THE PATHOLOGY OF POSTENCEPHALITIC OCULAR DISTURBANCES IN THE LIGHT OF RECENT ANATOMICAL AND PHYSIOLOGICAL RESEARCH.

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I.—The relative identity of the forced movements and forced positions seen in the lower quadrupeds after lesions of the supravestibular structures with the paralysis of lateral and upward movements seen in man after similar lesions.

WHY is it that in medical practice one rarely sees real forced movements after lesions of the vestibular nerve, its nuclei, and its ascending secondary and tertiary connections? Such forced movements in the three planes are known to be extremely common after a great variety of lesions in the lower vertebrates and in all invertebrates where the bodily structure is symmetrical and the power of independent locomotion sufficiently developed.

In answer to such a question different points must be considered.

(1) The erect posture with the vertebral column vertical below the cranium has undoubtedly brought about a fundamental reorganisation of vestibular functions. As a matter of fact two forms of forced movement, performed by fishes, birds and quadrupeds after a lesion of certain vestibular structures in two different planes (cf. the horizontal and frontal planes in Figs. 1 and 2) are performed in the same plane in some other mammals, *i.e.*, circus and rolling movements. This occurs in man and the erect arboreal simians. (2) With increased development of the prosencephalon compensatory and quasi-voluntary inhibitory movements develop, so that the strong and persistent rolling movements seen in the rabbit after lesion of the vestibular nerve are rarely if ever seen in the higher quadrupeds. This inhibitory effect of the higher centres on the lower naturally reaches its greatest development in man. (3) Primary lesions of the vestibular nerve such as may be inflicted experimentally are extremely rare in man. It is, however, very common to find pathological changes in the secondary and tertiary connections of the vestibular system. In my earlier work^{1,2,3} I pointed out that well-marked and strong movements of a forced character are only met with in the lower vertebrates after lesion of the peripheral vestibular nerve.

A lesion of the second neurone produces forced movements moderate in character, while after lesions of the third (prosencephalic) neurone they are still more moderate. The nystagmus which accompanies them exhibits itself as a slow movement in the direction of the forced movement, followed by a rapid jerk back.

Pathological affections of the vestibular tracts (*i.e.*, of one or more ascending tracts or of one or more nuclei) in man produce peculiar symptoms depending on the nature of the morbid process and on the neurones involved. Where the *first peripheral neurone* is slowly involved there is a tendency to fall to the affected side, as in tumour of the medulla, or the syndrome of the posterior inferior cerebellar artery (Wallenberg, Foix). Where the nucleus fastigius (or tecti) is involved there is a tendency to fall backwards. It must be remembered that recent anatomical and physiological research tends to show that nucleus to be a primary vestibular centre.*

As regards the *secondary vestibular neurone*, any lesion of the posterior longitudinal fasciculus produces in all vertebrates, as far as we can judge, circus movements to the *normal* side and rolling movements towards the *affected* side associated with a forced position of the head and eyes. (For the sake of simplicity forced movements in the vertical plane are at present disregarded).

In man such a lesion is usually caused by tubercular disease in the pons and is invariably productive of conjugate deviation of the head and eyes to the normal side (Bertelse, Rönne, Bruce, and others) and a tendency to fall to the affected side.

Lesions of the *third vestibular neurone*, *i.e.*, lesions on the oral side of the posterior commissure, produce in the lower animals forced movements, both circus and rolling in type, similar to those described as following lesions of the second neurone, but less vehement in character, while they take place in opposite directions. In the case of third neurone lesions the circus movements are towards the *affected* side, the rolling movements to the *normal* side. (See Figs. 1 and 2, and note the crossings at the posterior commissure). In some classes of animals forced movements in the vertical plane are the most pronounced after this lesion. In man pathological lesions affecting the third neurone are followed by symptoms which vary with the nature and localisation of such a lesion. In tabes and disseminated sclerosis there is disturbance of convergence (Barré and Duverger), in Parkinson's disease limitation of ocular movements in all directions coupled with disturbances of gait, while Prévost observed conjugate lateral deviation of the head and eyes in cases of apoplexy where the striate body was involved.

The third vestibular neurone in vertebrates connects the palæostriatal nuclei to the commissural, *i.e.*, supravestibular, nuclei. Further it is known that a lesion of this third vestibular neurone is followed by four different forms of forced movements, viz., lateral movement to either side, rolling movement to either side, movement upward and downward. It is therefore obvious

* This has been confirmed by van Gehuchten, Jr. (*L'Encéphale*, 1925, xx, 530, and *Proc. Kon. Akad., Amsterdam*, 1925, xxviii, No. 1). I purpose to demonstrate in a later publication as I did in a former², that anatomical and physiological observations made on different classes of animals tend to show that there are separate vestibular centres corresponding to lateral movement of the body and of the eyes from right to left and vice versa; for rotating movements to either side; and for upward and downward locomotion—each connected by secondary vestibular bundles with their particular supravestibular centres near the posterior commissure.

that after a lesion in this region in the lower animals, and of the frontal cerebral pole in man, so-called cerebellar symptoms may be expected ("vorbeizeigen," falling to the normal side, rolling movements, circus movements to the affected side). In man the forced movements in the horizontal plane are replaced in certain cases by tonic conjugate deviation of the eyeballs in one direction, and rolling movements by falling to one side and by concomitant "skew deviation" of the eyes (Magendie, Hertwig). Such a phenomenon is usually easily recognised as head, eyes, and occasionally extremities are deviated in the same way. Occasionally the complete primitive phenomenon may be seen with circus movements and rolling movements about the axis. Certain lesions in this region produce symptoms which are due to implication of the præcommissural vestibular structures, but which exhibit a special character. For example, there is the stiffness of the neck and opisthotonus found in tubercular meningitis, this being probably due to the lesion involving the basal longitudinal bundle (Wallenberg) which is situated superficially on the base of the forebrain; falling backward is seen where a tumour involves the genu of the corpus callosum; postural and oculomotor disturbances occur when epiphysis and hypophysis are involved.

II.—Which of the supravestibular centres have been localised and what is the result of a lesion in such centres?

The work of Cajal, Held, van Gehuchten and Boyce, supported by the later work of Ariens Kappers and that from the laboratory of Chiaruggi (Castaldi and Beccari), have shown that in the base of the mesencephalon of all vertebrates is a complex of cell-groups which are connected with the posterior longitudinal bundle and the posterior commissure. These connections have been recognised for some considerable time. In later work (*loc. cit.*) where anatomo-physiological methods of research have been combined it has been found that from at least two of these groups of cells at the level of the posterior commissure (nucleus commissuræ posterioris and nucleus interstitialis) a bundle of fibres descends into the posterior longitudinal fasciculus. In the first case the bundle is composed of thin fibres which send collateral branches to the nucleus of the third cranial nerve. It does not descend much below the level of the nucleus abducens, to which it (Fig. 1) sends collateral branches. This bundle is also known as the tractus commissuromedullaris. The second bundle is composed of thick fibres, collateral branches are sent to the nuclei of the third and fourth cranial nerves (Wallenberg), while the bundle itself can be traced far down the cord. It is known as the tractus interstitiospinalis (or Boyce's tract) (Fig. 2). Experiments on cats and pigeons have demonstrated a certain definite connection between lesions of these commissural cell-groups or nuclei and certain types of forced movement. A lesion of the nucleus commissuræ posterioris is found to be associated with circus movements to the side of the lesion, while a lesion of the nucleus interstitialis is associated with rolling movements to the side opposite to the lesion. Should the lesion be situated

more anteriorly and sever the connections between these nuclei and the globus pallidus the resulting symptoms, as regards changes in locomotion and posture, are the same. These fibres between the commissural nuclei and the globus pallidus just described have been demonstrated anatomically in the cat and pigeon^{3,4}. Riese⁵ has also identified these structures. It is suggested that these descending tracts in the posterior longitudinal fasciculus represent the final common path (Sherrington) associated with these two forms of locomotion and ocular movements.

At present there are no exact or dependable data concerning the centres or descending tracts governing forced movement in the vertical plane, *i.e.*, locomotion backward and forward, with concomitant deviation of the eyes upward and downward. It is, however, certain from experimental and clinical data that these centres and tracts are separate and distinct both from the nuclei and tracts just described, and from each other. Further there is definite evidence

Fig. 1. Schematic representation of tracts and centres dealing with forced movements in the horizontal plane. A lesion of the areas indicated produces circus movements to the left.

Fig. 2. Schematic representation of tracts and centres dealing with forced movements in the frontal plane. A lesion of the areas indicated produces rolling movements to the right.

that the primary vestibular centres involved in falling-backward and looking-upward movements are situated in the cerebellum (it is probably the nucleus tecti); the centre, involved in falling forward, near the raphe of the medulla oblongata (See fig. 3). The circumstance of the first centre being localised in the cerebellum has long proved a stumbling-block and a misleading factor in the investigation of cerebellar localisation. As yet the exact course of the fibres from these centres to their supravestibular centre is not known, but the evidence afforded by experimental work and from certain clinical cases indicates that the structures dealing with forced movements in the vertical plane ascend in the base of the mesencephalon very near the median line.

Fig. 3. Schematic representation of tracts and centres dealing with forced movements in the vertical plane. If the path including nuc. tecti, a mesencephalic nucleus, and nuc. septi accumbens be interrupted, falling backward ensues. If the path including nuc. rapheos, a mesencephalic nucleus, and nuc. tr. longit. basalis be interrupted, falling forward ensues.

III.—What light do recent anatomical and physiological researches on secondary and tertiary vestibular tracts throw on the pathogenesis of postencephalitic ocular disturbances, and vice versa?

Marinesco, Radovici and Drăganescu⁶ agree in the view that all efforts at classifying postencephalitic oculomotor lesions are doomed to failure because of our present ignorance of the physiology of the "centres in the basal gangliä."

So far the clinical data concerning these curious symptoms have been supplied mainly by the French school of neurologists. It is interesting and important to note that amongst these clinical reports cases occur illustrating all varieties of forced movements and forced positions which have been postulated experimentally as being certain of occurrence with partial lesions of the supravestibular centres near the posterior commissure and of their palæostriatal connections. (I have taken occasion elsewhere⁷ to deal more fully with this stage in the growth of knowledge of this region). Among these cases tonic spasm of the eyes is described with conjugate deviation, also skew deviation (this forced position of the eyes is associated with rolling movements in lower vertebrates) and conjugate upward and downward spasm of the eyeballs. It is peculiarly interesting to find that the complete syndrome of circus movements, rolling movements with concomitant deviation of the eyes, and opisthotonus with upward deviation of the eyes has also been repeatedly observed and described. The value of recent anatomical and physiological researches as an aid in localisation is evident when the frequency of the combination of tonic lateral position of the eyes with the upward or downward position is considered. Thus it is evident from the researches already referred to above that the two bundles involved in these two forms of forced movement are close together only at one point, viz., just in front of the posterior commissure. This being so it is evident that the lesion must be situated near the median line. The lesion will therefore lie in the metathalamic region near the commissura posterior. Further it has been demonstrated experimentally that the tracts involved in lateral deviation of the eyes and lateral movements branch off laterally by Forel's field.

It is curious, since the other symptoms are definitely not due to any lesion of the pyramidal tracts, that early workers on postencephalitic oculogyric crises were inclined to ascribe these forced positions in the vertical plane to lesions in the corpus striatum (G. Lévy, Hunt, Vogt, Stern, v. Economo). Later workers, among whom are Trétiakoff, Marinesco, Goldstein, Claude, Hohman⁸, MacKinley and Gowan came to the conclusion that alterations occurred mainly in the body of Luys. Hohman also noted changes in the nucleus of Darkschewitsch (nucleus commissuræ posterioris), nucleus interstitialis and reticularis. From the frequent combination of lateral and upward directions in ocular crises it is safe to infer that the lesion lies away from the striate bodies and further back in the region of the posterior commissure and hypothalamus. This is more especially the case where there is compound lateral and vertical deviation.

In the original work of Vogt⁹, which led to the general recognition of lesions destroying the lenticulopallidal and pallido-mesencephalic tracts as the causative agent in the syndrome of paralysis agitans the corpus striatum was recognised as a complex of centres from which primary automatic movements originated. To allow of the occurrence of these movements various writers

on this subject have postulated the existence of a great number of tracts between the globus pallidus and the mesencephalic centres. It has, however, been admitted by Vogt that of all those tracts and bundles postulated as existing, only one has been identified in its course and function, viz., the pallidofugal tract which passes by Forel's bundle towards the nucleus commissuræ posterioris. This tract was described first in 1914,^{3,4} as the main tract for lateral locomotion and lateral deviation of the eyes. It is interesting and important to find that the evidence afforded by clinical observations tends to bear out this conclusion reached by anatom-physiological research.

Vogt, Foerster and Economo claim to distinguish separate syndromes depending on lesions of the striatum and pallidum respectively. If this is the case it is necessary according to recent anatom-physiological researches to recognise at least four more syndromes related to the region between the commissural mesencephalic nuclei and the globus pallidus, all connected with forced movements of the eyeballs. These are:—

(1) Mesencephalic syndrome characterised by oculomotor paralysis and diplopia, and probably by disturbances of convergence and pathological sleep (Pötzl¹⁰).

(2) Metathalamic syndrome, characterised by compound ocular crises upward and downward in direction, and absence of oculomotor paralysis and diplopia.

(3) Syndrome of the Luysian body, characterised most frequently by lateral deviation, rarely by compound oculogyric crises.

(4) The syndrome of Forel's bundle, characterised by simple lateral deviation.

After the foregoing exposition it is hardly necessary to point out that I cannot accept the view taken by Szymanowsky, Zylberlast Zand and Poston that the encephalitic virus has a peculiar affinity for the *vestibular* fibres in the lower animals and the *oculomotor* nerves in man. Neither do I agree with Fischer, who explains the peculiar upward position of the neck in upward oculogyric crises as a deliberate posture assumed by the patient to avoid painful cramp. The suggestion made by Monakow¹¹ that in addition to anatomical lesions there is also some interference with the normal production of cerebrospinal fluid in the third ventricle has not as yet been supported by any substantial evidence.

IV.—*A comparison between the extrapyramidal paralysis agitans syndrome and the extrapyramidal postencephalitic syndrome.*

Here again the evidence afforded by clinical cases suggests that a more accurate localisation of lesions in the palæo- and neo-striatum may comparatively soon be possible. Dubief and Dana have described general vascular changes in the cerebrospinal axis in paralysis agitans; Winkler and Manschot described perivascular gliosis and atrophy of fibres in the lateral thalamic nucleus and globus pallidus. I have also pointed out¹² that from a physiological

point of view many symptoms of the disease indicate a lesion in the corpus striatum. Jeldersma was, however, the first to recognise distinct atrophy in the tracts of fibres passing from the nucleus lentiformis towards the thalamus, in the ansa lenticularis and Forel's bundle. This atrophy of fibres has also been recognised by Jeldersma in Huntington's chorea, and the main symptoms of this malady it is suggested are due to these changes. One thing is evident; the symptoms produced by or associated with lesions in this area fall into one of two categories—continuous phenomena or paroxysmal phenomena. This, however, applies to extrapyramidal paralysis agitans and extrapyramidal postencephalitic disorders equally (Stern¹³).

To make this clear the two types of symptoms are herewith enumerated and compared.

<i>Extrapyramidal striatal (Parkinsonian) symptoms.</i>	<i>Extrapyramidal substriate (postencephalitic) symptoms.</i>
No third nerve paralysis and diplopia.	Third nerve paralysis with diplopia (Barré Cords, Stern, Fischer).
General limitation of ocular movements.	Disturbances of convergence; difference in pupils (Collier).
No pathological sleep.	Pathological sleep (Pötzl).
No oculogyric crises.	<div> <div>Oculogyric crises</div> <div> <div>lateral, with torticollis and circus movement (Fischer, Babinski, Cassirer, Higier).</div> <div>downward, with propulsion (Paulian).</div> <div>upward, with opisthotonus and retrogression (Marinesco, Draganesco, Stoiesco, Bing, Schwarz, Westphal).</div> </div> </div>
Sialorrhœa.	Wilson's fragmentary and partial decerebrate rigidity (Mourgue, Marie, Lévy, Wimmer)
Adiadokokinesis.	Sialorrhœa.
	Adiadokokinesis.
	Spasm of masticatory muscles, chewing, yawning, stuttering.
Tremor, athetosis, chorea, spasmus mobilis, torsion-spasm, contractures.	Tremor parkinsonicus (Maas, Roger and Pourtales).
	Dysarthria (Economo, Lhermitte, Cornil).
	Athetosis (Lhermitte, Vogt, Marie, Levy, Spiller, Prince, Jakob, Foerster, Mendel).
Exaggeration of fixation reflex (Kleist).	Myoclonia.
Retardation of movement.	Striatal epilepsy (?) (Lhermitte, Cornil, Krebs, Thomalla, Krisch, Wimmer, Knapp, Stertz).
Deficient response to innervation or difficulty of passing from static to dynamic state (van Woerkom).	Tetanic convulsions (Vincent, Chavany, Stertz, Sterling).
Permanent paresis.	Glosso-palato-laryngeal and velum nystagmus.
Akinetic and hypertonic syndrome,	Akinetic and hypertonic syndrome (Vogt, Lhermitte, Foerster).
	Writer's cramp (Levy).

Forced laughter and weeping.
Pseudo-catalepsy.
Associated movements.
Psychical hypersensitiveness.

Intermittent claudication (?) (Magelhaes Lemos).
Fits of screaming (Kleist, Benedek, Schuster).
Hysterical fits (Vogt, Foix).
Katatonia.

From this table it is evident that the symptoms which must be ascribed to lesions of the region of the metathalamus, corpus Luysii, and Forel's fasciculus are lacking in the extrapyramidal paralysis agitans syndrome. On the other hand there is a great similarity between the two syndromes, which in the light of our present knowledge is not unexpected. It is obvious that all the symptoms depending on the atrophy described by Jellgersma in the fibre tracts from the striate body to the structures in the mesencephalon are bound to appear should a lesion involve the base of the mesencephalon. Further in the syndrome associated with lesions of the mesencephalon, metathalamus, corpus Luysii, and Forel's fasciculus symptoms must appear depending upon lesions affecting structures peculiar to the different regions, including pallidal and striatal structures. It is therefore evident that lesions situated in the præcommissural region must be more complicated symptomatologically; they are richer in symptoms than those of the striate bodies, because besides the symptoms of the latter they are bound to produce also their own.

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