

REVIEWS

The Lagena (the Third Otolith Endorgan in Vertebrates)

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Neirofiziolgiya/Neurophysiology, Vol. 40, No. 2, pp. 160-178, March-April, 2008.

Received January 14, 2008.

In this review, the structure and functions of the lagena (the third otolith organ) in an evolutionary lineage of the vertebrates are described and discussed. The lagenar macula appears first in the posterior part of the sacculus of elasmobranchs; in these animals, the lagena is considered to be involved in the balance support (orientation with respect to the gravitation force). The lagena as a separate endorgan has been described in teleost fishes; in some species, the lagena is connected with the sacculus, while in other species the interrelations of these structures can be dissimilar. The lagena supplements the functions of the sacculus; in fishes (animals with no special organ of hearing), it is involved in discrimination of sound oscillations, identification of the gravitation vector, and orientation in the course of movements within the vertical plane. In amphibians, the lagena is localized in the posterior part of the sacculus, near the auditory structures; it performs mostly vestibular and (to a much lesser extent) auditory functions. In amniotes, the lagena was first separated from the sacculus; it is localized in the cochlear canal, distally with respect to the hearing organ. Information on the functions of the lagena in amniotes is rather limited and contradictory. Central projections of this organ have been examined practically only in birds. Lagenar afferents project to the vestibular nuclei and cerebellum, while some fibers come to the auditory nuclei of the medulla. The lagena in birds can be related to their navigation abilities (birds are supposed to be capable of orienting within the magnetic field of the Earth due to the magnetic properties of the lagenar otoconia; this structure can also provide detection of movements along the vertical axis. The close proximity between the otolithic and auditory endorgans in the cochlear canal of amniotes can be indicative of the functional significance of these interrelations. This aspect, however, remains at present undiscovered. In mammals (except *Monotremata*), there is no lagena as an independent endorgan.

Keywords: inner ear, otolith organs, lagena, vestibular function, auditory function, vertebrates.

INTRODUCTION

As is generally known, there are two otolith endorgans, the utricle and the sacculus, in the inner ear of mammals. At the same time, the third otolith endorgan, called the lagena, is present in most other vertebrates. The lagena, similarly to other endorgans, is a group of sensory hair cells localized in the inner ear and covered with a membrane containing the otoconia. As is supposed, reception of mechanical accelerations (including the gravitational acceleration) is the main function of the inner ear endorgans. At the same time, it cannot be ruled out that these organs perform some other functions. In this review, we focus our attention on this aspect of the problem.

The lagena is present in the membranous labyrinth of the inner ear of all nonmammalian vertebrates. Despite the fact that the first (later on, generally accepted) description of the lagena was proposed by Retzius as early as in 1881, there is relatively limited information on the sensory role of this otolith-like formation [1]. For a long time, it was supposed that the inner ear membranous labyrinth (as an organ of equilibrium and a structure responsible for reception of mechanical oscillations) was formed in vertebrates on the basis of the lateral line organs of fishes [2, 3]. At the same time, in recent studies it has been stated that the inner ear and organs of the lateral line were developed in the course of evolution from a common system of superficial neuromasts independently of each other, and the dynamics of their development are rather specific [4]. As is supposed, a homolog of the membranous labyrinth in ancestors of living vertebrates looked like a parameningeal vessel

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opening on the surface of the head; it included a common macula with hair cells and neuromast organs [5]. The labyrinth characterized by such a relatively simple structure is typical of living *Cyclostomata*. According to the existing hypothesis, in the course of divergent evolution from common ancestors, the entire variability of the groups of modern vertebrates developed, and the respective specific modifications in the inner ear of the animals belonging to these groups appeared [3].

In this paper, we compare the structure and possible functions of the lagena in the course of development and complication of the membranous labyrinth of the inner ear in an evolutionary lineage of the vertebrates on the examples of representatives of all known classes of these animals.

STRUCTURE AND FUNCTIONS OF THE MEMBRANOUS LABYRINTH IN *CYCLOSTOMATA*

The first labyrinth, of a relatively simple structure, can be found in most primitive living fish-like marine vertebrates, *Agnathostomata*, or *Cyclostomata* [6]. According to modern classifications, *Cyclostomata* constitute a superclass (or a class) including classes (in other classifications, subclasses or orders) of hagfishes (*Myxine*, about 60 species) and lampreys (about 30 species) [7]. There is no lagena as an independent endorgan in the membranous labyrinth of these animals. It is, however, possible to observe the initiation of formation of the lagena in other vertebrates on the example of sophistication of the inner ear and beginning of differentiation of the common macula in the above animal group.

One of the patriarchs of studies of the vestibular system, Otto Löwenstein, who worked in the University of Birmingham for about 50 years, obtained fundamental information related to morphophysiology of the inner ear of *Cyclostomata* and other lower vertebrates. The membranous labyrinth in the hagfish is of an irregular toroidal form; it is localized in a capsule caudally with respect to roots of the X nerve and is oriented obliquely to the main head axis (Fig. 1A). The dorsal part of the labyrinth looks like a single semicircular canal (duct); anterior and posterior crests with no cupules in the site of connection with the otolith chamber can be differentiated in this canal [1, 6, 8]. Receptor cells located on a ventromedial wall of the otolith chamber in a common macula are covered by a common otolith composed of a gelatinous matrix

with mineral particles. The dimension of the latter in the hagfish *Paramyxine nelsoni* varies from 1 to 26 μm [9]. A specific feature of the mineral composition of otoliths of both hagfishes and lampreys is the following: these formations are built mostly of apatite, in contrast to otoliths of other vertebrates [10].

The hagfish macula comprises an anterior horizontal part, a middle part positioned vertically, and a horizontally oriented posterior part. Receptor cells on the edges of the posterior and anterior parts are directed toward the neighboring ampulla, while cells in the center of the macula are oriented, correspondingly, to their localization, i.e., dorsally located units are directed dorsally, and vice versa. Dissimilarities in the structure of the three parts of the common macula show that these parts in hagfish are to a certain extent similar to the utriculus, sacculus, and lagena, the structures differentiated in fishes and present in other (more evolutionary progressive) vertebrates, *Gnathostomata*. Sensory cells in the macula possess 12 to 25 stereociliae (4 to 10 μm long) and an 8- to 12- μm -long kinocilia [6, 8, 11]. Electrophysiological experiments demonstrated that, when the hagfish head is positioned in a “nose downward” manner, receptor cells of the anterior macula are excited, while posterior cells are inhibited. When the head is in a “nose upward” position, the situation is opposite. Responses of the macula to vibration were not observed [11].

Central projections of the labyrinth in the hagfish *Eptatretus burgeri* were examined using transganglionic transport of horseradish peroxidase. Afferent fibers to the anterior two-thirds of the macula and anterior crest come via the anterior (utricular) nerve, while those to the posterior one-third of the macula and posterior crest go in the posterior (saccular) nerve. Projections from both nerves significantly overlap in the ventral nucleus of the acoustico-lateral system. At the same time, a part of the posterior nerve fibers projects more caudally [12].

The labyrinth of lampreys (which, in general, are characterized by more active behavior, as compared with hagfishes; lampreys cover hundreds of kilometers within a spawning period) comprises two vertical semicircular canals and a common macular chamber [1, 6, 7]. The surface of the common macula is covered with a compact otolith membrane and is organized nearly in the same mode as that in the hagfish, but differentiation between three parts of the common macula in its anterior, intermediate, and posterior parts is clearer (Fig. 1B). These regions are, correspondingly, considered homologs of the utriculus, sacculus, and lagena in fishes [6]. In lampreys, the

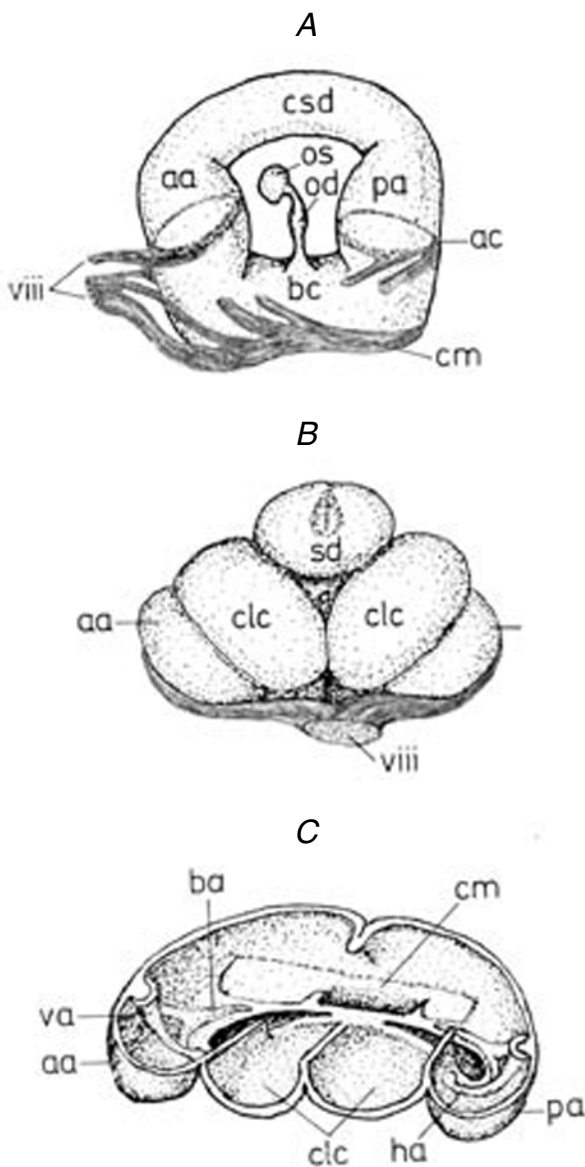


Fig. 1. Schemes of the membranous labyrinth in *Cyclostomata*. A) Labyrinth of a hagfish (*Myxine*); view into the medial part [1, 6]. *aa*) Anterior ampulla, *ac*) annular ampullary crest, *bc*) basal chamber, *cm*) common macula, *csd*) common semicircular duct, *od*) otic duct, *os*) otic sac, *pa*) posterior ampulla, and *viii*) vestibulocochlear nerve. B) Labyrinth of the marine lamprey (*Petromyzon*), view into the medial part [1, 6]. *clc*) Ciliated chamber and *sd*) common termination of semicircular ducts. Other designations are the same as in A. C) Lateral view into the basal part of the membranous labyrinth of the river lamprey (*Lampetra fluviatilis*) [13]. The dorsal part of the labyrinth and the lateral extremities of the ciliated chambers have been removed to expose the common macula and tripartite crests. *ba*, *va*, and *ha*) Basal, vertical, and horizontal arms of crests, respectively. Other designations are the same as in A and B.

anterior (greater) and central parts of the common macula are situated within horizontal and vertical planes and is a homolog of the lagenar macula in fishes (C). Polarization of hair cells in the anterior part of the common macula demonstrates polarization similar to that in the fish's sacculus (cells localized "higher" are oriented dorsally, while "lower" cells are directed ventrally). Polarization of the cells within a lagenar part of the common macula is in general analogous to that of the cell population in the anterior macular part; the only difference is the backward orientation of the medially localized cells [13]. Clear responses of the labyrinth in lampreys are evoked not only by changes in the head position (as is observed in the hagfish) but also by vibration [14]. In the stream lamprey *Lampetra planeri*, two types of hair cells were found in the common macula; some units possess a kinocilia (7 to 10 μm) and several stereociliae of about equal lengths, while other cells have a long kinocilia and short bundle of stereociliae whose length increases gradually [15]. The macula is covered by a common otolith; 40% of the latter in lampreys is constituted by organic materials. This index is considerably higher than the respective index in other fish-like animals (skates and guppy) where it is only 4 to 10%. At the same time, the amount of calcium in the otolith (5.33 mmol, on average) in lampreys is smaller than that in the above fishes (9.0 to 9.6 mmol) [16].

Central projections of the labyrinth in lampreys were found ipsilaterally in the ventral nucleus of the octavolateral medullary region, as well as in the molecular and granular layers of the cerebellum. Initially, it was supposed that crests of the semicircular canal are the source of thicker afferent fibers, while the macula is innervated by thinner fibers [13]. Later studies, however, showed that duct afferents are of nearly identical diameter (1.5-12 μm), similarly to other fibers of the VIIIth nerve [17]. In general, organization of the central projections of the acousticolateral system in lampreys is similar to that found in fishes and corresponds to the organization of central afferents of nerve VIII in all vertebrates. Fibers transmitting information on oscillations (auditory fibers) terminate more dorsally, while vestibular fibers project more ventrally [18].

Efferent vestibular neurons in river and marine lampreys were found only ipsilaterally, near Mauthner cells (about 20 units), and their axons go in the VIIIth nerve to the membranous labyrinth [17, 19].

Thus, in living *Cyclostomata* (hagfishes and lampreys, whose labyrinth is probably to a great extent similar to that in ancestors of all living vertebrates), there is a common chamber with one or two semicircular canals. Central projections of the macula, whose structure in lampreys demonstrates certain level of differentiation, transmit information on both changes in the head position and oscillations in the environment (vibrations). These projections are organized in the same mode as in other vertebrates. Fibers transmitting vibration-related information terminate in the medulla dorsally, while vestibular fibers reach more ventral areas.

STRUCTURE, FUNCTION, AND CENTRAL PROJECTIONS OF THE LAGENA IN FISHES

Fishes are the most numerous, with respect to the number of species (about 25,000), and complicated, from the taxonomic aspect, supraclass of vertebrates [7, 20]. This supraclass includes the class of *Chondrichthyes* (several hundreds of species) and the class of *Osteichthyes* (bony fishes), much more rich in the number of species. We note a subclass (according to another classification, supraorder) of *Teleostei*, a group that occupied a dominant position in the water world in the course of evolution. Considering the great importance of commercial fishing, intense fundamental and applied studies of fishes (including investigations of the structures of their inner ear) are carried out in many countries. In this review, classes of *Chondrichthyes* and *Osteichthyes* are considered together because the structure of their membranous labyrinth is similar in a number of features. At the same time, the inner ear of fishes as primary-water animals differs from that of amphibians that possess adaptations for life both in water and on the ground. In fishes, the labyrinth is first separated into superior and inferior parts; in most species, the lagena was differentiated from the common macula. The structure of the superior part of the labyrinth, including three semicircular canals and utriculus, is rather stable in all fish species and similar to that in other classes of vertebrates. At the same time, the inferior labyrinth part comprising the sacculus and lagena is characterized by considerable variability [5, 6]. In cartilaginous fishes, which, from a certain aspect, can be considered an intermediate group between *Cyclostomata* and bony fishes characterized by a higher organization [21] (in general, *Chondrichthyes* are an absolutely separate evolutionary branch of vertebrates), the sacculus is

an organizational center of the labyrinth, while the utriculus and lagena can vary considerably in their form (Fig. 2). The patterns of connection of such labyrinth with the external environment are their special features. In *Chimaerae*, specialized representatives of the cartilaginous fishes, the lagenar macula is not separated from the saccular macula, and the utriculus looks like a protrusion of the anterior part of the sacculus (A). In *Elasmobranchs* (sharks and skates), there are three maculae (the utricular, saccular, and lagenar ones); the latter is usually localized in a bend of the posterior wall of the sacculus (B). A common big otolith covers the lagenar and saccular maculae, and the level of differentiation of these maculae can be dissimilar [5, 6]. Hair cells in the thornback skate (see fox, *Raja clavata*) are oriented dorsally along the long axis of the sacculus and lagena within the dorsal part of the maculae and ventrally within their ventral part. In the utriculus (whose axis is perpendicular to the longitudinal axis of the sacculus and lagena), hair cells in the anterior and posterior parts of the macula are oriented forward and backward, respectively [22]. Electrophysiological experiments with recording of afferent activity from separate nerves going from the otolith organs showed that the utriculus, sacculus, and lagena in the above skate are sensitive to changes in the head position. Discharges in the lagenar nerve reached the maximum at a position close to the norm (horizontal) and decreased at tilts toward both sides [23]. Responses to vibration with frequencies of 10 to 110 Hz were found in afferents from the anterior two-thirds of the sacculus, *licinia utriculi* (an otolith-free part of this structure), and *papilla neglecta*. There were no vibration-related discharges in the lagenar nerve [24].

Projections of the inner ear structures in the clearnose skate (*Raja eglanteria*) were found in five nuclei of the medulla forming the nuclear complex of the VIIIth nerve, the magnocellular, descending, posterior, anterior, and periventricular nuclei. Afferents from the semicircular canals project ventrally, those from the saccular and lagenar maculae project dorsally, and utricular afferents project laterally. All endorgans, except the *papilla neglecta*, send afferents to all five nuclei, while the *papilla* projects only to the magnocellular nucleus, and terminals of its afferents are distributed most dorsally with respect to the afferents from other labyrinth structures. In the cerebellum, the semicircular canals are projected medially, and the otolith structures are projected laterally [25].

Bony fishes, especially those belonging to the subclass of *Teleostei*, have more adaptive

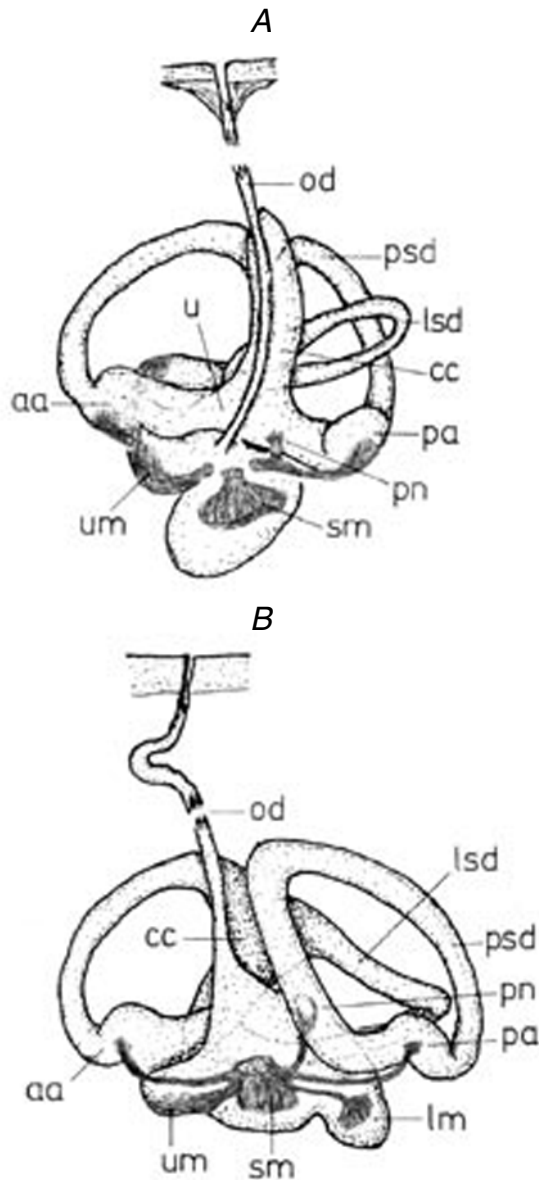


Fig. 2. Schemes of the membranous labyrinth in cartilaginous fishes. A) Labyrinth of a chimaera. *cc*) Common crus, *lsd*) lateral semicircular duct, *pn*) *papilla neglecta*; *psd*) posterior semicircular duct, *sm*) saccular macula, *u*) utricle, and *um*) utricular macula. Other designations are the same as in Fig. 1. B) Labyrinth in *Elasmobranchs*. *lm*) Lagenar macula. Other designations are the same as in Figs. 1 and 2A.

accommodations, including those of the inner ear [7]. In all fishes, otoconia are built from aragonite, i.e., calcium carbonate crystallized in a prismatic form. These structures differ from otoconia of other vertebrates because, together with a gelatinous matrix, they form an integral unit, the otolith *per se*. The macular region of each of the otolith endorgans

is covered by its own otolith. Such an otolith in the utricle has been called the *lapillus*, while the respective forms in the sacculus and lagena have been called the *sagitta* and *asteriskus*. Otoliths are growing within the entire period of life of fishes and do not undergo reabsorption [5, 6]. Mineralization of otoliths depends on the composition of endolymph [26] and is, to a certain extent, controlled by the CNS [27]. When the otolith organs of 15 species of Black Sea fishes were analyzed, the conservatism of these structures of the inner ear typical of the vestibular system pronounced during the entire process of growth of the fish was revealed. It was shown that, despite the fact that the mass of otoliths increases gradually during the growth, interrelations between the dimensions of an otolith and a macular area, otolith of the utricle and sacculus, and those of the lagena and sacculus do not change in a definite fish species [28]. Great attention is paid to the structure of otoliths because this is important for estimation of the age of fishes, their migrations, the dynamics of populations, etc. (see Payan [26]).

Each receptor cell of the macular area has several tens of short protrusions and a single longer protrusion, stereociliae and kinocilia, respectively. Sensory hair cells are distributed in the otolith organs in an ordered manner; one part of the macula contains cells with kinocilia directed toward one side, while kinocilia in another part of the macula are oriented in the opposite direction [29, 30]. Werner [31] calls the line separating regions of the macula with dissimilar orientation of hair cells the striola. Hair cells in the utricle and lagena are directed from the striola, while these cells in the sacculus are oriented toward this border. The density of receptor cells in the macula is the highest within the striola region, and in the lungfish *Protopterus* it is 120 cells per $10^4 \mu\text{m}^2$. This index is much higher than that in the extrastriolar region (14 units per $10^4 \mu\text{m}^2$) [32]. Hair cells in the striola area have big mitochondria localized around the nucleus. These cells are similar to hair cells of type I in amniots, while cells in the extrastriolar zones show certain similarity of type-II hair cells [33]. Otolith organs in bony fishes belonging to different orders demonstrate high variability, but three maculae, namely utricular, saccular, and lagenar ones, are typical of all fishes (Fig. 3). According to the significant specificity of the labyrinth of those bony fishes, which possess the swimming bladder and Weberian apparatus, and fishes without these organs, two morphological categories, a

typical labyrinth and an ostariophysine labyrinth, were classified [34]. The dissimilarities between these types of the labyrinth were found mostly in the lower part of the latter, while the upper part preserves common features described above. The typical labyrinth is characterized by domination of the sacculus; the lagena is separated from the latter to a greater or lesser extent (A, B) [6]. The ostariophysine labyrinth includes a relatively small sacculus connected with a big round lagena localized in a separate chamber and provided with a massive otolith (C). Sacculi of the left and right labyrinths of the ostariophysine fishes contact with a single sinus; mechanical oscillations are transmitted to the latter from the swimming bladder via a system of Weberian ossicles. The latter has resonance frequencies within 100 to 1,000 Hz and, correspondingly, amplifies oscillations of such frequencies [35]. The ability to perceive high frequencies in ostariophysine fishes (6-8 kHz) is better than in bony fishes with no swimming bladder; the frequency range for the latter is 800 to 3,000 Hz [36]. This circumstance is related to resonance properties of the swimming bladder and also to the presence of the Weberian apparatus, a system of Weberian ossicles effectively transmitting oscillations from the bladder to the inner ear [37]. The auditory sensitivity within the 300-500 Hz range in ostariophysine fishes is 40-45 dB with respect to a 1 μ bar level, which corresponds to the threshold energy of sound perception in humans in measurements at the same frequencies and is lower than the background noise level in the ocean [38].

In such a representative of ostariophysine fishes as the crucial and its domesticated form, goldfish (*Carassius auratus*), the lagena is of a round form and contains a somewhat heavier otolith than the sacculus. It was reported that the anterior part of the latter is innervated by thick fibers (15 μ m), while its posterior part and lagena possess thinner fibers (5 μ m) [39]. Subsequent studies did not support information on the existence of two different (in diameters) groups of afferents innervating various parts of the sacculus, but it was found that the branching of dendrites of primary afferents in the lagena is longer (74 μ m, on average) than that in the sacculus (50 μ m) [40]. Recording of electrical activity from fibers going from the anterior saccular part showed that they have no background activity, demonstrate fast adaptation, and generate maximum responses to stimulation with 700 to 800 Hz frequencies. Fibers from the posterior part of the

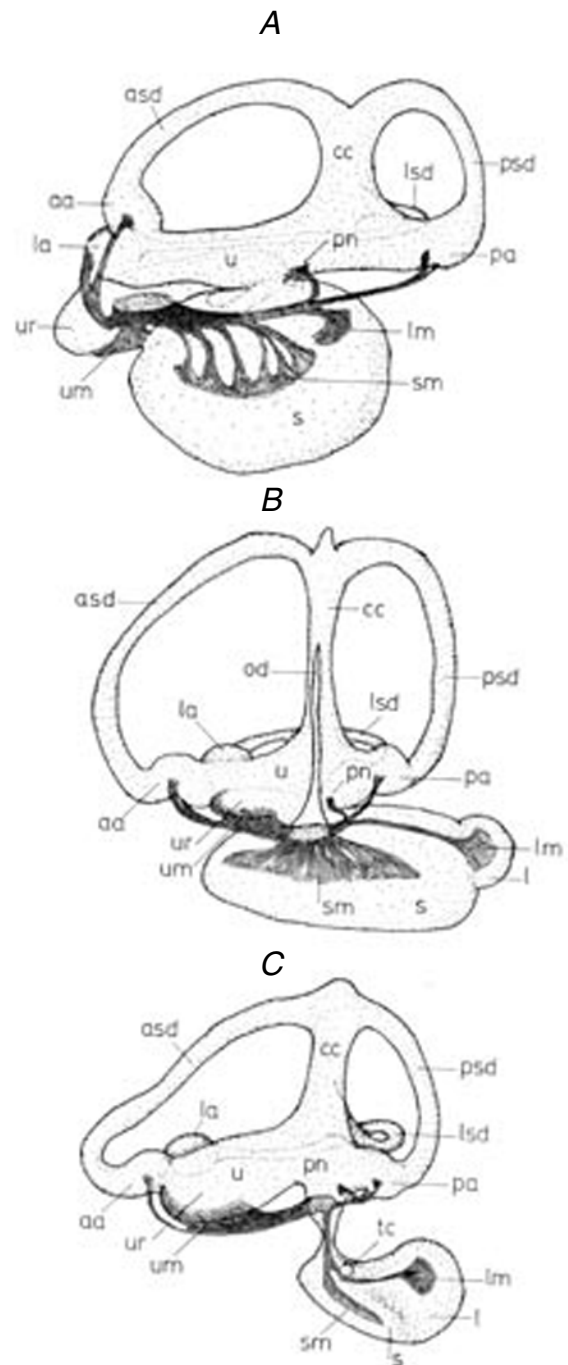


Fig. 3. Schemes of the membranous labyrinth in some *Teleostei*. A) A lungfish (barramunda, *Ceratosudus*), a "typical" labyrinth. *ur*) Utricular recess and *asd*) anterior semicircular duct. Other designations are the same as in Figs 1 and 2. B) A bony fish, perch, *Perca*, (a typical labyrinth). *l*) Lagena, *la*) lateral ampulla, and *s*) sacculus. Other designations are the same as in Figs 1, 2, and 3A. C) A bony ostariophysian fish, *Malapterus*. *tc*) Transverse canal. Other designations are the same as in Figs. 1, 2, and 3B.

sacculus and lagenar fibers manifested background activity, showed no adaptation, and clearly responded only to frequencies of 250-400 Hz, but responses in lagenar fibers were found only in the case where stimulation evoked noticeable vibration of the head [39]. An increase in the distance from the lagena or the edge of the sacculus exerted no influence on microphone potentials recorded from the labyrinth of the midshipman fish (*Porichthys notatus*), but these potentials were entirely eliminated when the sacculus was totally destroyed [41].

At the same time, it should be noted that in some species of ostariophysine fishes (e.g., in the marine catfish, *Arius felis*), the labyrinth has a dissimilar structure. The utriculus reaches rather large dimensions, while the sensory epithelium forms a broad strip around the equatorial region of the utricular chamber. It is supposed that just the utriculus (and not the sacculus and/or lagena) plays a crucial role in the perception of acoustic signals in fishes of these species. The range of sensitivity in these fishes covers 50 to 1,000 Hz, with the maximum within the 100-200 Hz region; this is much lower than in other ostariophysine fishes [42]. Projections of primary afferents from the otolith organs to the brainstem in the marine catfish are organized, however, in the same mode as in other *Sciluridae* [43]; the latter, in contrast to the marine catfish, do not use low-frequency sounds for communication and echolocation.

In two different orders of fishes possessing well-developed auditory perception but having no the Weberian apparatus (beaknose fishes, *Mormyridae*, and herrings, *Clupeidae*), the swimming bladder directly contacts with the labyrinth via its tube-like protrusions (with the utriculus in the herrings and with the sacculus in the *Mormyridae*). It is interesting to note that these fishes that live under quite dissimilar conditions (*Clupeidae*, mostly in the Atlantic ocean, while *Mormyridae*, in sweet-water African reservoirs) are capable of perceiving sound oscillations of frequencies up to 4 kHz [37]. In a representative of the *Cyhlidae*, *Dormitator latifrons*, the epithelia of the sacculus and lagena are oriented normally with respect to the horizontal plane of the fish, while the utricular epithelium is positioned within the horizontal plane of the animal [29]. In this species, the lagena is sensitive to these oscillations, and responses to acceleration of about $1.1 \text{ mm} \cdot \text{sec}^{-2}$ were recorded from the lagenar fibers. The clearest responses were observed at frequencies of 80-125 Hz and below 50 Hz, and their intensity depends on the stimulation frequency. Similarly to the saccular

macula, the lagenar macula demonstrates a directional sensitivity reflecting the morphological polarization of receptor cells perceiving linear accelerations within the vertical plane. As is supposed, in this fish species the lagena plays a significant role in the location of acoustic stimuli in the course of movements in the vertical plane, especially at high sound intensities, when responses of saccular sensory cells reach the saturation level [44]. Thus, some parts of the inner ear labyrinth (in some species, the utriculus, while in most species the sacculus and lagena) possess sensitivity to sounds [35].

The structure of the octavolateral brain region in fishes, similarly to that of the inner ear labyrinth, demonstrates considerable species-related peculiarities, and this circumstance makes it difficult to identify the corresponding nuclei in different species. In general, however, the medulla and central projections of the VIIIth nerve in fishes have a uniform structural pattern; this is also true with respect to other vertebrates, higher in the evolutionary grade. The auditory compartment is localized more dorsally, while the vestibular compartment is presented ventrally. Central projections of the lagena have been detected in fishes in the dorsocaudal regions of the octavolateral region, in proximity to terminals of the afferents of other otolith endorgans (mostly of the sacculus), and also in the cerebellum [45, 46]. Efferent neurons of the above-mentioned region obtain inputs from both sides and are projected ipsilaterally to the endorgans of the inner ear [46].

Thus, the lagena was differentiated as an independent endorgan of the inner ear in some species of the bony fishes. In other species of the bony fishes and in cartilaginous fishes (sharks and skates), the lagena is localized in a posterior wall of the sacculus and demonstrates different levels of separation from the latter. The functions of the lagena are dissimilar in different species of fishes. The lagena in skates is considered an organ of equilibrium. In general, fishes possess no specialized organs of hearing, and in many species the sacculus and, partly, the lagena and utriculus are believed to be the structures involved in the perception of acoustic oscillations. Central projections of the lagena in fishes are found in the dorsocaudal area of the octavolateral region, near the termination region of other otolith endorgans, and also in the cerebellum. As is supposed, functioning of the lagena supplements the auditory function of the sacculus; the lagena can also be involved in detection of the gravitation force and orientation upon realization of movements within the vertical plane.

STRUCTURE, FUNCTIONS, AND CENTRAL PROJECTIONS OF THE LAGENA IN AMPHIBIANS

Amphibians are an ancient group of vertebrates, which possess specific morphofunctional peculiarities reflecting adaptations of these animals to life in both aqueous and ground environment. Frogs and toads, *Anura*, are the most numerous representatives of this class; the number of their species (about 3500) considerably exceeds the number of *Urodela* (tritons and salamanders, 470 species) and *Apoda* amphibians (gymnophione, 170 species) [47]. A significant contribution to studies of the amphibian inner ear labyrinth was made by scientists of the USA, Germany, Japan, Spain, Hungary, and the former USSR.

It should be noted that the sacculus in amphibians, similarly to what is observed in fishes, is greater than the utriculus; the hypoglossal-mandibular bone is transformed into an ear *columella* [6, 48]. Elements of the auditory system in tailless amphibians (*Anura*), whose behavior is more “ground,” are better developed than those in *Urodela* and *Apoda* where these elements can be reduced to a different extent [49].

The lagena in amphibians is localized in the lagenar diverticulum situated medially in the posteroventral wall of the sacculus [6, 48]. In frogs and toads, the lagena is better developed than that in salamanders and gymnophions [49]. In the grass frog (*Rana temporaria*), the lagena looks like a cone with a round head and flat medial wall motionlessly fixed to the bone capsule. The arch-like lagenar macula (about 400 μm long) is located on the medial wall [48]. The macula of otolith organs is covered with a gelatinous membrane with inserted otoconia containing crystals of calcium carbonate. The utricular otoconia are built from cylinder-shaped crystals typical of calcite, while the otoconia in the sacculus and lagena contain aragonite [50, 51].

The dorsal part of the amphibian labyrinth preserves features typical of primitive vertebrates, while novel structures that are considered the first specific auditory organs, the *amphibian* and *basillar papillae*, appear in the ventral part of the labyrinth (in the sacculus) of these animals (Fig. 4).

The *amphibian papilla* is localized on the dorsal and medial walls of the sacculus above the lagenar diverticulum; it is situated in proximity to the utricular/saccular common junction. The *basilar papilla* is localized near the lagena, ventrally and caudally with respect to the *amphibian papilla* [48]. Close proximity between the *basilar papilla* and lagena is

also observed in other classes of vertebrates. In the bullfrog (*Rana catesbiana*), the number of sensory cells in the *amphibian papilla* is greater than that in the *basillar papilla* (600 and 60 units, respectively) [52]. The *amphibian* and *basillar papillae* were shown to contain receptors of low- and high-frequency oscillations, respectively [53, 54].

The question on the genesis of the *amphibian* and *basilar papillae* has been discussed for a long time. It is supposed that the *amphibian papilla* is a derivative of the *papilla neglecta*, while the *basillar papilla* of the amphibians can be considered a homolog of the *basillar papilla* in all tetrapods and in the coelacanth *Latimeria chalumnae*, the only living species of fleshy-finned fishes (subclass *Crossopterygii*). Their extinct representatives, as is believed, could move on the bottom and climb onto solid ground using paired fins. The *basillar papilla* of the *Latimeria* is localized in the lagenar protrusion on the membrane separating the perilymphatic space from the endolymphatic volume. This *papilla* includes a group of cells covered with the membrane with no otoconia and innervated with a branch of the lagenar nerve [55].

Concepts on the vestibular function of the lagena in amphibians have been formed on the basis of earlier observations of the motor behavior of frogs with impairments of different parts of the inner ear. After partial bilateral destruction of the labyrinth with the lagena left intact, the leveling-out reflex is preserved, while after complete bilateral labyrinthectomy this reflex disappears [56].

In the lagena of frogs, a part of the receptor cells are sensitive to changes in the head position in the vertical plane, while other cells demonstrate sensitivity only to oscillations of the body. Lagenar afferents whose activity varies with a change in the head position are usually classified into three groups, tonic (23.5%), phasico-tonic (20.6%), and phasic (41.2%) [57]. Intracellular recording from primary lagenar afferent units combined with Lucifer yellow staining allows one to divide hair cells into separate groups depending on localization of such cells in the macula and characteristics of their kinocilia, and also according to the types of responses of primary afferent fibers innervating these hair cells [58, 59]. Two lines of cells within the region of central strip of the striola have bulb-shaped kinocilia and are innervated by fibers whose discharges are modified by oscillations. Such hair cells with bulb-shaped kinocilia were found in the sacculus, *amphibian papilla*, and *basilar papilla*, i.e., in the structures relating to the auditory function [58]. Within the region of striola, peripherally to the central

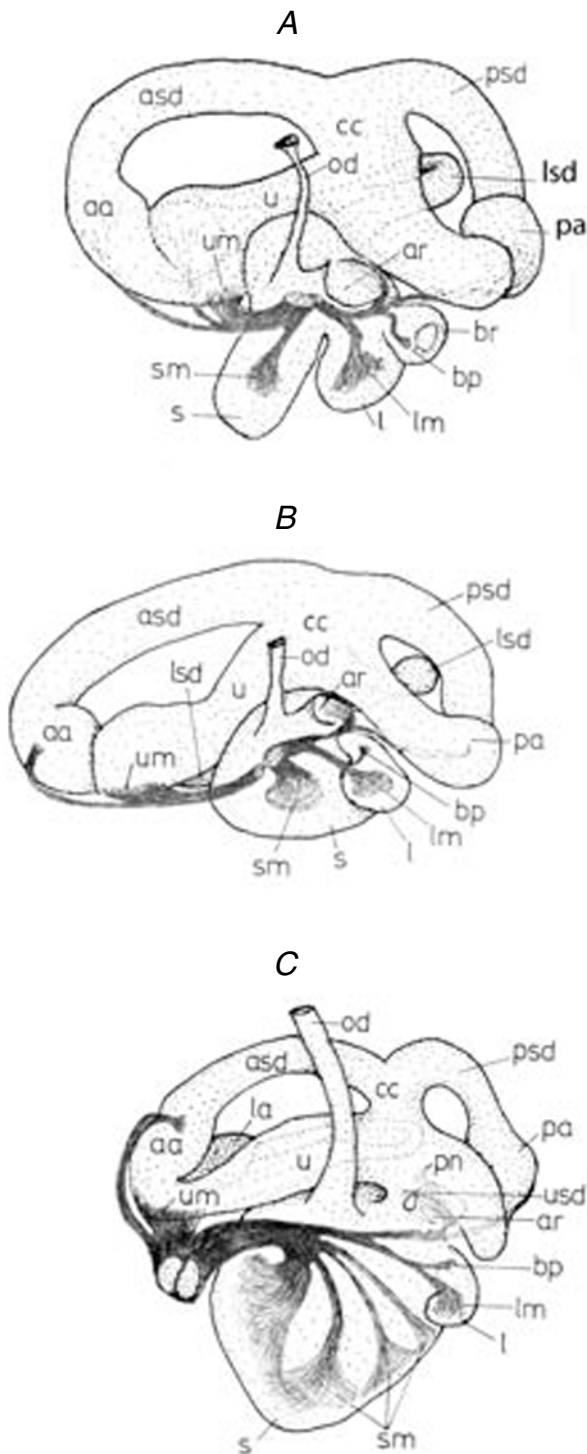


Fig. 4. Schemes of the membranous labyrinth in amphibians. A) *Anura*, B) *Caudata*, and C) *Apoda*. Novel structures arrived in amphibians: *ar*) amphibian recess, *bp*) basilar papilla, *br*) basilar recess, and *usd*) utriculo-saccular duct. Other designations are the same as in Figs 1-3.

strip, cells with a short kinocilia or a long kinocilia with no bulb-shaped enlargements are localized. Such cells are innervated by phasic or phasico-tonic afferents. Extrastriolar regions contain hair cells with long kinocilia having no bulb-shaped enlargements [59]. Lagenar afferents sensitive to oscillations have steeper amplitude/frequency characteristics than lagenar afferents sensitive to changes in the head position (dorso-ventral microshifts with 10 to 1,000 Hz frequencies were used as the stimuli) [60]. It should, however, be mentioned that in other studies no responses to vibration were found under conditions of recording of the activity from single fibers of the lagenar nerve, while recordings from the anterior and posterior branches of the VIIIth nerve showed the respective clear responses of primary afferents. Such responses were probably of a saccular and/or utricular nature or were produced in the *amphibian papilla*. Fibers of the latter group were also sensitive to low-frequency acoustic stimulation [61].

Two groups of cells, which are targets for projections from the inner ear labyrinth, were classified in the frog medulla using experimental degeneration and silver impregnation. The ventral region includes four vestibular nuclei looking as long parallel cell columns [62, 63]. The dorsal region consists of cells of different types gathered in a single auditory nucleus. Afferents of the VIIIth nerve, after entering the brain, are distributed caudally and rostromedially [64]. In the bullfrog (*Rana catesbiana*), the VIIIth nerve consists of two branches. The anterior branch is mostly vestibular; it contains fibers from the utricle and crests of the anterior and lateral semicircular canals, while the posterior branch includes fibers from both *papillae*, inferior part of the saccular macula, lagena, and posterior canal [65]. The greatest number of fibers of the VIIIth nerve (4,000) is of utricular nature, while a smaller part (2000) comes from the lagena. The number of afferents from the semicircular canals, *amphibian papilla*, and sacculus is from 1,000 to 1,500, and the smaller group (800) goes from the *basilar papilla* [66, 67].

The role of lagena in the amphibian vestibular system is supported by the data on clearly expressed convergence of inputs from the lagena and one of the semicircular canals and also from the sacculus or utricle obtained in experiments with intracellular recording from neurons of the vestibular nuclei under

conditions of selective electrical stimulation of the lagenar nerve and one of the canal and/or utricular (saccular) nerves. Seventy-five percent among 113 neurons of the vestibular nuclei, which were monosynaptically activated upon stimulation of the lagenar nerve, also generated monosynaptic EPSPs after stimulation of the nerves from one or a few semicircular canals. At the same time, convergence of the inputs from the sacculus and one of the other endorgans was observed in no more than 5% of the total number of neurons monosynaptically activated by saccular stimulation. It is supposed that the lagena in frogs plays nearly the same role as the sacculus in mammals (e.g., in cats). Convergence of afferent influences from the utriculus and sacculus was found in 25% of neurons of the vestibular complex in cats; this is comparable with the data on convergence of lagenar and utricular afferents in the frog (11% among 153 neurons). A great majority of vestibular neurons possessing direct inputs from the lagena were antidromically activated upon stimulation of the spinal cord, i.e., they formed descending vestibulofugal projections [68]. This finding agrees with the results of earlier studies allowing experimenters to believe that the lagena in frogs is not involved in vestibulo-ocular processing [69].

Each endorgan, except the sacculus, sends a considerable number of afferents to all the four vestibular nuclei. Lagenar fibers are distributed relatively evenly in the anterior and medial vestibular nuclei, lateral ventral nucleus, and in the middle and caudal parts of the descending vestibular nucleus. The utriculus also sends projections to all vestibular nuclei, but, in respective studies, the density of labelled fibers was found to be higher in the dorsal region of these structures. The sacculus is projected mostly to the ipsilateral auditory nucleus and, to a considerably lesser extent, to rostral parts of the lateral and descending vestibular nuclei. Efferent neurons, whose mean diameter is $19.4 \pm 2.5 \mu\text{m}$, were found in ventral regions of the vestibular nuclei; their number did not exceed 3-4 per endorgan. Using two different markers (one was introduced in the crista of one of the canals, while another was applied to the region of one of the maculae), overlapping of projections from the maculae of the otolith organs and cristae of the semicircular canals was demonstrated [64]. Projections from the lagena and sacculus were found in rostral parts of the cerebellum, while the utricular projections went to caudal parts of the latter [70].

Data on the lagena in amphibians can be summarized in such a way. This organ is localized in the posterior

wall of the multichamber sacculus near the auditory receptors. Lagenar fibers were shown to be sensitive to displacements in the vertical plane and to vibration. A "vestibular" role of the lagena is also supported by the existence of its central projections to all four vestibular nuclei and the cerebellum. In addition to the involvement in vestibular sensory processing, the amphibian receptor apparatus of the lagena probably participates, to a certain extent, in the discrimination of acoustic signals.

STRUCTURE, FUNCTION, AND CENTRAL PROJECTIONS OF THE LAGENA IN REPTILES

The *Reptilia* is a class of the terrestrial vertebrates completely adapted to life and reproduction on the ground. At present, more than 8,000 living species are known [20]; they are grouped in four subclasses (according to other classifications, orders). Among them, *Squamata* (lizards and snakes, 7,000 species) are the most numerous; turtles and tortoises (*Chelonia*, more than 200 species), and crocodiles (*Crocodyliae*, more than 20 species) are less variable. The fourth group, the beak-headed reptilian (*Rhynchocephalia*), is represented by a single relict species, *Sphenodon*, or *Gatteria* [20, 71]. A significant contribution to our knowledge about the inner ear of reptiles was provided by I. L. Baird (University of Pennsylvania, USA), E. G. Wever (Princeton, USA), and G. A. Manley (Technical University of Munich, Germany).

Reptiles (turtles, snakes, lizards, and crocodiles) demonstrate considerable variability in both dimensions of the entire body and relative dimensions of different organs, including the inner ear. This circumstance is probably partly related to the evolutionary history of these animals; living species of reptiles represent different ancient lines of vertebrates that served as the basis for the formation of *Amniota*. No clear dependences were found between their mode of life, on the one hand, and mass of the body and dimensions of the endorgans of the membranous labyrinth, on the other hand [21]. For example, the length of the *basilar papilla* is equal to 1% of the rostral-caudal body length in large reptiles and to 2% in small species. At the same time, the mass of the otoconia demonstrates certain correlation with the body length of these animals [72].

Evolutionary modifications of the inner ear labyrinth influenced mostly its ventral part, while the dorsal part preserved the pattern typical of all

higher vertebrates. The arch-like utriculus is smaller than the sacculus; the dimensions of the semicircular canals increased somewhat. In the ventral part of the labyrinth, a novel structure can be found; this is the cochlear canal, which is similar to the sacculus in shape and dimension. The cochlear canal attaches to the posterior wall of the sacculus and is connected with the latter by the saccular-cochlear canal, or *ductus reuniens*. The dimensions of the cochlear canal and *ductus reuniens* demonstrate great variability in representatives of different reptilian orders and families. The lagena is localized in the most distal part of the cochlear canal. The proximal part of the latter contains the *basilar papilla* and also the periotic connective tissue forming the basilar membrane and supporting limb [6, 73, 74] (Fig. 5).

The U-like lagenar macula looks like a band crossing the anterior, medial, and lateral walls of the lagena. Two types of sensory cells are found in the otolith endorgans of reptiles; these cells are identical to hair cells of types I and II in the endorgans of mammals [21]. The lagenar and utricular maculae are covered by an otoconial membrane containing calcite, while aragonite predominates in the saccular otoconia [75].

In the tuatara (*Sphenodon punctatus*), a unique living representative of the *Rhynchocephalia* order, the most ancient reptiles demonstrating a composition of anatomical features typical of amphibians and "classic" reptiles, the lagena is somewhat longer than the sacculus [6]. In the tuatara, turtles, and snakes, the lagena is separated from the *basilar papilla* by a noticeable narrowing of the cochlear canal; the latter canal in lizards, however, includes the lagenar and limbic parts that are not separated by any formation. Probably, the lagenar and limbic parts of the cochlear canal unite in the course of evolution, and the latter canal forms more close connections with the more developed middle ear. It should be noted that in amphibians the lagena and *basillar papilla* are localized in the sacculus in close proximity, but they are not connected with each other and are localized in separate invaginations of the mentioned structure, and this feature differentiates the above animals from reptiles [74]. The labyrinth of crocodiles is characterized by relative increases in the dimensions of both the cochlear and semicircular canals, as compared with those of the otolith endorgans. Elongation of the cochlear canal, which in crocodiles begins to look like a boomerang, makes their inner ear labyrinth similar in pattern to the labyrinth of the birds. The lagena in the elongated cochlear canal of crocodiles is fixed to two lateral sides of the surrounding cavity, and

the basilar membrane is localized on the base of the lagena [6, 21, 73].

According to Wever [21], the *basilar papilla* in reptiles is a fundamentally new structure, with no analogs in fishes and amphibians. But, as was mentioned earlier, Fritzsche believed that the *basilar papilla* appeared as an independent structure in the lagena as early as in crossopterygian fishes; in these creatures, it is similar to the *basilar papilla* of all tetrapods [55]. The dimensions of the *basilar papilla* lying in the cochlear canal proximally with respect to the lagena demonstrate considerable species-related differences. For example, the short papilla in iguana lizards (*Scleropus magister*) includes only 60 sensory cells, whereas in geckos (*Gekko gekko*) the *papilla* is five times longer and contains 1,600 sensory units. At the same time, the frequency/threshold curves plotted by recording the potentials from the round window cover a nearly identical frequency range in both species, but with a lower threshold and with the maximum sensitivity within a 400 Hz region in *Gekkonidae* [21].

The existing concept on the structure and functions of the inner ear labyrinth in reptiles was formed mostly based on a comparison of this complex with the respective structures in birds [21].

In summary, we note that reptiles possess an evolutionarily novel structure, the cochlear canal, where the lagena and *basilar papilla* are localized. In evolutionary older reptiles (tuataras, turtles), the lagena and *basilar papilla* are separated by a narrowing of the cochlear canal, while in lizards and crocodiles the cochlear canal is composed of the connected lagenar and limbic parts. It should be recognized that the functions of the lagena and central projections of its receptor apparatus in reptiles have practically not been examined.

STRUCTURE, FUNCTIONS, AND CENTRAL PROJECTIONS OF THE LAGENA IN BIRDS

Birds constitute the second class of vertebrates in species diversity (after fishes). This class includes about 10,000 species and is composed of a supraorder *Impennes* (including only one order, penguins) and a supraorder of typical (*Neognatha*) birds, including a great majority of the species gathered, according to one of the most detailed classifications, in 40 orders [20, 76]. Studies of the inner ear in birds were successfully carried out for many years in the USA, Germany, Japan, the Netherlands, the Scandinavian

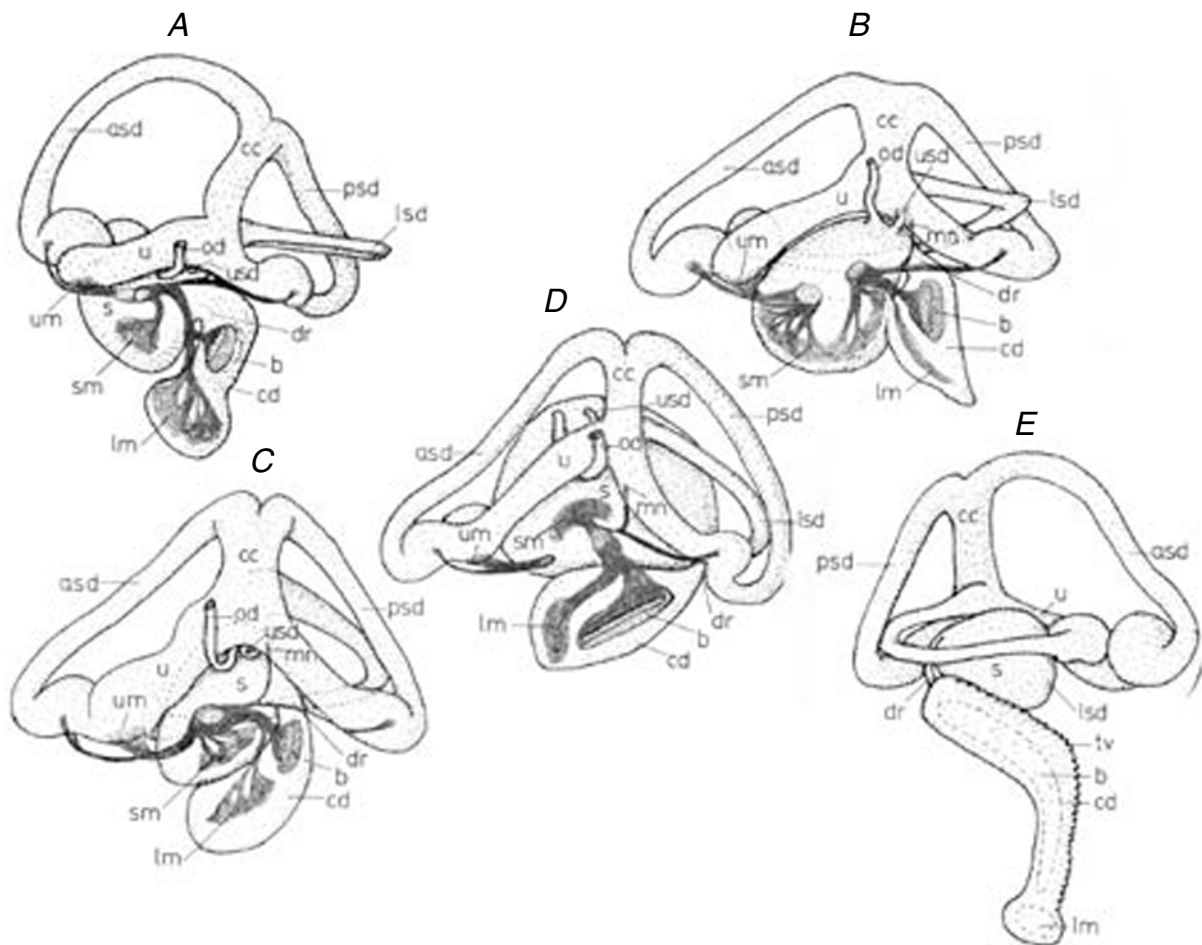


Fig. 5. Schemes of the membranous labyrinth in representatives of different orders of reptiles. A) Tuatara (*Sphenodon*). The following structures arrived first in reptiles: *cd*) cochlear duct, *dr*) reunient duct, and *b*) basilar-papilla membrane. Other designations are the same as in Figs 1-3. B-D) A turtle, a snake, and a lizard, respectively. *mn*) *Macula neglecta*. Other designations are the same as in Figs. 1-4 and 5A. E) A crocodile. *tv*) *tegmentum vasculosum*. Other designations are the same as in Figs. 2, 3 and 5A. In A-D, medial aspect, and in E, lateral aspect.

countries, and the former USSR.

The labyrinths of the inner ear in birds belonging to different orders are rather similar to each other. The bone capsule of the inner ear, which in general corresponds to the membranous labyrinth localized in this capsule, demonstrates relative lengthening in the dorso-ventral direction. In the bird skull, this capsule is likely to be rotated backward, as compared with the analogous capsules in fishes and amphibians (Fig. 6A). In the inferior part of the labyrinth, the cochlear canal predominates; it is directed anteroventrally, has a banana-like shape, and is expanded in its distal part, where the lagena is situated. The sacculus is smaller than the utriculus and is localized ventromedially with respect to the anterior part of the latter and rostrally to the cochlear canal. Within the region of its posterior wall, the sacculus is connected with the cochlear canal

by a wide *ductus reuniens* [5, 6, 73].

The inner ear labyrinth of birds attracts special interest because their navigation abilities (e.g., the capability of very accurately finding the nesting place after long transigrations) are related to a probable sensitivity of the inner ear organs to the influence of the magnetic field of the Earth. The content of iron and manganese compounds in the lagena of birds is shown to be much greater than that in the utriculus and sacculus [77].

When the lagenar nerve is impaired in pigeons, it results in the loss of their ability to return to the nest. Analogous results were observed in pigeons with implantation of a miniature magnet in the inner ear (in the lagenar region); the lagenar nerve was in this case left intact. It is supposed that the lagena, which possesses the corresponding properties, can serve as a

sensor of the magnetic field of the Earth [78].

The inner ear labyrinth has been studied in most detail in the pigeon (*Columba livia*). The lagena is localized in this species in an expanded apical part of the cochlear canal (distally with respect to the *basilar papilla*). The lagenar macula is of a U-like shape, with a flat longitudinal surface and short edges converted outside. The longitudinal surface of the macula is situated within the plane of the posterior semicircular canal, and lateral horns are positioned normally to the main longitudinal surface of the lagena and utriculus [78-80]. The lagenar macula is about 1.5 mm long, and its width does not exceed 0.7 mm [79]; the *basilar papilla* is about 3.8 mm long [81]. The area of the lagenar macula is, on average, smaller (0.93 mm²) than the area of the utricular macula (1.29 mm²) but greater than that of the saccular macula (0.56 mm²) [79]. Other authors mention very close figures on the dimension of the lagenar macula (0.98 mm²) and report that the lagena contains about 16,800 sensory cells [82]. The otolith membrane containing otoconia composed of calcite crystals partially covers the lagenar macula, while the remaining part of the latter is covered by a gelatinous matrix. The border between the two above-mentioned parts of the otolith membrane approximately corresponds to localization of the striola dividing the field of receptive cells into two parts, and these cells have dissimilar orientation of cilia [79].

Morphometric studies showed that hair cells in the lagena of birds belong to two types, I and II, which is typical of the vestibular organs, including the utriculus and sacculus, in all amniotes [83-85]. The striola is localized centrally, along the longitudinal axis of the lagena. Sensory cells in the lagena, similarly to that in the utriculus, are directed from the striola, while in the sacculus these cells are oriented toward the striola. Within the striolar region, hair cells of type I predominate; these cells form long longitudinal bundles, while only cells of the type II are found in the extrastriolar regions [79, 86-88].

The number of primary lagenar afferents in birds corresponds to about 10% of the general number of fibers in the cochleo-lagenar part of the VIIIth nerve; it varies from 10,000 to 12,000 in different species [89, 90]. As is supposed, one lagenar fiber innervates, on average, about 15 sensory cells [82], while in the *basilar papilla* one primary afferent is usually connected with one sensory cell. The number of the latter is about 12,000 [21].

Functions of the lagena in birds have not been finally elucidated. According to the studies of the

activity of primary lagenar afferents with the use of electrodes filled with a marker, lagenar hair cells are insensitive to sound signals [91]. Electrical properties of the membrane of lagenar hair cells of types I and II were found to be similar to analogous properties of hair cells of other vestibular endorgans, cristae of the semicircular canals, and utriculus [92, 93].

From the anatomical aspect, central projections of the lagena in birds have been studied in detail. According to the cytoarchitectonics, four vestibular nuclei (superior, ventrolateral, descending, and medial) and several smaller cell groups were classified in the medulla of birds [94, 95]. Using degeneration techniques, it was shown that the lagena in pigeons (*Columba livia*), similarly to two other otolith

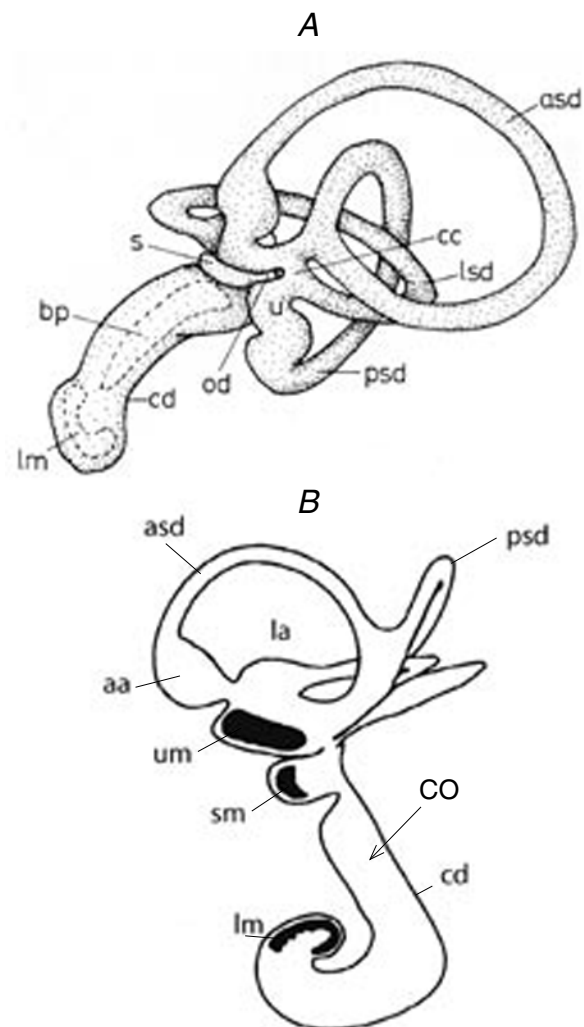


Fig. 6. Schemes of the membranous labyrinth of birds and monotreme mammals (medial aspect). A) A bird. Designations are the same as in Figs. 1-5. B) A monotreme, the echidna (*Tachyglossus aculeatus*) [105]. CO) Cochlea. Other designations are the same as in Figs. 1-3 and 5A.

endorgans, projects to dorsolateral portions of the superior, medial, and descending vestibular nuclei. Single lagenar projections to the medullary auditory nuclei were also found [96, 97]. These results coincide, in general, with the data of radiographic studies using [^3H]. These experiments demonstrated that lagenar afferents project approximately to the same regions of the medulla as afferents from the sacculus and utriculus. Some labelled lagenar fibers were also found in the external cerebellar nucleus [98]. As was observed in experiments with application of a mixture of horseradish peroxidase and cholera toxin on the cochleo-lagenar nerve, lagenar fibers terminate within the same cellular fields as afferents from the sacculus and utriculus [95]. It should be taken into account that the data on the presence of projections from otolith organs to the cochlear nuclei were obtained on mammals [99-101]. At the same time, only some of the authors agree with the statement that the lagena in birds sends afferents to the medullary auditory nuclei [80]. Selective applications of a marker (DiI) exclusively to the lagena showed that, in this case, labelled fibers were found only in the vestibular nuclei. In the case where the marker was applied not only on the lagena but also on the *basilar papilla*, the pattern of distribution of the fibers coincided with that obtained with the use of degeneration methods; labelled fibers were also observed in the ventral parts of the medullary auditory nuclei.

Efferent vestibular neurons have been found in birds bilaterally, ventrally with respect to the vestibular complex in the *nucl. reticularis pontis caudalis* [95, 98]. Vestibular efferent fibers are localized in the medulla near axons of motoneurons of the facial nerve. As is supposed, both efferent units projecting to the labyrinth and motor efferent neurons (motoneurons) of the nucleus of the VIIth nerve have the same precursors [102]. Efferent neurons sending their axons to the lagena are localized more dorsally and medially, in the so-called dorsal efferent group, while efferents projecting to the *basilar papilla* are situated ventrally and laterally, in the ventral efferent group [98, 103].

When summarizing the data on the lagena in birds, we should mention that this endorgan is localized in the cochlear canal distally to the *basilar papilla*. The functions of the lagena in birds have not been conclusively defined. The existing data of morphological studies allow one to suppose that this structure is connected mostly with the vestibular nuclei and cerebellum and, to a considerably lesser extent, with the auditory nuclei of the medulla. It is

supposed that the lagena in birds is a possible sensor of the magnetic field of the Earth and can be related to their navigation abilities. It cannot also be ruled out that the lagena is involved in the detection of accelerations in the vertical plane.

STRUCTURE AND FUNCTIONS OF THE LAGENA IN LOWER MAMMALS

In mammals, the lagena have been found only in the *Monotremata* infraclass, representatives of the only order of egg-laying mammals (several species of echidnas and the platypus that live in Australia, Tasmania, and New Guinea [104]. The large dimensions of the utriculus is specific to the inner ear of the echidna *Tachyglossus aculeatus*; this endorgan is the greatest, as compared with those in all living vertebrates, and contains the greatest number of sensory cells (>50,000). In other respects, the membranous labyrinth of *Monotremata* is similar to that in birds (Fig. 6B). The lagena contains receptor hair cells of types I and II, which are typical of vestibular organs of all amniotes. Polarization of hair cells in these mammals is also similar to that in birds; in the utriculus, these cells are oriented from the periphery toward the center, while in the lagena orientation is peripheral. Hair cells possess a kinocilia and 40-60 stereociliae filled with microfilaments, and having no microtubules. These cells are innervated by terminals of two types, bouton- and cup-like endings. The absence of the striola in the sacculus and lagena, as well as the relatively homogeneous distribution of cup-like nerve terminals across the macula are peculiarities of the otolith structures in the echidna. This is typical of higher mammals but differentiates the above animal from birds and reptiles where cup-like terminals are localized within the striola region [105].

The Corti organ in monotremes and other mammals demonstrates clear similarity. The relatively small length of the Corti organ and the small number of outer hair cells can be mentioned as specific features of the hearing organ in monotremes, while these animals do not differ from placental mammals in the number of inner hair cells related to discrimination of acoustic oscillations [106]. The middle ear of monotremes and reptiles has similar features. In the echidna, the malleus and anvil are united and fixed to the *os petrosum*; the stirrup is of a column-like shape, and the stapedius muscle is absent [37]. Experimental studies of the functions of the middle and inner ear

and of the central projections of separate parts of the membranous labyrinth in monotremes have not been carried out.

CONCLUSION

The lagena is the third otolith formation localized in the lower part of the inner ear labyrinth; it is present in some fishes, amphibians, reptiles, birds, and monotremes. It is situated approximately at a direct angle with respect both to the utriculus, which is usually oriented within the horizontal plane of the animal, and to the vertically positioned sacculus. Morphological polarization of hair cells in the lagena is identical to that observed in the utriculus, but it is opposite to that in the sacculus. The inner ear otolith endorgans demonstrate significant functional plasticity in the evolutionary lineage of vertebrates. For example, the appearance of the ability to perceive oscillations and then the formation of the hearing organs occur on the basis of functioning of the otolith endorgans, whose main role is provision of the vestibular function. Fishes have no specialized hearing organs, and oscillations of the sound range are perceived, to a different extent, by the utriculus, sacculus, and lagena. The lagenar macula is first differentiated in cartilaginous fishes; its function is related to the balance support. The lagena as a "competent" third otolith endorgan is present in a series of bony fishes. In general, in fishes the lagena is always connected with the sacculus. The plasticity of otolith receptors is clearly observed in bony fishes whose labyrinth, in general, is the balance organ, but separate otolith endorgans manifest different sensitivity to sound oscillations. The removal of the sacculus and lagena in ostariophysine fishes does not result in disorders of equilibrium, since the utriculus is responsible for the maintenance of equilibrium. In most species of these fishes, the sacculus and, partly, the lagena are involved in the perception of oscillations. In clupeal and gnatostomal fishes having no Weber apparatus, as well as in some ostariophysine fishes, this function is performed by the utriculus. The afferent and efferent innervation of the lagena is close to that of other otolith endorgans, especially of the sacculus, but also has some specific regions of the medullary projections.

In amphibians, the lagena is localized in the sacculus (the latter is related mostly to the auditory function) between two evolutionary novel structures, the *amphibian* and *basillar papillae*, the first hearing organs in the series of vertebrates. The close proximity

of the lagena to the auditory organs is further observed in all groups of vertebrates, including the most primitive mammals, *Monotremata*. Results of examinations of central projections of the lagena and those of microelectrode studies demonstrate that this endorgan in amphibians is mostly related to the vestibular system and, to a lesser extent, to the auditory system.

In amniotes, the lagena (first in vertebrates) is separated from the sacculus and is localized in a distal part of the cochlear canal, which is longer in birds and monotreme mammals than in reptiles. The *basilar papilla* occupies a proximal part of the cochlear canal; in monotremes, it demonstrates significant similarity with the Corti organ in higher mammals. The functions of the lagena in amniotes have practically not been experimentally examined; the question of the relation of this endorgan to the auditory system also has not been conclusively elucidated. Central projections of the lagena in birds are directed toward cell territories related mostly to the vestibular and, to a much lesser extent, auditory function. The presence of the lagena and *basilar papilla* in the cochlear canal in birds and reptiles is indicative of a possible functional significance of such close localization of these two endorgans in animals of the above two groups. There are indirect indications on the possible involvement of the lagena in the perception of movements in amniotes in 3D space, especially within the vertical plane, and also in the realization of navigation abilities of migrating birds (due to the magnetic properties of their lagena).

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