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Review

Anatomical and physiological development of the human inner ear

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ABSTRACT

We describe the development of the human inner ear with the invagination of the otic vesicle at 4 weeks gestation (WG), the growth of the semicircular canals from 5 WG, and the elongation and coiling of the cochlea at 10 WG. As the membranous labyrinth takes shape, there is a concomitant development of the sensory neuroepithelia and their associated structures within. This review details the growth and differentiation of the vestibular and auditory neuroepithelia, including synaptogenesis, the expression of stereocilia and kinocilia, and innervation of hair cells by afferent and efferent nerve fibres. Along with development of essential sensory structures we outline the formation of crucial accessory structures of the vestibular system – the cupula and otolithic membrane and otoconia as well as the three cochlea compartments and the tectorial membrane. Recent molecular studies have elaborated on classical anatomical studies to characterize the development of prosensory and sensory regions of the fetal human cochlea using the transcription factors, PAX2, MAF-B, SOX2, and SOX9. Further advances are being made with recent physiological studies that are beginning to describe when hair cells become functionally active during human gestation.

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Contents

Abbreviations: WG, weeks gestation; VGNs, vestibular ganglion neurons; IHCs, inner hair cells; OHCs, outer hair cells; SGNs, spiral ganglion neurons; GER, greater epithelial ridge; LER, lesser epithelial ridge

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1. Introduction

The inner ear is a complex structure that comprises sensory organs that detect angular and linear accelerations (vestibular system) and sound (auditory system). To detect these sensations both organs use hair cell mechanoreceptors to convert or transduce mechanical movement (head motion or sound waves) into electrical signals. However, there are significant differences in the morphology, location, physiology, and innervation of hair cells of the vestibular and auditory systems. Much of our understanding of the development of these two inner ear systems has been derived from rodent models. Here, we review the more limited information on the morphological development of the inner ear, from rudimentary otic placode to fully formed semicircular canals, vestibule, and cochlea of the membranous labyrinth, in the human embryo and fetus, as well as recent advances describing physiological maturation.

2. Morphological development of the inner ear

Classic anatomical studies have described human inner ear development (Bast and Anson, 1949; Streeter, 1906). In the embryo the otic vesicle forms as an invagination of ectodermal cells at the level of *rhombomere* 5 by four weeks gestation (4 WG) (Bruska et al., 2009). At this stage of development, the otic vesicle has two pouches, one dorsal the other ventral. A projection extends from the dorsal pouch that will form the primordial *endolymphatic duc*t (Bruska et al., 2009; Streeter, 1906). Between 4 and 5 WG, the dorsal pouch enlarges into a triangular shaped mass that will form the basis of all three semicircular canals (Streeter, 1906). As this triangular-shaped region develops there is concomitant resorption of the medial walls to form, in chronological order, the anterior, posterior, and horizontal semicircular canals (Streeter, 1906). At the same stage of development the vestibule, which will contain the future utricular and saccular maculae, also enlarges. An initial constriction between the immature saccular macula and the developing cochlea will eventually form the *ductus reuniens* (Streeter, 1906). Over the following two weeks of growth, there is continued remodeling of each semicircular canal and by ~7 WG, a swelling or *ampulla* containing the sensory organ or *crista ampullares*, associated with each semicircular canal, is evident. At this time a cleft also forms in the vestibule, partitioning the utricular macula from the saccular macula (Streeter, 1906). The cochlea elongates as a tubular structure from the ventral pouch and with continued growth, begins to rotate between 8 and 9 WG (Kim et al., 2011; Yasuda et al., 2007). By 10 WG, the cochlea has formed a full 2.5 turn coil (see Fig. 1 Streeter, 1906). Between 9 and 18 WG there is a three-fold increase in labyrinth length, after which there are no further length changes (Jeffery and Spoor, 2004). Between 17 and 19 WG, other indices of labyrinth size, such as canal and cochlea radius, have ceased to change and are comparable to adult form and size. In the following two weeks, bony ossification of the surrounding cartilage encapsulates the entire membranous labyrinth, forming the bony labyrinth (Jeffery and Spoor, 2004).

3. Development of vestibular organs

The general description above provides an outline of membranous labyrinth maturation from ~4 to 20 WG of human embryonic and fetal development. Since the vestibular system is ontogenetically and phylogenetically older than the auditory system, we will

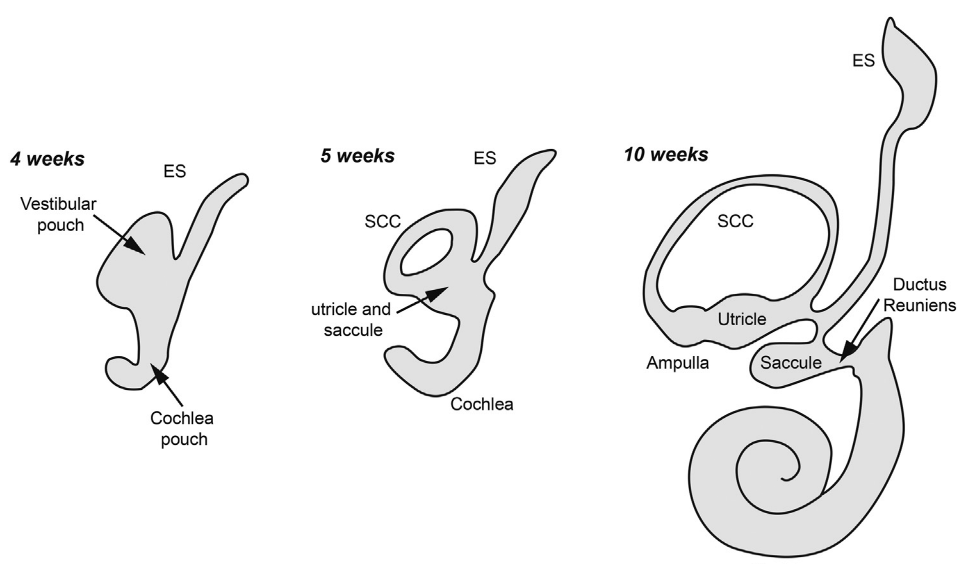

Fig. 1. Schematic representation of the development of the human inner ear from 4WG to 10WG. Initially, the inner ear develops from an otocyst at 4WG, with a dorsal pouch that will become the vestibular organs, and a protrusion that will form the endolymphatic sac. A ventral pouch becomes the cochlea. By 5WG, the semicircular canals are beginning to form and the medial walls undergo resorption. A constriction, the ductus reuniens develops between the saccule and cochlea. By 10WG, a partition forms between the utricle and saccule. The semicircular canals are complete, although they have not reached mature size. The ductus reuniens separates the vestibular organs from the cochlea that has reached a full-2.5 turns by 10WG. Length of inner ear: 9 mm at 4WG, 12 mm at 5WG, and 30 mm at 10WG *Modified from* Streeter (1906).