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THE EXPERIMENTAL BASIS FOR THEORIES ON VESTIBULAR FUNCTION.*

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EVERYONE who is compelled to use hypotheses regarding the function of the vestibular organ for further experimental research and for clinical purposes, feels the necessity of reviewing, from time to time, the facts from which these theories have been deduced, and of determining whether the basis is still a solid one.

About a hundred years ago, Flourens was the first to show that lesions of the internal ear were followed by motor disturbances. In 1870, however, in a short but suggestive paper, Goltz stated that the vestibular organ was a special sense organ of equilibration. Shortly after, three independent investigators, Mach, Breuer, and Crum Brown, developed the theory of the function of the semicircular canals, which remains, to the present day, the fundamental basis of all the work done on this part of the labyrinth. Breuer had made, at this early time, a sharp distinction between the function of the ampullæ and of the otolithic maculæ. To the ampullæ, he ascribed all reactions and sensations evoked by rotatory movements; to the maculæ, the reactions to different positions in space and the sensations of progressive movements.

Of the subsequent investigators, two especially must be named; Högyes carefully worked out the mechanism of the rotatory reactions and compensatory positions of the eyes, depending on labyrinthine stimulation; Ewald, at the end of a long series of experiments, came to the conclusion that the

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labyrinths exercised an influence upon muscle tone. Ewald believed that the labyrinth-tone depended on the ampullæ, but later, in a paper from his laboratory (N. Ach.), the otolithic origin of this tone was also discussed. The well-known researches of Bárány on caloric stimulation of the vestibule have also contributed very much to our knowledge.

In the last fifteen years, with the aid of many co-operators, a great number of experiments have been conducted at Utrecht on the reflexes connected with posture and attitude, with righting-function and distribution of muscle tone, and on the rôle played in these functions by different sense organs, and especially by the labyrinths. In 1923 my friend, Dr de Kleijn of Utrecht, had the honour to present to the Section of Otology an account of some results,* so far ascertained, and I can assume, therefore, that the chief points, as far as they touch the otologist, are known to you.

The following groups of reflexes, arising from the labyrinths (and absent after labyrinth extirpation), have been investigated :—

TABLE I.

I. *Reflexes responding to movements*—	*Apparatus of semicircular canals.*
1. Rotatory reactions.	
(*a*) on head	(Otolithic apparatus may also be stimulated by movements.)
(*b*) on eyes	
(*c*) on limbs	
(*d*) on trunk	
2. Progression reactions.	
II. *Reflexes resulting from position*—	*Otolithic apparatus.*
1. Tonic labyrinthine reflexes on the body musculature.	
(*a*) on limbs	utricle.
(*b*) on neck (and trunk) . .	utricle.
2. Labyrinthine "righting" reflexes.	
(*a*) asymmetrical . . .	saccule.
(*b*) symmetrical	utricle.
3. Compensatory eye positions.[1]	
(*a*) vertical	saccule.
(*b*) rotatory	?

[1] In rabbits and guinea-pigs. In monkey and man, "*a*" and "*b*" must be exchanged.

In the first group, the reflexes, which are transient, are evoked by *movements* (more exactly spoken of as accelerations): in the second, the reflexes depend upon *positions* of the head

* See R. Magnus, *Körperstellung*, Berlin, Springer, 1924; a review of which appears in this number of the *Journal*.

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in space; the latter reflexes are tonic, and last as long as the head keeps a definite position.

In the first place, we must try to find out whether the different groups of reflexes can be connected with certain structures in the vestibular organ, especially as to which are reflexes from the canals, and which of them come from the otolithic maculæ.

For this purpose, one can use a method first described by Wittmaack. By centrifuging anæsthetised guinea-pigs, it is possible to detach the otolithic membranes from the maculæ, and to leave the ampullæ and cristæ of the canals intact. In every single case, at the end of the experiment, it must be shown, by careful microscopic examination, that the epithelium of the maculæ is completely freed from the otoliths, and that the detached membranes are found in other parts of the *endolymphatic* space, whereas the ampullary apparatus is not damaged. In later experiments, it was ascertained by Dr de Burlet, at Utrecht, that it is possible, by placing the head in different positions on the centrifuge, to throw the membranes purposely in certain directions and to find them again at the expected places.

Physiological investigation of successfully centrifuged guinea-pigs has shown that, after detaching the otolithic membranes, all reflexes responding to movements are still present and unchanged, whereas all reflexes resulting from position are absent. From this we must conclude that the reflexes of the first group (Table I.) are elicited in the canals, and those of the second group in the otolithic apparatus. This is in accordance with current views, as far as the rotatory reactions are concerned, but is in contrast to common opinion for the progression reactions.

The experiments leave no doubt, however, that very definite reactions to rectilinear accelerations can be observed after centrifuging and detaching the otoliths, and that these reflexes, therefore, must be evoked in the canals. These experiments, however, by no means exclude the possibility that the otolithic apparatus also may be excited by movements, and this is indeed very probable. But, unfortunately, we cannot prove it experimentally, because we know of no method by which to destroy the canals and at the same time leave the otoliths intact. So far as the function of the otolithic apparatus is concerned, we can safely conclude that all reflexes resulting

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from position are dependent upon them, and that the maculæ therefore are, with different positions of the head in space and with different inclinations against the horizontal plane, in different states of excitation, which remain unchanged as long as the macula keeps its position. The otolithic apparatus is, therefore, the place of origin of labyrinthine tonic reflexes.

Before entering into a discussion of the intrinsic mechanism of the otolithic organ, it is necessary to know in what state of excitation or non-excitation the sensory epithelium of the maculæ is, if *no* otoliths pull or press on it. This question can be settled in centrifuged guinea-pigs with all four otolithic membranes detached. Directly after the centrifugalisation, the animals show symptoms of macular stimulation, for instance, eye deviations, turning of the neck, rolling movements, etc. But these soon disappear, usually after one to two hours, always by the following morning. After that time no symptoms can be detected, which point to a remaining stimulation in consequence of the trauma by the centrifugalisation. In order to be sure that no such traumatic stimulation is still present, we wait seven to eleven days. If, then, one labyrinth is paralysed by injecting a small amount of cocain into one middle ear, the other labyrinth with detached otoliths is the only one left in action.

There are then two possibilities. If the sensory epithelium without connection with its otoliths does not produce excitation, paralysis of one labyrinth cannot give rise to symptoms arising from the maculæ of the intact side. If, on the other hand, the epithelium still produces stimuli, the symptoms of unilateral macular excitation must appear, because the compensation by stimuli from the other side has been removed. The latter appears to be the case in the described experiments, which always result in turning of the neck and in vertical eye deviation. The conclusion is, that the sensory epithelium of the maculæ is able to produce excitations of its own without any connection with otolithic membranes, and that the stimuli, reaching the medulla from both sides, compensate each other intracentrally, so that no asymmetrical symptoms arise. The epithelium of the maculæ resembles, in this respect, the retina, which also can produce stimuli without any light.

The function of the otolithic membrane consists, therefore, in increasing or decreasing the state of excitation of the sensory cells, according to their situation in space, by pulling

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at or pressing upon the macula. This mechanism makes it conceivable that the otolithic apparatus is practically not fatiguable, because the production of stimuli always goes on, depending upon some metabolic changes in the sensory cells, and is only changed in intensity by the mechanical action of the membranes.

The following data, for which I am indebted to Dr de Burlet, give an impression of the extreme minuteness and sensitivity of the whole apparatus :—

TABLE II.

	Utricle.	Saccule.
Size of macula (macacus)	2·06 mm.^{2}	1·8 mm.^{2}
,, ,, (guinea-pig)	0·48 mm.^{2}	0·49 mm.^{2}
Weight of otolith membrane (rabbit) . .	0·07-0·05 mgr.	0·06 mgr.
$CaCO_3$ crystals in otolith membrane (rabbit)	31·8-38·6 per cent.	30 per cent.
Specific gravity of ,, ,,	1·32-1·39	1·27

The size of the maculæ is $\frac{1}{2}$ to 2 mm.^{2}, each membrane has a total weight of about $\frac{1}{16}$ of a mgr., and the arragonit-crystals ($CaCO_3$) embedded in one membrane weigh about $\frac{1}{50}$ of a mgr. From these data it should be possible to calculate the changes of positive or negative pressure, which are sufficient to influence the whole macula or a single epithelial cell: the result would be a very small figure for the threshold of this sense organ.

We have now to discuss the question, in how far we can ascribe the different groups of otolithic reflexes (Table I., Group II., Nos. 1-3) to the different maculæ, viz., of the utricle and saccule respectively. For this purpose we can use the careful measurements of Dr de Burlet and his co-operators on the position of the maculæ in the skull of guinea-pigs, rabbits, cats, and monkeys. We tried to fix, experimentally, for each one of the different otolithic reflexes, the positions of the skull in space, in which the reflex has its maximum and its minimum, and we investigated the position of the maculæ in these maximum and minimum positions of the skull. The results were as follows:—

The *tonic labyrinthine reflexes on the extensor muscles of the limbs*, which can easily be studied in the decerebrate preparation of Sherrington, have their maximum in the back position of the head with the snout a little above the horizontal

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plane. In this position, the maculæ sacculi have no characteristic position, but both maculæ utriculi lie in the horizontal plane. After unilateral labyrinth extirpation, the position of the maximum does not change; from this we can deduce that the maculæ, from which these reflexes arise, are approximately in the same plane. This also points to the utricles. In the minimum position for these reflexes, the maculæ utriculi again lie horizontally. We may safely assume, therefore, that the tonic reflexes on the limb muscles come from the utricles, and that the maximum and minimum of stimulation are reached with horizontal position of the maculæ; that is to say, that the way in which the otoliths influence the epithelium is by pulling or pressing, and not by shifting, as the older theories assumed.

If one believes that the essential effects of these reflexes are on the *static* muscles, the extensors, it follows that the maximum of the stimulation is reached, when the membrane hangs and pulls on the macula. But there are also reflexes—weaker indeed—on the flexors, which have their maximum, if the otoliths press on the epithelium. In the case of the tonic reflexes on limb-muscles, we cannot therefore decide with certainty in what position the maximum of excitation is reached: we can only suspect that it is the hanging position, a conclusion which will appear the right one on investigating other reflexes.

In the same way we come to the conclusion that the *tonic labyrinthine reflexes on neck and trunk* depend also on the utricles.

Of the *compensatory eye-positions*, the site of origin of the rotatory reflexes (II. 3*b*) has not yet been made out. Experiments investigating this are now in progress.

The *vertical eye deviations* appear to depend on the sacculi. If one labyrinth is extirpated, the well-known vertical eye deviation follows. This is maximal if the head is in the lateral position, with the intact labyrinth below; it is zero, or minimal, if the intact labyrinth lies above. But with both labyrinths intact, no eye deviation is present, with the head in the normal position. This change of the minimum position after unilateral labyrinth extirpation, proves that the maculæ in question cannot be situated in one plane, and that these reflexes must arise in the sacculi. With one labyrinth destroyed, the eyes are not deviated at all in lateral position

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with the *macula sacculi lying horizontally* and the *otolith pressing on the epithelium.* This is the *minimum* position. The maximum of excitation is reached, if the membrane pulls at the macula. In this case it can, therefore, be proved that the maximum of excitation is present, if the otoliths *hang.*

The *asymmetrical labyrinthine "righting" reflexes* bring the head from lateral positions into the normal standing position. After unilateral labyrinth extirpation, they tend to bring the head in such a position that the intact macula sacculi lies horizontally with pressing otolith. This is the minimum position, in which the reflex comes to an end. Here again the same mode of stimulation is found.

The *symmetrical "righting" reflexes* act so that, of all possible symmetrical situations, the head is always held in such a position that the maculæ utriculi lie horizontally, and the otoliths are pressing. The conclusion that these reflexes arise in the maculæ utriculi is also confirmed by another line of experiments to be described presently.

This review, perhaps too short and aphoristic, shows that the utricles are the place of origin of the tonic reflexes on the body musculature and of the symmetrical righting reflexes, whereas the sacculi give rise to the asymmetrical righting reflexes and the vertical compensatory eye-positions. The place of origin of the rotatory eye-positions has not yet been found.

In regard to the reflexes of the sacculi and the symmetrical righting-reflexes of the utricles, it can be proved that the minimum of stimulation in the sensory cells is attained if the otolithic membrane presses upon them, and that the excitation becomes maximal with the otoliths hanging. In the case of the tonic reflexes on the body muscles, the same is probably true. In this way, a first conception has been attained as to the way in which the otolithic apparatus can fulfil its task.

The distribution of the functions of the different otolithic maculæ has been deduced only from one line of evidence, viz., the comparison of the experimentally found maximum and minimum positions with the situation of the maculæ in these positions found by anatomical investigation. It would be a great advantage if a confirmation of these results could be obtained in quite a different way. This happens to be the case.

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Injection of a small amount of cocain into one middle ear of a guinea-pig, induces unilateral labyrinth paralysis. But all the symptoms do not appear at once and at the same time; they come on in definite stages, corresponding to the anatomical situation of the sense organs in the internal ear. In the first stage, a vertical eye deviation and a unilateral paralysis of the asymmetrical righting reflexes develop, depending upon a paralysis of the macula sacculi, which is situated just opposite to the foramen ovale, and will therefore first be reached by the diffusing cocain. In the second stage, the symptoms of paralysis of the utricle are added: (1) Turning of the neck in consequence of unilateral absence of the tonic reflexes on neck muscles, and (2) unilateral abolition of the symmetrical righting-reflexes.* *This sequence is in accordance with the distribution of functions between the maculæ, as stated above.* In the second stage, the canals are not yet paralysed; they can still be stimulated by rotation and by syringing with cold water. In the third stage, the excitability of the canals disappears, the lateral canal being the first, one of the vertical canals the last to be affected. Finally, the whole vestibular organ is out of function.

These experiments yielded also other interesting results, which I cannot describe here. Only one point must be mentioned.

In the second stage, in which both the maculæ sacculi and utriculi are paralysed, but the ampullæ of the canals are still in function, the eyes are deviated, but no trace of nystagmus can be detected. But at the moment the excitability of the canals begins to disappear, a very strong nystagmus shows itself. Thus the well-known nystagmus, after unilateral labyrinth extirpation, does not depend on the otolithic maculæ, but on the apparatus of the ampullæ. This leads to an interesting sequence.

If the ampullary epithelium on one side is put out of action, the symptoms arising therefrom must depend on the ampullary epithelium of the other intact side. The nystagmus is not only present if the head is moved or rotated, but also if it is not moved at all. Therefore, the sensory cells of the cristæ ampullares possess the function of producing excitations, if there is no current or pressure-change in the endolymph space

* Only to be seen in animals in which the other labyrinth has been extirpated beforehand.

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of the canals. The epithelium of the cristæ has the same physiological behaviour as that of the maculæ. It gives rise to continuous stimuli flowing through the nerves to the central nervous system. The difference of function between the canals and the otolithic maculæ depends on the mechanical arrangement of the apparatus connected with their epithelium. In the canals, currents or pressure-changes are evoked by accelerations, last only a short time, and pass away. The state of excitation in the epithelium changes, therefore, temporarily, and soon comes back to the original value, so that only transient reactions can be evoked. The otolithic membranes, on the contrary, preserve their pulling or pressing action as long as the head keeps a definite position, and can induce a constant change in the state of the macular epithelium, which in this way can cause tonic reflex actions.

The experimental work on the described lines has thus established definite ideas on the functioning of the different parts of the vestibular organ, which may form the basis for further research and for clinical investigation. But, like all hypotheses, they continually want confirmation by new facts, and have to be modified as soon as conflicting observations are made. Possibly they can be of value for diagnosis and treatment in human beings, and the clinical examinations will surely extend and perhaps correct them. In every case we must not forget an old saying of Goethe: "Hypotheses are scaffolds which are erected before the building and taken down when the building is ready. They are necessary for the workmen, but one must not take the scaffold for the building."

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