e-Neuroforum 2014 · 5:51–52
DOI 10.1007/s13295-014-0062-8

E. Friauf
Abteilung Tierphysiologie, Fachbereich Biologie, Technische Universität Kaiserslautern, Kaiserslautern

Hearing

The sense of hearing is of crucial importance for orientation and survival in the environment, as well as for communication among conspecifics. Hearing informs, warns, orients, and establishes contacts. The importance of the human auditory system becomes most drastically evident upon failure. The philosopher Immanuel Kant (1724–1804) once noted:"Blindness cuts us off from things, but deafness cuts us off from people." And the American writer Helen Keller (1880–1968), who became deaf-blind at the age of 19 months, arguably because of scarlet fever or meningitis, commented that her loss of hearing was much worse than her loss of vision. Hearing impairment, the complete or partial loss of hearing, is the most frequent sensory deficit in humans. At present, around 14% of the population are affected, with severe economic side effects and social impact.

The normal human hearing range is tremendously broad. Young humans can perceive sound signals within a frequency range from ca. 20 Hz up to ca. 20 kHz, equivalent to ten octaves. The range of an 88-key grand piano extends from subcontra A_0 (27.5 Hz) up to C_8 (4186 Hz), thereby covering 'only' slightly more than seven octaves. In other species (bats, whales), the upper frequency limit can exceed 100 kHz. When it comes to sound pressure, the dynamic range is also enormously broad. In humans, it ranges from ca. 20 µPa at the absolute hearing threshold up to more than 200 Pa at the threshold of pain, thus covering more than six decades. With regard to sound intensity, values differ even trillion-fold (ca. 10^{-12} W/m^2 at hearing threshold, 1 W/m^2 at pain threshold). At the absolute threshold described for humans, the air molecules vibrate with amplitudes of about 1 nm, and the ear drum moves with incredibly small, sub-atomic amplitudes of just 10 pm. The ability to detect frequency differences is also astounding. Trained musicians can distinguish two tones that differ by only 0.1%, i.e., a 1000 Hz tone from a 1001 Hz tone. Values of 1% are common for untrained subjects. Many communication calls represent extremely complex acoustic signals in which the frequency content may change within milliseconds, thus contributing considerably to the information-carrying signal. An individual with normal hearing can interpret such communication calls very well, even in a noisy environment. These hallmarks, combined with a number of other temporal aspects, make the auditory system so remarkable.

The portion of the mammalian inner ear responsible for hearing is the coiled cochlea. The cochlea is the site of mechanoelectrical transduction, which is the conversion of physical stimulus (sound) into electrical impulses in neurons. The transduction process occurs within microseconds, 1000-fold faster than photoelectrical transduction in the retina. In order to localize a sound source in space, mammals and birds can evaluate temporal differences between the two ears of as little as 10 µs. This is remarkable and all the more so since the duration of action potentials, by which the nervous system encodes information, is within the millisecond range. Crucial to hearing are the hair cells, epithelial receptor cells equipped with mechanosensitive hair bundles that convert sound stimuli into electrical responses. Each human cochlea, in which the sensory epithelium is about 3.5 cm long, harbors only around 16,000 of those hair cells, only a quarter of which, namely the inner hair cells, perform the fundamental hearing process. Of particular neurobiological interest is the temporal precision with which information processing and transmission take place in the inner ear and central auditory pathway. Several of the special and (in some cases) extreme adaptations that enable the outstanding performance of the auditory system have been identified, e.g., fast glutamate receptors, a variety of voltage-activated potassium channels, as well as morphological specializations like giant synapses. The great majority of adaptations, however, are so far unknown. In order to analyze the processes that enable ultrafast and temporally precise information processing, the German Research Foundation (*Deutsche Forschungsgemeinschaft*, DFG) launched the Priority Program 1608 (PP1608) entitled"*Ultrafast and temporally precise information processing: normal and dysfunctional hearing*" in 2012 (http://www.pp1608.com). Central to PP1608 is the question of how temporal precision in auditory signaling is achieved by the underlying molecular and cellular substrates and neuronal circuitries. To this end, the consortium is attempting to identify these substrates and analyze their function and dysfunction in both the peripheral and central auditory system. It unites scientists from physiology, anatomy, human and mouse genetics, and computational neuroscience. The 20 participating groups are located in Aachen, Berlin, Göttingen, Hamburg, Hannover, Homburg/Saar, Kaiserslautern, Lausanne, Leipzig, Marburg, Munich, Oldenburg, Ulm, and Würzburg. The focus of the consortium is on the inner ear, the auditory nerve, and the auditory brainstem up to the midbrain. Research is predominantly performed on mammals, including humans. Nevertheless, the fruit fly Drosophila is also used as a well-established model organism. Investigations are performed at various complexity levels, from single gene products via molecular machineries to the levels of cells and neuronal circuits.

In addition to impaired cochlear mechanisms, the decline of temporal precision within the central auditory system appears to play a crucial role in age-related hearing loss (presbyacusis). Therefore, PP1608 may also contribute to finding solutions in the emerging field of 'fighting sensory disabilities.' Promoting young researchers is a central component of the priority program. To this end, not only have annual summer schools been set up, but also several Workshops, which may additionally be open for doctoral students and postdoctoral fellows outside of the consortium. The next workshop entitled"Targeted protein expression and conditional gene deletion in the lower auditory brainstem" will take place from November 30 to December 3, 2014.

This special issue of Neuroforum uses four articles as examples to shed some light on the topics addressed in the PP1608."Hereditary hearing loss in humans: the importance of genetic approaches for clinical medicine and basic science" is the title of the first contribution by Christian Kubisch. Approximately 1100 babies are born annually with hearing disorders in Germany (ca. 1 in 600), and around two thirds of these disorders are thought to be of genetic origin. Many forms of hereditary hearing disorders have been elucidated over the past 20 years using genetic approaches. The identification of the relevant deafness genes and characterization of the gene products have contributed significantly to a better understanding of the physiology of hearing, both at the molecular and the cellular level. The second review, authored by Hans Gerd Nothwang, Jutta Engel, Marlies Knipper, and Eckhard Friauf, is entitled"L-type calcium channels in the auditory system." This review article summarizes our current knowledge of the role of two voltage-activated calcium channels, $Ca_v1.3$ and $Ca_v1.2$, in the cochlea and during maturation of the auditory pathway. $Ca_v1.3$ is essential for the transmitter release from the inner hair cells onto the axons of the auditory nerve, yet it is also present within the auditory centers of the brain. The loss of $Ca_v1.3$ results in deafness. The effects of mutations in the genes encoding for the two types of calcium channels, be they systemic or conditional (region-specific), are discussed in detail. The third contribution, by Felix Felmy and Thomas Künzel and entitled"Giant synapses in the central auditory system," deals with morphological specializations in the synaptic contacts between neurons, which occur in four relay stations in the auditory brainstem of mammals and birds. Giant synapses of this kind, named 'endbulbs of Held' and 'calyces of Held' after their discoverer Hans Held (1866-1942), make contacts with the cell bodies of downstream neurons which comprise numerous active zones required for transmitter release. By so doing, they guarantee the precise transmission of action potentials. The review also tackles some biophysical properties which efficiently contribute to the reduction of temporal imprecision in eliciting action potentials."Drosophila hearing: mechanisms and genes" by Maike Kittelmann and Martin Göpfert is the fourth and final article. Over the course of insect evolution, hearing has probably been independently invented 20 times. Within the various insect groups, tympanal organs for hearing are located on the proboscis (hawk moths), the thorax (praying mantis, beetles), the forewings (green lacewings, butterflies), the forelegs (crickets, katydids), and the abdomen (cicadas, geometer moths). The fruit fly Drosophila perceives acoustic communication signals with two antennal ears on its head. These acoustic organs are composed of around 250 mechanosensitive sensory cells which detect particle velocity. Due to the evolutionary relationship to hair cells of vertebrates and the sophisticated genetics, Drosophila is a superb model organism for exploring the molecular basis of hearing.

In conclusion, the aim of PP1608 is to obtain comprehensive insights into the underlying mechanisms of ultrafast auditory processing with high precision. This includes the mechanisms whose dysfunction leads to temporal auditory processing disorders—be it in the cochlea, the auditory nerve, or the brain. The consortium aims to achieve a fundamentally improved understanding of the causes of hearing disorders and to find tools for better therapeutic treatment. A better understanding of the (patho)-physiology of auditory information processing is indispensable if we want to develop effective treatment strategies for hearing disorders. I would like to thank the German Research Foundation for financial and ideational support. Likewise, thanks are due to all members of the PP1608 for their productive research activities; I wish them continued success in the future.

Corresponding address

Prof. E. Friauf
Abteilung Tierphysiologie, Fachbereich Biologie,
Technische Universität Kaiserslautern
Postfach 3049
67653 Kaiserslautern
Germany
eckhard.friauf@biologie.uni-kl.de