Chapter 1

General introduction

Background

Menière’s disease is a disease of the inner ear characterized by a classical triad of vertigo attacks, tinnitus and a fluctuating hearing loss. Since the first description by Prosper Menière in 1861 (1), this disease has been the object of many clinical and experimental studies.

In humans, the hearing loss has been researched extensively. This is due to the fact that there are many standardized hearing tests, which can be measured repeatedly. Most hearing tests are non–invasive, unobtrusive and good quantifiable. Tinnitus, on the other hand, is extremely difficult to research since it is a subjective symptom and the nature and intensity cannot be measured objectively.

The vertigo attacks are a result of a dysfunction of the vestibular part of the inner ear. The vestibular system can be investigated with various methods, but for obvious reasons the vertigo attacks are difficult to research in the acute stage. In more stable situations, some aspects of the vestibular system can be measured (2). The most widespread methods of investigation are the calorigram and rotational tests in combination with the electronystagmo-gram. These tests are labour–intensive and the calorigram is uncomfortable especially in Menière’s patients. They usually also rely on the vestibulo–ocular reflex, which requires an intact ocular system. The calorigram can measure a singular vestibular organ, while the rotational test measures the combination of both vestibular organs. A disadvantage is that both test outcomes vary greatly and are not easily quantified and standardized.

In experimental animal research on Menière’s disease, the main focus has also been on the cochlea (3). One of the main reasons is that, as in humans, the cochlear stimulus is easily given in the form of acoustic clicks or tones. Acquisition of the response by measuring of the compound action potential on the round window is relatively easy as well. The main problem in testing the vestibular function is the stimulus. There are two functional parts of the vestibular organ, the otolith organs and the semicircular canals. They are developed to react to different stimuli, respectively to linear and angular acceleration, but they are not totally independent of each other. Technically
the administration of quantifiable, reproducible acceleration stimuli is difficult and laborious. The response acquisition is also more complex since the responses of all vestibular organs converge in the vestibular nerves, which are deeply immersed in the temporal bone.

Morphologically, the ultrastructure of the vestibular organs has been described as early as 1956⁴⁻⁵. Unfortunately, the vestibular organs are also more difficult to locate and isolate than the cochlea. Only the macula of the saccule is fixated to the bone, while all other vestibular organs are only bound to the membranous labyrinth, which makes the preparation more difficult. The macula of the otolith organs are covered by the otholithic membranes which can be removed easily, but in the ampullae’s the sensory hair cell bundles of the crista ampullares are long and deeply embedded in the cupula which makes the surface of the crista extremely difficult to visualize in scanning electron microscopy. Since there are five vestibular organs, a choice has to be made which organs to prepare for scanning electron microscopic research, since it is virtually impossible to acquire high quality images of all vestibular organs from the same specimen.

The combination of both morphological and functional evaluation of the vestibular system has been performed rarely in experimental animal research, mainly because of the above mentioned reasons.

This thesis investigates several methods to investigate the vestibular system under physiological and pathological conditions in animal experiments. It is mainly focused on the otolith organs, especially the utricle. The guinea pig was chosen as experimental animal, since this animal has a vestibular organ similar to the human and is used most frequently in experimental animal research in Menière’s disease.

**Objectives of this study**

In this thesis a morphological and functional evaluation of the vestibular system in the guinea pig is performed under physiological and pathological conditions. To evaluate the function of the vestibular organ, short latency vestibular evoked potentials to linear acceleration stimuli were used. Light-microscopy, as well as transmission, scanning and freeze-fracture electron microscopy was used for morphological evaluation. To quantify the morphological changes the surface area damage ratio was developed. Different methods of inducing vestibular dysfunction were performed to evaluate the possibilities of the developed measurement instruments.
Chapter 2 gives a short overview of the anatomy and function of the vestibular system in the guinea pig and various methods of investigation. Chapter 3 describes the highly detailed morphological characteristics of the sensory epithelium in the normal guinea pig with emphasis on the glycocalyx and stereociliary interconnections by means of transmission, scanning and freeze–fracture scanning electron microscopy. Chapter 4 describes the functional evaluation of the vestibular system by measurements of short–latency evoked potentials to linear, alternating, acceleration stimuli in normal guinea pigs. Chapter 5 describes the effect of systemic gentamicin on the function and morphology on the utricle in the guinea pig. Chapter 6 describes the morphological alterations of the inner ear after the application of systemic gentamicin using scanning and electron microscopy in a higher detail. Chapter 7 describes the histopathology of the vestibular sensory epithelium with the focus on repair and regeneration mechanisms after systemic gentamicin induced injury. Chapter 8 describes the effect of injection of artificial endolymph in the scala media on the vestibular function as measured by short–latency evoked potentials to linear acceleration. Chapter 9 summarizes the results of the studies and conclusions are presented.
**Reference List**

1. Menière P. Mémoire sur des lésions de l’oreille interne donnant lieu à des symptômes de congestion cérébrale apoplectiforme. (A report on lesions of the inner ear giving rise to symptoms of cerebral congestion of the aploplectic type).


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5. Lim, D.J. Threedimensional observation of the inner ear with the scanning electron microscope.