Abstract

Age-related hearing loss, presbyacusis, is becoming one of the most common health disabilities in elderly people. Despite intensive research, age-related changes are still poorly understood and, given the continuous aging of the population, it is desirable to improve our knowledge of the mechanisms of presbyacusis. Consequently we decided to study age-related changes that appear in the structure and function of the central auditory system in the brain of experimental animals.

In the first experiment we tested the hypothesis that during aging there is substantial decline of GABA-mediated inhibition in the central auditory system of the rat. We evaluated levels of both isoforms of glutamatedecarboxylase (GAD65, GAD67), a key enzyme in GABA synthesis. Western blot analysis revealed an overall decrease in levels of both isoforms in the inferior colliculus as well as the auditory cortex in aged rats. The same pattern was found when we used immunohistochemistry analysis; there was a decrease in the number of GAD65 and GAD67-ir neuronal bodies and a decrease in the density of the labeling. The results were similar for both GAD isoforms and both studied strains – the normally aging Long Evans strain (LE) and the Fischer 344 (F344) strain known for accelerated aging.

In the next experiment we evaluated age-related changes in two calcium binding proteins, calbindin (CB) and calretinin (CR), present in the auditory system predominantly in GABAergic neurons. Their neuroprotective function has been extensively studied, however, their role during ageing is yet to be fully uncovered. Our results showed a significant decrease in CB and CR protein levels and a decrease in the number and volume of CB-ir and CR-ir neurons during aging in the upper parts of the auditory pathway, both in LE and F344 rats. Like in the study with GAD, the changes displayed a uniform pattern. First, the decline observed was found in both the subcortical and cortical levels of the auditory pathway, but also in the visual cortex. Second, both strains displayed comparable age-related changes. Third, the western blot protein analysis was in line with the immunohistochemistry cell analysis. In addition, CB declined more significantly than CR.

The third experiment focused on behavioural observations of well known age-related decreases in responsiveness to auditory stimuli. We evaluated both the aforementioned rat strains at three different stages of their life using the acoustic startle reflex test (ASR) and prepulse inhibition (PPI). Our results confirmed different age-related changes of the startle responses in LE and F344 strains. F344 rats showed lower ASR amplitudes compared to LE rats across all types of acoustic stimuli presented. ASR amplitudes decreased faster at each age in F344 than in LE rats and PPI was manifested to a lesser extent in F344 than LE rats.

However, relative decline remained the same for both strains, reaching significancy only in aged animals.

The same methodology was used in the fourth study in an attempt to evaluate changes in the responsiveness to acoustic stimuli of adult rats exposed to noise stimuli during early development. Such changes could reflect altered representations of various parameters of sound in the central auditory system. Audiogram data showed that, in adolescence, auditory thresholds of exposed rats were not different from those of unexposed animals. However, in exposed rats ASR amplitudes were smaller at higher intensities of white noise and higher frequencies of tonal stimuli (≥ 4 kHz). Moreover, PPI was expressed more at lower prepulse intensities (20–30 dB SPL) in exposed rats. In summary the results of our studies reveal age-related changes in the central auditory system of rats and gives suggestions as to what type of behavioral methods can serve in the detection of these changes.

Keywords: audition, aging, Fischer 344, Long Evans, GAD, GABA, calbindin, calretinin, ASR, PPI, early noise exposure