



**Karolinska  
Institutet**

**The Department of Neuroscience**

# **The Effect of Caloric Restriction on Age-related Hearing Loss and the Impact of Repeated Sound Exposures**

**AKADEMISK AVHANDLING**

som för avläggande av medicine licentiatexamen vid Karolinska  
Institutet offentligen försvaras i Hillarpsalen, Retzius väg 8,  
Karolinska Institutet

**Fredagen den 8 november, 2013, kl 09.00**

av

**Paula Mannström**

Leg. Biomedicinsk analytiker

*Huvudhandledare:*

Professor Mats Ulfendahl  
Karolinska Institutet  
Institutionen för neurovetenskap

*Bihandledare:*

Professor Brun Ulfhake  
Karolinska Institutet  
Institutionen för neurovetenskap

Med. Dr. Mette Kirkegaard  
Aarhus Universitet, Danmark  
Institut for molekylærbiologi og genetik

*Betygsnämnd:*

Docent Esma Idrizbegovic  
Karolinska Institutet  
Institutionen för klinisk vetenskap,  
intervention och teknik

Docent Elina Mäki-Torkko  
Linköpings Universitet  
Institutionen för klinisk och experimentell  
medicin  
Teknisk audiologi

Docent Maria Ankarcrona  
Karolinska Institutet  
Institutionen för neurobiologi, vårdvetenskap

**Stockholm 2013**

## **ABSTRACT**

The auditory system is the sensory system responsible for hearing and crucial for communication between individuals. While aging, many organs of the body start losing their function, including the hearing organ. The severity of age-related hearing loss depends on numerous factors. Intense noise and different ototoxic drugs are well-known damaging external factors, which can be avoided if precaution is taken. However, the moderate sound levels that surround the environment in every-day life are difficult to avoid, and the knowledge about their impact on the age-related hearing loss is limited. There are however ways of delaying age-related hearing loss. Caloric restriction is a proven method of prolonging life expectancy and to delay the age-related diseases, such as the age-related hearing loss.

The structural effects of caloric restriction on inner ear tissues of aging Sprague-Dawley rats were investigated. The age-related degenerative shrinkage of the metabolic important structure stria vascularis was delayed by a life-long, 70% dietary restriction. Moreover, the restricted feeding regime preserved hearing function at median life-expectancy age, compared to age-matched littermates.

The impact of repeated moderate sound exposures on hearing was investigated in the female Sprague-Dawley rat. The aim was to develop an animal model, to mimic human life-time noise exposure. Different exposure intensities were compared to determine an appropriate level, which could be repeated several times without causing a permanent hearing loss. At the intensity level of 104 dB SPL, the exposures were repeated six times, six weeks apart, with hearing thresholds returning to normal levels. Interestingly, exposures at this level made the animals more resistant to later overstimulation with intense noise.

The elderly population increases every year in the developed countries. Thus, there is significant need, not only to investigate the causes of age-related hearing loss, but also to explore ways to delay or prevent the disability. The life-time noise exposure model will thus be a realistic tool for this purpose. Caloric restriction and other possible intervention therapies can further be investigated, and its impact on age-related hearing loss can be studied.