ganglion reflexes," *i.e.*, of a structure capable of receiving sensory impulses and sending forth motor stimuli.

The identity of the pituitary body as a sensory center is emphasized first of all by the fact that lesions of the cortex do not influence general sensibility.

"Innumerable cases have been reported of lesions of the motor cortex," writes C. K. Mills,[603] "without the slightest impairment of sensibility. In several cases of excision of the human cortex in the Rolandic region by surgical operations, careful studies of the patients by the writer and others failed to show any impairment of sensation." As we all know, a large number of cases of extensive injury of the cerebrum fully sustain this assertion by the absence of sensory phenomena. Again, Charcot and Pitres[104] state that "the paralyses of cortical origin are accompanied sometimes with disorders of cutaneous or muscular sensibility, but these sensory disorders, which are eventually associated with motor paralyses, do not show a *direct* or *necessary* connection with lesions of the motor zone." We have seen also, that the pigeon deprived of its hemispheres can feel and shake off a fly that chances to alight on the feathers of its head; that Goltz's dog, similarly mutilated, reacted promptly to tactile sensation, limped when hurt, promptly raised its feet when these were placed in cold water, etc. On the other hand, Schäfer[106] concludes a comprehensive review of the question with the remark: "This no doubt lands us in the unsatisfactory position that we are unable certainly to say in what part we are to localize cutaneous sensibility, or even *if it is localized at all in the cortex.*"

This obviously suggests that the posterior pituitary, *i.e.*, the neural lobe, might in the light of my views, fulfill this function. Yet, a decapitated frog, *i.e.*, one deprived of its basal ganglia and part of the central gray matter, and, therefore, of the pituitary body, will raise one of its limbs and adjust it to a spot upon which some irritant has been placed in order to rub it. We must not lose sight of the fact, however, that *all* protoplasm is endowed with reflex attributes and that nerve impulses only *multiply* their inherent properties. We have in this auto-protective motion of the decapitated frog, therefore, but an expression of its latent capabilities. As stated by Foster,[107] "the phenomena presented by a frog possessing the middle portions of the brain differ widely from those presented by a frog possessing a spinal cord only. We may, perhaps, broadly describe the behavior of a frog from whom the cerebral hemispheres only have been removed by saying that such an animal, though exhibiting no spontaneous movements, can, by the application of appropriate stimuli, be induced to perform all, or nearly all, the movements which an entire frog is capable of executing." Of the frog possessed of its spinal cord only, he says: "When placed on its back it makes no attempt to regain its normal posture; in fact, it may be said to have completely lost its normal posture, for when placed on its belly it does not stand with its fore feet erect, as does the other animal, but lies flat on the ground. When thrown into water, instead of swimming it sinks like a lump of lead. When pinched or otherwise stimulated it does not crawl or leap forward; it simply throws out its limbs in various ways. When its flanks are stroked it does not croak; and when a board on which it is placed is inclined sufficiently to displace its center of gravity it makes no effort to regain its balance, but falls off the board like a lifeless mass. Though, as we have seen, the various parts of the spinal cord of the frog contain a large amount of co-ordinating machinery, so that the brainless frog may, by appropriate stimuli, be made to execute various purposeful co-ordinate movements, yet these are very limited compared with those which can be similarly carried out by a frog possessing the middle and lower parts of the brain in addition to the spinal cord." The author also states that "the phenomena presented by animals deprived of their cerebral hemispheres show that this machinery of co-ordination is supplied by cerebral structures lying between the cerebral hemisphere above and the top of the spinal cord below," and subsequently refers to the "foundation of the machinery in question" as "the tegmental region *from the bulb upward.*" The tegmental region, that through which ascends the *fillet*, is likewise

[103] C. K. Mills: "The Nervous System and its Diseases," Phila., 1898.
[104] Charcot and Pitres: "Les centres moteurs corticaux chez l'homme," Paris, 1895.
[105] Schäfer: "T. B. of Physiol.," vol. ii, p. 728, 1900.
[106] Schäfer: *Ibid.*, vol. ii, p. 768.

[107] Foster: *Loc. cit.*, p. 637.

referred to by Foster[108] as a "probable path of sensations of one kind or another from *the body at large.*"

The neural lobe may well be, therefore, the organ in which, repeating Schäfer's words, we can "localize cutaneous sensibility" and in fact sensory impulses received from mucous membranes, muscles, etc., since in Goltz's dog all functions, digestion, salivation, urination, etc., which involve reflex actions, were performed normally. As stated in the preceding section, moreover, this lobe is the only organ "lying between the cerebral hemisphere above and the top of the spinal cord below," as Foster says, that is capable structurally of carrying on the functions of a center. Finally, that it is actually the seat of sensibility is clearly suggested by the presence of various disorders of sensation when the pituitary body is diseased.

In acromegaly, for example, very severe headache of a neuralgic type is commonly observed. It is usually limited to the head but may extend over the entire body, as in a case reported by Hymanson,[109] or be localized, as in that observed by Pirie, who specifies "the face, chest, back and loins." The facial neuralgia is essentially within the domain of the fifth pair as emphasized by Gubler.[110] Rosenhaupt[111] found that when this characteristic pain was present, the skin of the face was hypersensitive. Breton and Michaut[112] noted that pressure on the points of exit of the fifth caused intense pain, with typical signs of acromegaly. In one of M. Allen Starr's cases[113] the pain was agonizing and was constant over the forehead and back of the eyes. In another instance, recorded by O. T. Osborne,[114] the pain is stated by him to have been "directly over the pituitary body" while the autopsy "revealed a plate of bone making pressure at this very point."

Disorders of sensibility of other kinds may likewise occur. Paræsthesia of the lower extremities and back was observed by Pearce Bailey[115] in a case of tumor of the pituitary, in which this organ was found, after death, to have been the seat of an

[108] Foster: *Loc. cit.*, p. 716.
[109] Hymanson: Med. Record, July 1, 1899.
[110] Gubler: Correspondenzblatt f. d. Schweizer Aerzte, Dec. 15, 1900.
[111] Rosenhaupt: Berl. klin. Woch., Sept. 28, S. 893, 1903.
[112] Breton and Michaut: Gaz. des Hôpitaux, Dec. 13, 1900.
[113] M. Allen Starr: Med. Record, Feb. 3, 1900.
[114] O. T. Osborne: *Ibid.*, Mar. 4, 1899.
[115] Pearce Bailey: *Ibid.*, Apr. 16, 1898.

extensive hæmorrhage. In his case of acromegaly, Pirie noted "shooting pains in combination with paræsthesia, tingling and numbness" of the arms and legs, and "a remarkable perversion of thermic sensibility" in the lower limbs, front of the abdomen and chest to about the level of the fourth rib, the patient having "no sensation of heat in these regions," and he refers to Sternberg as remarking "particularly on the occurrence of pain and paræsthesia as valuable signs for diagnosis in the *early* stages of the disease." Many similar instances could be quoted.

This is strikingly controlled by the fact that removal of the pituitary abolishes sensation even of the most sensitive nerve of the body, the fifth pair. Thus Cyon not only observed in the course of his investigations in a very large number of animals (though working in different lines) that removal of the pituitary annulled nasal sensory phenomena, sneezing, etc., but he also specifies[116] that all the nerves, *including the fifth* and glossopharyngeus, "lost their *reflex* influence after the pituitary body had been removed." The inference is obvious in view of the fact that section of the fifth deprives the nasal surfaces of sensibility. Whether severed between the nasal surfaces and the bulb, or between the latter and the pituitary body or destroyed along with the latter amounts to the same thing: we are brought to the inevitable conclusion that the fifth is also under the domain of the pituitary body—a fact which in turn explains why lesions of this organ can provoke sensory phenomena throughout the entire organism, for the fifth is but a portion of the great system of common sensation.

All these phenomena belong, however, to the domain of *common sensibility.* Do other special senses show evidence of being related in any way with the pituitary body?

Smell is sometimes impaired and even lost in acromegaly, as shown by cases reported by Joffroy,[117] Leszynsky,[118] Roxburgh and Collis,[119] and others. A study of the question—the details of which I will not inflict upon the reader—showed that the sense of olfaction *per se* could be influenced indirectly, the morbid effects being due to ischæmia and impaired nutrition of

[116] Cyon: Richert's "Diction. de physiol.," vol. iv, p. 131, 1900.
[117] Joffroy: Le progrès médical, Feb. 26, p. 129, 1898.
[118] Leszynsky: Med. Record, Mar. 4, 1899.
[119] Roxburgh and Collis: Brit. Med. Jour., July 11, 1896.

the olfactory area through involvement of the sympathetic center in the neural lobe. Another source of disorder in the nasal cavities is brought about through the sensory fibers of the mucous membrane. As stated by Haycraft,[120] "the fifth is the nerve of common sensibility to the nose, and in the case of disease or *section* of this nerve, irritants such as pepper, chlorine, and ammonia, produce no irritating effect." This statement is suggestive in view of the fact that removal of the pituitary body by Cyon produced, we have seen, identically the same effect.

While there is no ground for the conclusion that the pituitary body receives odoriferous impressions as far as available evidence is concerned, therefore, the common sensibility impressions are clearly referable to this organ.

Vision is impaired in a large proportion of cases of acromegaly—91 times in 174 cases according to Hertel[121]—and blindness is a frequent result. Optic nerve disorders are, at least in part, ascribable to pressure of the enlarged organ on the optic chiasm. Bi-temporal or one-sided temporal hemianopsia for form and color is also observed. The symptoms may appear early and follow a progressive course; conversely, the disease may have existed many years before visual disturbance appears. As shown by the statistics of Hertel, they may not appear at all, though the typical symptoms of acromegaly be present. In such a case, reported by Ferree Witmer[122] for instance, the eyes were examined by W. Campbell Posey. "As a result of the ophthalmological examination," says the latter, "it is evident that there is no pressure anywhere on the optic tract." Interesting in this connection, is the fact that among the symptoms recorded in this case was a "marked reduction of the common sensibility" and that "the sensibility of the fauces was also considerably diminished." In another case of acromegaly observed by Packard and Cattell, reported by Spiller,[123] "the visible fields for form and color were normal; the pupils responded freely to light in accommodation and in convergence" and yet common sensibility was markedly reduced. Thus tests to determine the rate of sense perception showed "a retardation of reaction time to forty

[120] Haycraft: Schäfer's "T. B. of Physiol.," vol. ii, p. 1247, 1900.
[121] Hertel: Archives f. Ophthal., Bd. xli, Abt. i, S. 187, 1895.
[122] Ferree Witmer: Intern. Med. Mag., Jan., 1898.
[123] Spiller: Jour of Nerv. and Mental Dis., Jan., 1898.

per cent. below the normal." At the autopsy a round-celled sarcoma about the size of an English walnut was found in the pituitary body which pressed upon the optic nerves.

Apart from the impressions of common sensibility, the anatomical connections of the visual tract do not present features which suggest a direct functional connection with the pituitary body. Indeed, Goltz's dog, though sensitive to a bright light, could not actually see. This does not apply of course to the oculo-motor muscles which in common with other muscles, are also related through the bulb, with the latter. Hence the strabismus often observed in acromegaly and neoplasms of the pituitary.

We are again brought to conclude, therefore, as far as the main functions of the eye are concerned, motion and common sensibility are the only ones related directly with the pituitary body.

Hearing is occasionally impaired in acromegaly, but a feature which stands out prominently in this connection is that disorders of sensibility appear always to be present concurrently—even when the very frequently observed symptom, tinnitus, fails to appear. In Pirie's case, for example, tinnitus accompanied the marked sensory disturbances to which reference has been made. In Hymanson's it also coincided with numbness of the hands. In Lackey's[124] tinnitus and impairment of hearing occurred in conjunction with numbness of both feet and hands. Deafness may also appear along with cutaneous hyperæsthesia as in Breton and Michaut's case. Conversely, Gibson states that his patient "was not at all deaf" and that "ordinary sensibility to touch, pain, heat, cold and electric stimuli was intact;" in Grinker's[125] case the special senses were normal and "the pain, touch and temperature senses" likewise. All these phenomena are readily accounted for by the fact that aside from the auditory nerve distributed to the cochlea, the vestibule and semicircular canals, the membrana tympani receives fibers from the fifth pair. "Although the innervation of the membrana tympani has not been conclusively established," write McKendrick and Gray,[126] "there is little doubt it is supplied with sensory nerves by the

[124] Lackey: Phila. Med. Jour., July 22. 1899.
[125] Grinker: Chicago Med. Recorder, Dec., 1903.
[126] McKendrick and Gray: Schäfer's "T. B. of Physiol.," vol. ii, p. 1157, 1900.

fifth, and also by the tympanic plexus, formed by fibers derived from the otic ganglion, from the petrosal ganglion of the glosso-pharyngeal, and from the carotid plexus." The aural symptoms of acromegaly, therefore, are not preversions of the sense of hearing, but disorders of general sensibility.

Taste is rarely referred to as being morbidly influenced by disorders of the pituitary, but it is probable that the condition of this sense is seldom inquired into. It is occasionally mentioned, however, among the symptoms of acromegaly and tumor. In Gibson's case, the food had to be highly seasoned before it could be tasted. In a case which proved to be one of melanotic sarcoma of the pituitary observed by Agostini[127] impairment of taste coincided with auditory, visual and olfactory paræsthesia and with "obtuse general sensibility." Here again we have not only glosso-pharyngeal fibers and the lingual terminals of the chorda tympani, but also the lingual branch of the 5th, which supplies the anterior two-thirds of the tongue with common sensibility.

This terminates the list of special senses. It has become apparent that the only special sense clearly related with the posterior pituitary is that of general sensibility.

Although this organ thus asserts itself as a terminus for impressions included within the precincts of a single special sense out of the five, the function it fulfills in this connection is a far-reaching one as interpreted from my standpoint, since it means "the sensations of one kind or another from the body at large," including those from the gastro-intestinal mucous membranes, the muscles, etc.

We can now understand why Mills could write that "innumerable cases have been reported of lesions of the cortex" or excision of portions thereof failed to produce "the slightest impairment of sensibility," and why Schäfer was unable to say whether cutaneous sensibility was localized at all in the cortex. The foregoing facts obviously show that the cortex is not the organ through which such sensations are perceived. Indeed, Cyon's observation in relation to the loss of sensibility of the nasal mucous membrane after removal of the pituitary is but a limited example of the morbid influence of this procedure: Vassale and

[127] Agostini: Rivista di patol. Nerv. e Ment., Fasc. iv, 1899.

Sacchi[128] found that the animals submitted to it remained *totally indifferent to excitation*—evidence that their general sensibility had been destroyed. It is plain, therefore, that the posterior or neural lobe of the pituitary body receives impressions of general sensibility from the body at large.

Sensory impulses of this kind awaken normal *motor* stimuli in animals deprived of their brain. Thus in Goltz's dog, there was no loss of muscular co-ordination although the animal was not, of course, deprived of its pituitary. And yet, this phenomenon always attends removal of this organ, even though the cerebellum and the semicircular canals be normal. The pituitary body must, therefore, exercise an all-pervading influence over motor phenomena. What is the nature of this influence?

Clinical data throw considerable light upon this question provided several confusing facts are borne in mind and misleading cases are avoided. First among the former, is the reserve of functional elements with which the pituitary body, in common with the "ductless glands," is endowed, which makes it possible for this organ to carry on its functions even though considerable of its substance is destroyed. Thus, Vassale and Sacchi[129] in the course of their experiments on cats and dogs, in which total extirpation of the pituitary invariably proved fatal, only partially destroyed it in one of these animals, as previously stated. The characteristic phenomena were observed for about three weeks, after which the animal gradually recovered and remained healthy. At the end of eleven months it was killed and the incomplete destruction was confirmed. Friedmann and Maas[130] also refer to three animals which were killed after two and one-half, three and four months after a supposed destruction of the organ; but this was found to have been incomplete.

This partial destruction may be due to disease. As emphasized by Burr and Riesmann,[131] the pituitary body can also carry on its functions, even though a part of it be diseased. Thus in a case of tumor of this organ in which no signs of acromegaly were present, they found a considerable portion of its elements

[128] Vassale and Sacchi: Rev. sper. di fren., p. 83, 1894.
[129] Vassale and Sacchi: *Ibid.*
[130] Friedmann and Maas: *Loc. cit.*
[131] Burr and Riesmann: Jour. of Nerv. and Mental Dis., Jan., 1899.

intact. In a case reported by Walton, Cheney and Mallory[132] a part of the pituitary body was also found normal.

Another clinical feature which tends to obscure the rôle of the pituitary body is the extension of a morbid process in this organ to structures above, or the presence, simultaneously, of cerebral, bulbar or spinal lesions. The cases quoted herein are of such a nature as to prevent confusion on this score; they include only such disturbances as those witnessed experimentally either during stimulation or after extirpation in normal animals.

Irrespective of these sources of confusion, the functional relationship between the pituitary and the muscular system may easily be discerned. Thus, while Pironne[133] found experimentally in common with other observers, that "the results of removal" are "disturbances of mobility, great depression, rapid emaciation, cachexia and death," Rath[134] enumerates the symptoms of tumor of the organ in the order of their frequency as follows: headache, generally frontal and temporal; vomiting; vertigo; disturbances of motion, spastic and paretic; disturbances of speech; disorders of the pupil; paralysis of the ocular muscles; diabetes mellitus and insipidus. The ocular motor disturbances, "vomiting," "motion" and "speech," bring into play almost all the muscles of the organism governed by the cranial nerves, including the tenth (vagus) and fifth. In Agostini's case of sarcoma of the pituitary, muscular asthenia was a prominent symptom, although the characteristic signs of acromegaly were absent. In another case of tumor reported by Howard and Southard,[135] "some unsteadiness of gait" was noted four years before death, suggesting not only muscular weakness but impairment of co-ordination. In Walton, Cheney and Mallory's case,[136] an angiosarcoma had destroyed the pituitary in part, without giving rise to clearly-defined symptoms of acromegaly; and yet the patient's gait was "slow and dragging" and the muscular weakness increased until "extreme prostration" was reached. In a case characterized as "ataxia but without any signs of acromegaly," observed by T. W. P. and J. Lawrence,[137] the pituitary was found enlarged and the posterior lobe was destroyed. Masay[138] observed that after removal of the pituitary body, the animals (dogs) though they tried to do so, were "unable to stand," the ataxia being "complete."

[132] Walton, Cheney and Mallory: Boston Med. and Surg. Jour., Dec. 7, 1899.
[133] Pirrone: La riforma medica, Feb. 25, p. 205, 1903.
[134] Rath: Archiv f. Ophthal., Bd. xxxiv, Hft. 4, S. 81, 1888.
[135] Howard and Southard: Amer. Jour. Med. Sci., Oct., 1904.
[136] Walton, Cheney and Mallory: *Loc. cit.*
[137] T. W. P. and J. Lawrence: Brit. Med. Jour. Apr. 8, 1899.

Such paralytic phenomena also occur in advanced acromegaly. Here, muscular asthenia is a prominent feature. Even in cases such as those reported by Virchow, Dana, Woods Hutchinson and others in which there is marked increase in bulk and muscular strength, in wrestlers, giants, etc., this symptom forms part of the cachectic stage into which the patient ultimately lapses. "In the earlier stages in *some* cases," writes Woods Hutchinson,[139] "there is a decided increase in both muscular bulk and power, but this rapidly reaches a maximum and thereafter quickly declines." But he also concludes in accord with Dana, Tamburini and Harlow Brooks, that acromegaly and giantism are "the result of a normal or glandular hypertrophy of the entire pituitary body beginning in and chiefly affecting the anterior lobe, but even extending to and affecting the posterior or nervous lobe." All cases of acromegaly which do not die of some intercurrent disease, in fact, lapse into what amounts practically to muscular impotence.

And we have here but the uncomplicated type. Along with the muscular asthenia we may have mixed symptoms. Where in other words there was merely "increasing weakness," with "no evidence of paralysis" we now witness besides, phenomena recalling neuroses and muscular dystrophies of various kinds—syringomyelia; unilateral, bilateral or localized paralyses; progressive muscular atrophy, etc. In some cases related by Duchesnau[140] for instance, "atrophy of the muscles was so marked, that it had been mistaken for syringomyelia, progressive muscular atrophy" and other kindred disorders. In a case reported by Pirie[141] (who quotes Duchesnau's), the muscular weakness not only became intense, but this was attended by atrophy of various muscles of the hands, arms, calf, thigh, and of the glutei.

On the whole, it is evident that the "neural" or posterior lobe of the pituitary, when diseased alone or in conjunction with

[138] Masay: *Loc. cit.*, pp. 16, 17.
[139] Woods Hutchinson: N. Y. Med .Jour., Mar. 12, Apr. 2, 1898; July 21 and 28, 1900.
[140] Duchesnau: Thèse de Lyon, 1891.
[141] Pirie: Lancet, Oct. 5, 1901.

the anterior lobe, can provoke a great variety of motor disorders, a fact which, in view of the loss of muscular co-ordination, the marked relaxation of all muscles and the profound asthenia that follow extirpation of the pituitary—including of course the neural lobe—clearly point to the latter as the seat of general motor centers. Its influence is not limited to the skeletal muscles, since, as we have seen, it governs also the sympathetic system, whose terminals are distributed to the muscular coat of the arterioles.

We can now understand why organic lesions, gradually as they destroy the cellular elements of the posterior pituitary, give rise to promiscuously-distributed disturbances of sensibility and motility. It receives sensory impulses from all muscles, skeletal, gastric, intestinal, diaphraghmatic, cutaneous, ocular, etc., and from the mucous membranes, then converts and co-ordinates all these impulses into motor stimuli which it sends back to the muscles, to sustain the many functions with which they are connected and to enhance their activity, when need be.

The view still prevails in the minds of many that the cerebellum is the co-ordinating center of muscular movements. Foster says, in this connection, that experimental and clinical investigations "have thrown little or no light on the exact nature of the part which the organ plays in the complex process, but perhaps rather show that *we are at present wholly ignorant of how co-ordination is brought about.*" He states also, however, referring to the pituitary body: "Concerning the purposes of the organ as a whole, we know absolutely nothing." The foregoing evidence, contributed since he wrote these lines, clearly suggests that the true co-ordinating center is the neural lobe of the pituitary body.

Foster[142] terms "the machinery of co-ordinated movements" structures "lying between the cerebral hemisphere above and the top of the spinal cord below;" but as to *how* "this machinery is related to the various elements which go to make up this part of the brain" he says "the only answers which we receive are of the most imperfect kind." Physiologists, in fact, have furnished no answer. Experimental evidence, however, has brought them to structures *immediately overlying the pituitary body*

[142] Foster: *Loc. cit.*, p. 651.

and connected with it, but structures presenting no organization capable, after removal of the brain, of accounting for the continuation of all somatic functions. We have seen that Ramon y Cajal—though unaware of the functional importance of the pituitary body—found that it was connected by afferent and efferent, *i.e., sensory* and *motor* fibers with the great nucleus situated immediately above this organ, which nucleus, as previously shown, is itself connected by nerve-paths with "the top of the spinal cord below." The neural lobe of the pituitary thus asserts itself as the chief center of the "machinery of co-ordinated movements," as well as the seat of common sensibility.

The vast scope of these functions is summarized in the following postulates: (1) *the cortex is not the only organ through which cutaneous and internal sensations are directly perceived;* (2) *these sensations, which include pain, heat, cold, pressure (constituting touch), hunger, thirst and the muscle and spatial senses, are perceived by and through the neural or posterior lobe of the pituitary body;* (3) *this organ also receives all sensory impulses which reflexly incite and sustain the secretory activity of all glands (gastric, intestinal, pancreatic, salivary, lachrymal, lacteal, etc.), and the contraction of all muscles, striped and unstriped, peripheral or internal (including those of the vessels and heart, the stomach, intestines, bladder, etc.);* (4) *the processes thus governed by the posterior pituitary body, are not mere reflex phenomena such as those elicited from subsidiary nerve-centers, e.g., those in the medulla oblongata and spinal cord; they include all functions which require conscious and to a certain extent intelligent co-ordination.*

This involves the conclusion that *the neural lobe of the pituitary is the general center of all the cranial nerves concerned with common sensation and motion,* besides the sympathetic center studied in the preceding section, with which the cranial centers are in close functional association, as will be shown.

The manner in which these nerves carry on their functions in the peripheral organs, and their functional relations with the sympathetic terminals will be studied in the eighteenth and twentieth chapters.