unfamiliar. These observers have shown that in a case of complete severance of the cord, after recovery from the effects of shock caused by a sudden lesion as that produced by a gunshot wound, a period of reflex activity sometimes ensues. In this period such phenomena as reflex evacuation of the bladder or of the rectum and profuse sweating in various parts of the body may occur after a strong stimulation of the sole of the foot. Other phenomena, such as flexion of the thighs on the abdomen and of the legs on the thighs, may also occur. The sweating which occurs in these cases, especially that which is seen in the parts of the body supplied by the spinal cord above the side of the lesion, is brought about through the activity of the sympathetic nervous system, the chain of the sympathetic ganglia taking their course outside of the central nervous system. The other reflex phenomena might be regarded as of a primitive sort, that is, as due to the direct influx of powerful peripheral stimuli. The permanent state of the reflexes after complete transection of the cord is one of lowering or loss.

In his discussion, Dr. Dercum, like Dr. Lloyd, gives close attention to the bearing of comparative anatomy on the question of the functions of the cerebellum. It is well known that Dr. Dercum, in the true scientific spirit from the beginning of his professional career, has based his neurologic views on his evolutional studies and on comparative anatomy and biology. It is a pleasure to me to know that these studies first made many years ago indorse the conclusions regarding the cerebellum and the entire brain at which I have arrived during my sixty years of neurologic work.