He agreed with Mr. Hallpike on the essential need for carrying out the caloric test with both hot and cold water. Mr. Hallpike had misunderstood him as regards the clinical importance of directional preponderance. What he had wished to stress was that this might be found in normal persons, and should not, therefore, be considered out of its proper place in relation to the whole clinical picture. He had been reminded of the difference between his own caloric test findings and those of Mr. Hallpike and his collaborators in normal subjects. This difference might, he suggested, be due to the fact that in the latter's investigation a selected group of healthy young men had been used.

Recording of Responses from Individual End-organs of the Vestibular Apparatus

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A critical review of the extensive literature on the equilibrium function of the vertebrate labyrinth (Lowenstein, 1936) showed that up to that time investigations in this field had dealt with the effect of surgical injury to the labyrinth and its effect on the known reflex responses of body, limbs, and eyes to rotation and tilting. This evaluation of "deficiency" phenomena led to the establishment of the classical theories of labyrinth function, which formed the backbone of general physiological and specialized clinical and otological opinion in this field of sense physiology. The method of the "elimination experiment" so widely used in experimental physiology is limited in its usefulness by the indirectness of approach. It was therefore not surprising to find a considerable number of open problems and contradictions, the elucidation of which could only be achieved by a more direct approach. With the elaboration by Adrian and his school of the method of oscillographic recording of action potentials from sensory nerves such a direct approach became possible and has been the chief method used in a series of investigations dealing with a number of such open questions of labyrinth hysiology.

The first problem attacked concerns the mode of function of the semicircular canals of the vertebrate labyrinth (Lowenstein and Sand, 1936).

It was found possible in the spinal dogfish to record directly from the branch of the VIII nerve supplying the ampulla of the horizontal semicircular canal, while the entire animal was subjected to rotation tests on a turn-table. Thus, for the first time in the history of labyrinth physiology, direct evidence became available concerning the mode of function of a component part of the complex vestibular organ. This led to the settlement of the controversial question of uni- *versus* bi-directionality of semicircular canal response. It could be shown that the canal response to angular acceleration is inherently bi-directional and, what is more, the intimate mechanism of this response could be clearly demonstrated. It was found to be based upon the presence in the "resting" animal of a spontaneous discharge of action potentials, the frequency of which can either be increased—in the case of the horizontal canal—by ipsilateral or decreased by contralateral acceleration. The functional significance of such a resting discharge in this clear-cut case helped in furnishing sense physiology with a concept which has by now become a universally accepted principle of sensory function in general. The demonstration of a continuous influx of afferent discharge from the labyrinthine sense endings raised anew the question of the tonic function of the labyrinth and the disputed role of the semicircular canals as a source of tonus. This tonic function of the semicircular canals could be established by elimination experiments in the pike labyrinth (Lowenstein, 1937), where it was found possible to sever by operation the nerve branch supplying the horizontal semicircular canal, and to demonstrate in the surviving animal the existence of well-circumscribed, lasting tonus asymmetries of the eye-muscle apparatus. The eye reactions of such a pike during and after rotation were found to be in complete agreement with the electrophysiological properties of the ampullary sense organ of the dogfish.

It was, of course, desirable to extend the functional analysis to all three pairs of semicircular canals The problem of access to the nerve twigs supplying the various ampullæ led to the elaboration of the new technique of the "isolated labyrinth preparation". Control experiments had shown that the labyrinth of an elasmobranch fish remains functionally active for a matter of hours after an interruption of the blood supply. Thus it became possible to work on a labyrinth contained in a part of the isolated skull of the ray (*Raja clavata*), a method which opened up many chances for analysis such as described in a paper on the individual and integrated activity of the semicircular canals of the elasmobranch labyrinth (Lowenstein and Sand, 1940*a*). The basic mechanism for canal function was confirmed for all six canals and the precise delimination of function in the interaction of the various canals during rotation in all planes of space could be mapped out. These findings could also be correlated with the known facts concerning the vestibular eye-muscle reflexes in vertebrates.

So far, recordings had been taken from the whole of the nerve branches supplying the sensory structures (cristæ) of the canal ampullæ. Such records of massive impulse discharges give valuable qualitative information. But for the purpose of quantitative analysis of the stimulus-response relationship in a sense organ, impulse records have to be obtained from single sensory units within a certain organ. The study of the responses from such single-fibre preparations to angular accelerations and rotations at constant speed were carried out in the isolated labyrinth of the ray (Lowenstein and Sand, 1940*b*) and led to a quantitative description of the behaviour of the cupula terminalis in the canal ampulla, which put on a safe basis the disputed torsion-pendulum theory of the cupular function. Thus, the sensory activity of the semicircular canal was found to provide a framework adequate to account for the time-relations of nystagmus and after-nystagmus, as utilized in the clinical analysis of vestibular defects (Lowenstein, Groen, and Vendrik, 1952).

The successful application of the method of the isolated labyrinth combined with the single-unit recording from individual vestibular nerve branches encouraged a still more ambitious research programme concerning the function of the less accessible and infinitely more delicate otolith organs of the labyrinth. A whole host of conflicting experimental and theoretical evidence obtained from representatives of the various vertebrate classes renders this the most obscure chapter of labyrinth physiology (Lowenstein, 1950). Fortunately, it was found possible to gain sufficient access to the nerve branches supplying the otolith organs in the isolated labyrinth preparation to obtain satisfactory single-unit recordings from all three otolith organs and to study the quantitative stimulus-response relationships, and the interaction of the three organs during changes of spatial orientation (Lowenstein and Roberts, 1950). It could be demonstrated that all three otolith organs, viz. the utriculus, sacculus, and lagena participate in the maintenance of equilibrium. Sense-endings in the maculæ generally show a resting discharge, the frequency of which is increased or decreased by positional changes. The functional ranges of *utriculus* and *sacculus* overlap. Both contain sense-endings responding to lateral and fore-and-aft tilting. There are two main types which have their maximum of discharge activity in Side-up and Nose-up and Side-up and Nose-down positions respectively. Organs having a maximum in the Side-down position were encountered, but did not appear among the position-receptors proper. Apart from "static" position-receptors, the maculæ contain receptors responding to a change of position in one and the same manner, irrespective of the direction of the change. They are described as "out-of-position" receptors. The receptors in the *lagena* also respond both to lateral and to fore-and-aft tilts. They have their maximum of activity usually in or near the normal position and can be described as "into-level" receptors.

During the analysis of the equilibrium function of the otolith organs it became apparent that, apart from responding to changes in the direction of gravitational pull, some of the structures also respond to vibrational stimulation. A detailed study of the vibrational responses (Lowenstein and Roberts, 1951) led to results which can be summarized as follows:

Vibration responses in the form of impulse discharges can be recorded from nerve twigs leading from part of the macula sacculi, the macula neglecta, and the lacinia of the macula utriculi of the isolated elasmobranch labyrinth. The otolith-bearing part of the macula utriculi, the posterior portion of the macula sacculi and the adjoining macula lagenæ do not respond to vibrational stimuli. They contain gravity receptors only. An appreciable number of the sense endings show a resting activity in the absence of vibrational stimulation. There exists, however, convincing evidence that, at any given time, many sensory units are quiescent. These can be recruited to take part in the vibrational responses, and they show a considerable range of thresholds. Under the obtaining experimental conditions vibration responses were recorded to stimulus frequencies extending rarely higher than 120 cyc./sec. Vestibular microphonics were observed up to a signal frequency of 750 cyc./sec. but only responses in the form of nerve impulse discharges were accepted as evidence for vibration sensitivity. At low-intensity stimulation the response consists of an increase in the discharge frequency of the "spontaneously" firing units. Higher intensities lead to the recruitment of previously quiescent sense endings and to a marked synchronization of the response frequency with that of the stimulus. This synchronization closely resembles the responses described for the mammalian cochlea, where it occurs at the lower end of the audible spectrum. Adaptation to sustained vibrational stimulation and a "silent period" after cessation of prolonged stimuli have been observed and the latter has been quantitatively analysed. It can be claimed that the theoretical implications of these results may be of considerable importance in relation to the problems of the evolution of hearing and pitch discrimination in vertebrates.

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