illustration, to the "capsule of the lobe thickened in places, *from which* extend threads that end in knobs," etc. That the varicose threads and the capsule are structurally continuous, the latter thus dipping, through a multitude of protoplasmic projections, into the deeper elements of the lobe is evident.

We have seen that many features suggest a relationship between the *anterior* pituitary and the adrenals, through nerves at present considered as appurtenances of the sympathetic system. That the anterior lobe contains but one kind of nerve connected with this function—besides its vasoconstrictors—is shown by the following statement of Berkley's: "In the glandular portion of the body, nerves, other than those belonging to the sympathetic system, are not found. They are very fine *varicose* fibers, with numerous ramifications and branchlets coming off from the main stems at a right or slightly obtuse angle." These fibers must, therefore, represent, considering their general morphology and location, not terminals of the connecting nerves and distributors of energy, but *collectors* of energy, *i.e.*, of sensory impulses. They are probably the fibers which Cajal traced to the floor of the third ventricle. If Fig. *l* in Plate III, which represents a section of the glandular portion of the anterior lobe, is consulted, it will be seen that these nerves present the two main characteristics of the capsular threads of the posterior lobe: *i.e.*, they are also varicose and their tips are likewise knobbed. Since, therefore, the nerves so disposed in the anterior pituitary are collectors of energy, *the varicose and knobbed threads of the capsules of the posterior pituitary must also be collectors of energy.* This is further sustained by the analogy between the two organs to which reference has already been made.

That a direct nervous connection between the posterior pituitary and the infundibular tissues, etc., exists by way of the capsule of the former is thus probable—thus making it possible for impulses generated in the depths of the lobe to reach the ventricular structures, irrespective of the sharply defined connective-tissue separation between the lobe proper and the infundibulum. Indeed, such a separation seems a necessity, inasmuch as an impulse, transmitted through the intermediary of the capsule must, owing to the skull-cap shape of the latter,

come from every part of the underlying structures and only reach the basal structures through paths that are continuous with the capsule's tissues, and irrespective of the nerves which arise directly from the two lobes and pass upward by way of the interior of the infundibulum. That a profuse padding of cellular tissue is Nature's resource under such conditions is well illustrated by the following remark of Déjerine's: "The vessels of the central nervous system are surrounded by two sheaths of a different kind: the *internal* is connective in nature and belongs to the mesodermic layer; the *external*, neurogliar in nature, is developed at the expense of the external, or ectodermic, layer." The capsule has been compared to the cerebral cortex, perhaps with justice, as we shall show.

Berkley, referring to the various cellular structures in the deeper portion of the lobe supplied with long extensions, says: "The axis-cylinder extensions of all the cells in the inferior portion of the lobe turn upward. . . . Those belonging to the larger proportion of the smaller cells of the superior border turn upward and intermingle with the marginal fiber net-work. . . . All the axis-cylinder processes and the long dendrites have a general tendency upward and forward, both dendrites and neuraxons branching as they proceed onward: but all traces of the dendrites of the inferior and median cells of the lobe are lost some little distance below the superior edge, and then the neurons only are intermingled with the extensions of the smaller superficial cells, passing them, however, before the border is finally reached, where they spread out into a most extensive fret-work of fine *varicose* fibers, still retaining something of their previous longitudinal arrangement from the threads of the uptending fibers being coarser than the lateral and intermingling branches. It is doubtful whether any of these fibers pass beyond the limit of the lobe into the infundibulum; our sections give no evidence of such an arrangement." This upward tendency of all cells, and the evident concentration of their functional activity at the upper extremity, seem to us to further emphasize the identity of the posterior lobe as a powerful source of energy. Its junction with the end of the infundibulum becomes, under these circumstances, the normal pathway for all the energy that the organ can accumulate. Capsule and protoplasmic extensions or processes all serve a similar purpose, but the neck of the organ is its own functional limit.

We must not lose sight of the fact, however, that other nerves penetrate the organ. This is shown by the fact that Berkley says, in this connection: "the nerve-fibers accompanying the larger arteries are sometimes distinctly seen coming from the infundibular tract into the body of the posterior lobe of the gland and ramifying through it." That there is no connection between these and the nervous structures previously described, however, is shown by the additional statement: "Connections between the fibers of the vascular supply and the nerve-cells of the organ we have never been able to observe. That these are the nerves through which the organ receives its own functional energy—*i.e.*, the impulses to its vessels and alveoli,—as in the case of other organs, is probable."

The prevailing view that the embryonal supporting substance of the brain and spinal cord, the ependymal neuroglia, almost entirely atrophies and disappears in the adult mammal would tend to counteract my belief that the capsule and its underlying structures are important factors of the posterior lobe's functions. Berkley, alluding to the writings of various observers in this connection, and referring to the infundibulum and other tissues of the third ventricle which he had just described, says: "After reading these statements, it was something of a surprise to find the above-described beautiful specimens of several types of ependymal neuroglia extending from *all portions of the middle and inferior regions of the cavity of the third ventricle* and reaching to the periphery, all portions, bodies, branches, tentacles, and subpial endings being readily distinguishable. The region examined is, therefore, very interesting not only from the great variety of neuroglia-cells that may be seen within a very limited area, but from the fact that varieties of the ependymal neuroglia-cells, *previously supposed to have entirely disappeared* from the central nervous system *in the adult* mammal, are found present in perfect condition in the brain of a very high order of animal, and *are not confined, as has previously been supposed, to those of adult reptiles, amphibia, and fishes.*"

If all the data I have submitted are considered collectively, it seems to me that the following conclusion is warranted: *Removal of the hemispheres in an animal does not arrest its power to execute normal bodily movements under external stimulation, because these movements are dependent upon functional structures situated in the base of the brain and in the spinal cord and which the posterior pituitary probably governs.*

Of course, this appears to contradict at once a great mass of experimental and clinical testimony, but the contradiction is only apparent. Removal of the motor areas in the rabbit gives rise to no detectable differences in the movements; the injured animal is similar to an intact one. In the dog, the same procedure, according to Foster, causes "loss or diminution of *voluntary* movement in the corresponding part of the body"; but this is only temporary, and the animal may recover to such a degree that the temporarily paralyzed limb cannot be told from the normal one. Careful examination of the brain after death shows that no regeneration of the lost part had occurred. Even removal of the whole motor area causes no appreciable difference between the movements of the two sides of the body to a casual observer. In the monkey the results have been unequal: "While in some instances recovery of the movement has, in the monkey, as in the dog, after awhile taken place, in other instances the 'paralysis' has appeared to be permanent." . . . "The facts, however, within our knowledge relating to the permanence of the effect are neither numerous nor exact enough to justify at present a definite conclusion," as stated by Foster. "On the other hand, the positive cases, where recovery has taken place, are of more value than the negative ones, since in the latter the recovery may have been hindered by concomitant events of a nature which we may call accidental." I might add that a single case of recovery in the monkey, when the motor area has been completely removed, demonstrates that, generally speaking, the structures are functionally similar in all higher animals, including man, judging from such instances as the crow-bar case, or one reported by Brown-Séquard,[11] in which an entire

[11] Brown-Séquard: Société de Biologie, 1876.

lobe was destroyed and in which the only symptoms were amaurosis and slight headache. This emphasizes the identity of the cerebral hemispheres as an aggregate of centers which record impressions and are the seat of reason, intelligence, and volition, but it also suggests that the word "motor" is only applicable in its literal sense to the areas in the lower cerebral mechanism: *i.e.,* the intermediary through which the mandates from the hemispheres are executed.

I have previously referred to the misleading information afforded by the use of electrical stimulation. Nowhere in the organism does this seem to be more applicable than to the brain. This feature and the complexity of the processes involved are fully emphasized in the following lines of the late Dr. Foster: "Some writers appear to entertain the conception that in a voluntary movement, such as that of the forelimb, all that takes place is that the 'will' stimulates certain cells in the cortical area, causing the discharge of motor impulses along the pyramidal fibers connected with those cells, and that these motor impulses travel straight down the pyramidal tract to the motor fibers of the appropriate nerves, undergoing possibly some change at the place in the cord where the pyramidal fiber makes junction with the fiber of the anterior root, but deriving their chief, if not their whole, co-ordination from the cortex itself: that is to say, being co-ordinated at their starting-point. That such a view is untenable and that the simplicity of the electrical phenomena is misleading are shown by the following two considerations, among others: On the one hand, as was shown in a previous section, the co-ordination of movements may be carried out apart from the cortex, namely: in the absence of the hemispheres; and we can hardly suppose that there should be two quite distinct systems of co-ordination to carry out the same movement: one employed when volition was the moving cause, and the other when something else led to the movement. On the other hand, the analogy of speech justifies us in concluding that the cortical processes do take advantage of co-ordination effected by the action of other parts of the nervous system."

Referring directly to the general character of the processes involved, Professor Foster says: "Hence, while admitting, as we must do, that in the intact animal the cortical area and pyramidal tract play their part in carrying out voluntary movements, their action is not of that simple character supposed by the view referred to above. On the contrary, we are driven to regard them rather as links—important links, it is true, but still links—in a complex chain. As we have already urged, we may probably speak of the changes taking place in the pyramidal fibers as being, on the whole, of the nature of efferent impulses; but *we would go beyond the evidence if we concluded that they were identical with the ordinary efferent impulses of motor nerves.*"[12] All the features emphasized in these quotations, especially in the last lines, appear to me to isolate the hemispheres from the *source* of motor impulses *per se,* and to confirm what experimental evidence obtained after removal of the hemispheres had suggested: *i.e.,* that the *lower* cerebro-spinal structures constitute the executive intermediary through which the cortical mandates are actively realized. Yet, as is well known, these lower structures, in turn, manifest their activity through the centers imbedded in them; what is there to replace the energy in the form of motor impulses which is erroneously supposed to be awakened by the "will" in "certain cells of the cortical area"?

Professor Foster partially answers this question when he says: "The discussion in a previous section has shown that much of the co-ordination of the body is carried out by the *middle portions of the brain,* and on these the motor area must have its hold as on the spinal mechanisms. The details of the nature of that hold are at present unknown to us." It would appear from the facts reviewed that what might be termed the *central* brain and the spinal cord constitute an entity—a mechanical entity, perhaps—made up of working centers, beginning with the olfactory bulb and the other nervous structures distributed to the nasal mucous membrane anteriorly, and terminating with the end of the spinal cord: *i.e.,* the neural tract of lower forms. Motility, unconscious co-ordination, and sensation—but only, in the case of the latter, to the extent of *transmitting* sensory impressions to their re-

[12] The italics are my own.

spective perception-centers—would enter within the scope of this central brain.

As to the source of the transmitted energy or impulses,—apart from the sensory connections with underlying structures which the cortex possesses,—the predilection of most writers to ascribe to the cortical areas motor functions but demonstrates the need of such an agency to logically account for the phenomena witnessed. To ascribe to the central brain or its centers *per se* attributes of a similar kind would simply amount to shifting to it a convenient, but unknown, quantity, and a fictitious one besides, in the sense that it supplies nothing to account for something. In the only nervous system that I have so far traced to its origin, that of the suprarenal glands, the conversion of chemical energy into nervous impulses was found to be a functional attribute of the anterior pituitary body. That so extensive a system as that represented by the central brain and cord should likewise need a center such as that represented by the posterior pituitary body for the conversion of some form of energy of external source to satisfy the needs not only of its efferent, but also its afferent, impulses seems clear.

That the middle brain is the source of the motor phenomena witnessed is not only suggested by the fact that normal muscular contractility promptly recurs after removal of the hemispheres, but also by the following experiment by Professor M. Duval: "If a part of the gray substance of the cortex designated as the center of certain movements is cauterized, the same movements are obtained when the electrodes are applied upon the eschar thus produced. . . . This experiment shows," says the author, "that the gray cortical substance is not a necessary experimental condition for the production of localized movements." Indeed, he states that the underlying white substance of certain parts will also cause circumscribed motions in certain groups of muscles, etc.

Can the removal of the cortex of one side be followed by the assumption of compensative functions by the opposite side? After the usual period of paralysis, due to shock, the normal motions promptly recurred, precisely as they had on the other side. To ascertain whether the cortex at all possessed motor attributes Vulpian passed an electrode through it, that part in contact with the cortex being insulated. The underlying white substance was thus alone stimulated. He found that the latter was far more easily excited than the cortex. It seems clear that in these experiments *the increased excitability was due to the closer proximity of the central brain.* "All the functions of the brain can persist," says Brown-Séquard, "after the complete destruction of an entire lobe."[13] Experimental and clinical evidence, however, only eliminate motility and co-ordination from the hemispheres. The cortex, as regards cerebral localization, merely loses the "motor" attribute suggested by the term "motor area," and is shown, by its functional relations with the underlying structures, to be a vast sensitive surface, to the "areas" of which the term "sensory" might be more fittingly applied.

The practical bearing of this may be illustrated by an experiment that will recall some of the familiar features of the earlier portions of this work and at the same time point to the central brain as the source of motor phenomena. This experiment, referred to by Professor Foster, is as follows: "It has been observed that in certain stages of the influence of morphine the cortex and the rest of the nervous system are in such a condition that the application of even a momentary stimulus to an area leads not to a simple movement, but to a long-continued tonic contraction of the appropriate muscles." As previously shown, many drugs raise the blood-pressure and thus congest the adrenals and indirectly the brain. Cerebral hyperæmia, we have seen, is the source of the majority of phenomena that follow the ingestion of drugs that are sufficiently active to stimulate the adrenals. The intense headache of quinine and other agents is obviously due to this congestion of the cerebral vessels; muscular contractions, tetany, etc., are also familiar results of suprarenal overactivity; indeed, digitalis, one of the most active suprarenal stimulants, is particularly active in predisposing muscles to contraction and in experimental animals suitably dosed a minimal current without the drug will produce maximum effects—prolonged tetany—with it.

[13] M. Duval: *Loc. cit.*, p. 115.

In the course of the statements to which I have referred, Foster, after ascribing the temporary paralysis observed after operative interference to a condition "of the nature of shock," remarks: "But, even giving full weight to this consideration, there remains the fact that the cortical area is *associated* with various co-ordinating and other nervous mechanisms belonging to the limbs by such close ties that these are thrown into disorder when it is injured. And, side by side with this, we may put the remarkable fact, previously stated, that during an *abnormal* condition of the cortical area—simulation of the area—instead of producing the appropriate movements confined to the limb may give rise to movements of other parts *culminating in epileptiform convulsions.*"[14]

If the word "associated" is given its full meaning, limbs and co-ordinating mechanism constituting one class, and the cortical surface the other, *the hemispherical mantle of gray matter being considered solely as a great sensory surface,* the demands of experimental evidence seem to me to be satisfied. What are epileptic convulsions after all but manifestations of excessive *motor* activity? . . . Can the latter be credited to the cerebral cortex, as is now taught in text-books? Obviously not, since experimental evidence proves that the cortex has no motor properties *per se.* But irritation of this sensory surface or an accumulation of physiological toxics, which periodically becomes sufficiently great to so stimulate the vasomotor center as to cause violent hyperæmia, not only of the sensory cortex, but also of its executive mechanism, the middle brain, are the clearly defined causes to which physiological and chemical evidence points. Could the cortex without the middle brain give rise to the same phenomena? That such is not the case is shown by the preservation of all motor functions, including co-ordination, after removal of the hemispheres. Indeed, it is only when the middle brain is removed that the experimental animal thus deprived of its sentient cortex and of its dynamic center practically loses its identity as a living thing. Hence it seems clear that *the motor phenomena caused*

[14] All italics are my own.

by stimulation of the motor areas of the cortex are manifestations of activity of the central gray matter at the base of the brain, incited therein by sensory impulses from these cortical areas.

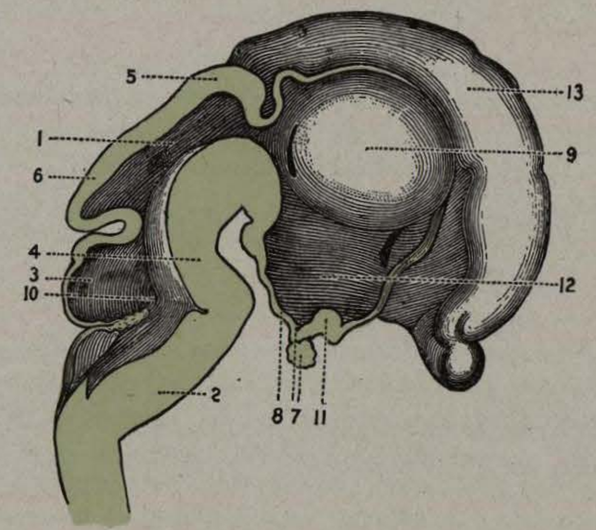
What constitutes this lower brain? The co-ordination, so evidently preserved in animals deprived of their hemispheres, points to the cerebellum as a possible member of the group of organs to be considered in this connection. Including this organ, therefore, and beginning with the anterior structures, we would now have: the posterior pituitary body; the infundibulum; the central gray matter, forming "a bed for the development of the nuclei of the cranial nerves"; the tegmental system,—*i.e.,* the reticular formation in the medulla continued to the subthalamic region, and to which belong the red nucleus and other bulbar nuclei. All this forms what Foster so aptly characterizes as "a more or less continuous column of gray matter" connected with the spinal cord by various ties, besides being, as it were, "a continuation of the spinal gray matter." It is as evident that the optic thalami and corpora quadrigemina are also members of the group, since these related organs appear to be necessary for the success of the experiment in which both cerebral hemispheres are removed. Thus, referring to the frog, Foster says: "In this animal it is comparatively easy to remove the cerebral hemispheres, including the parts corresponding to the corpora striata, leaving behind, intact and uninjured, the *optic thalami* with the optic lobes, the representatives of the *corpora quadrigemina,* the small cerebellum, and the bulb. If the animal be carefully fed and attended to, it may be kept alive for a very long time: for more than a year, for instance."

If, with this list before us, we now examine the annexed illustration, originally from His's work, and, therefore, not recently drawn, a rather suggestive coincidence appears, indicating, perhaps, a total independence, in the embryo, of the region containing all the structures enumerated from the vesicle which subsequently develops into the hemisphere of the same side. In mammals the latter is at first insignificant, but it develops very rapidly, soon overlapping the middle structures. The outline of the latter is colored bluish gray. The name of each part is given on the cut: a feature that will better convey the mutual relations of the various structures included in this system than a verbal description.

Again, the location of the posterior pituitary at the very head of the entire spinal system, as shown in the illustration, adds further testimony to that already submitted to demonstrate the functional relationship between the nervous structures lying in the posterior pituitary, including the floor of the fourth ventricle, and the bulb.

A summary of all these facts, *i.e.*, (1) that the posterior pituitary body has a phylogenetic history which distinctly identifies it as a part of the entire neural tract; (2) that it presents clearly defined histological characteristics of an active neural organ; (3) that these characteristics extend to the infundibulum, the tuber cinereum, the floor and sides of the third ventricle; (4) that these structures are continuous with the reticular substance of the tegmental region, the medulla, and the cord; (5) that the posterior pituitary body has been found to be in direct relation with the olfatory center and the bulbo-spinal axis in all classes of vertebrates; (6) that a current passed between the olfactory and medullar centers may cause heart-inhibition and death; (7) that various nerve-centers are included in the structûres with which the pituitary is functionally connected in all vertebrates; (8) that sudden death is caused by a puncture in the region of the vagal bulbar center through interruption of the efferent and afferent impulses through which the cardio-pulmonary system is incited to activity and governed; (9) that electrical excitation of the exposed pituitary body causes an instantaneous rise of the blood-pressure of over 100 mm. Hg.; (10) that removal of the pituitary causes the opposite, *i.e.*, an immediate and great fall of the blood-pressure; (11) that division of the base of the brain across the path of nerves known to originate in the pituitary body prevents the action of drugs, such as antipyrin, which lower the temperature, and also the action of pus and other septic materials which cause fever; and finally (12) that all functions carried on normally after removal of the brain are caused to cease by removal of the pituitary, seems to me to warrant the conclusion that:—

The posterior pituitary body is the chief center of the spi-



MEDIAN AND VERTICAL SECTION OF A TWO AND ONE-HALF MONTHS' EMBRYO. *[His.]*

[Considerably Enlarged.]

1, Aqueduct of Sylvius. 2, Medulla Oblongata. 3, Cerebellum. 4, Pons Varolii. 5, Anterior Tubercula Quadrigemina. 6, Posterior Tubercula Quadrigemina. 7, Infundibulum and Pituitary Bodies. 8, Tuber Cinereum. 9, Optic Thalamus. 10, Fourth Ventricle. 11, Hypoglossal Nerve [Twelfth Pair]. 12, Third Ventricle. 13, Hemisphere Vesicle.