NENS Exchange Grant - Final Report

PhD student: Meike Marie Rogalla

Time of training stay: 2nd - 30th of June

Home Institution: University of Oldenburg, Graduate School 'Oltech': PhD Program Neurosensory Science and Systems, Neurobiology of Hearing Group, Department of Neuroscience, Cluster of Excellence 'Hearing4all'

PhD project supervisor: K. Jannis Hildebrandt

Host Institution: University of Salamanca, Auditory Neurophysiology Lab, Instituto de Neurociencias Castilla Y León (INCYL)

Host Supervisor: Manuel Sánchez Malmierca

Project Title: Evaluation of stimulus-specific-adaptation in the inferior colliculus using a frequency oddball paradigm

In June 2019, I had the honor to spend a methodical training in the Laboratory of Manuel Sánchez Malmierca at the university of Salamanca. During the four weeks in Spain, I focused on the technique of single unit recordings in the rodent auditory system using paradigms for stimulus-specific adaptation (SSA). The purpose of this training was the learning the named techniques to apply them in my home lab on my PhD project.

Over 5 % of the world population suffer from disabling hearing impairment. Those patients that cannot benefit from a hearing aid due to deafness, the restauration of auditory function can only be achieved by electrical sensory implants, like cochlear implants (CI) or auditory brainstem implants (ABI). But the state-of-the-art approaches, especially those stimulating the central nervous system, suffer from limited spectral resolution due to widespread of current or channel crosstalk. My PhD projects aims to develop an auditory midbrain implant that uses optogenetic stimulation at two different points within the tonotopy of the inferior colliculus in the to generate a frequency shift in perception. In my home Institution, my work covers the construction of implants, craniotomies and the behavioral evaluation of those implants in the awake behaving mouse. To further evaluate the stimulation pattern evoked by the optogenetic stimulation and the properties of the implantation site, single unit recordings of the IC are necessary. I chose the lab of Manuel Sánchez Malmierca not only to get a methodical training for the single-unit recordings but also to benefit from the expertise regarding the anatomy of the auditory midbrain and response properties of auditory neurons in the central nervous

system. I wanted to benefit not only from the technical expertise in the lab, but also from the extensive knowledge on SSA. For me particularly, it would be of higher interest to evaluate a possible SSA generated by optogenetic stimulation of the inferior colliculus of the mouse (oSSA). To get a further understanding about the percept which is generated by my implants the comparison of acoustic and optogenetic stimulation in behavior and physiology is required.

During the first weeks of my stay I gained further insights into the lab routine and into the construction of electrodes for the single-unit recordings. I constructed my own electrodes that also used later in my own experiments. Additionally, I participated in several surgeries and recordings. During that time, I developed an Idea about the required anesthetics, how to isolate single units during recordings and how to construct paradigms for the evaluation of SSA ('oddball' paradigms). I also developed my own ideas of the specific paradigms I would be interested in. SSA can be defined as the diminished firing of a neuron towards repetitive stimuli while still responding to new ones (Fig 1.) The oddball paradigm for the evaluation of SSA consists of pure tones from two different frequencies. One frequency is played repetitively, named the standard, the other one is played rarely, which is called the deviant (Fig.2). During my own recordings I varied the deviance probability and observed how the strength of the SSA is influenced by the probability of deviant occurrence.

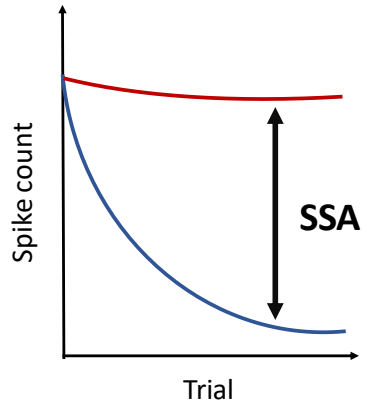


Fig.1 Stimulus Specific Adaptation. SSA neurons show a reduced firing when a specific stimulus is repeated (blue) but do not show adaptation in response to new stimuli (red).

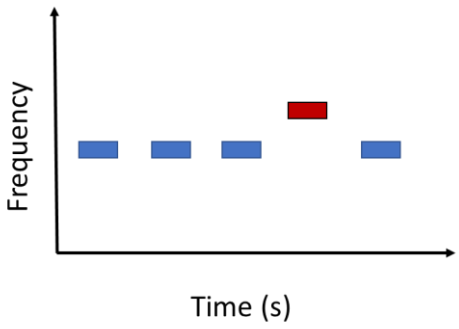


Fig.2 The Oddball Sequence. During an oddball paradigm, two different stimuli are presented: a repetitive one of a given frequency (standard, blue) and one of a different frequency that is rare (deviant, red).

With the excellent assistance and guidance of Ana Belén Lao Rodríguez, I performed single-unit recordings in adult female Long-Evans rats. I performed the surgery and isolated units in the inferior colliculus. After obtaining the frequency-level tuning of the neuron (frequency response area, FRA, see Fig. 3) I presented different versions of the oddball sequence with different deviant probabilities (10%, 30%, 50%).

For the analysis of the data and the determination of the common SSA index (CSI), I had very helpful support from David Pérez González, who introduced the computations and gave an introduction into the necessary scripts and the data structure. What could be observed from my

acquired data is the decrease of the CSI with increasing deviant probability how it was expected (Fig 4).

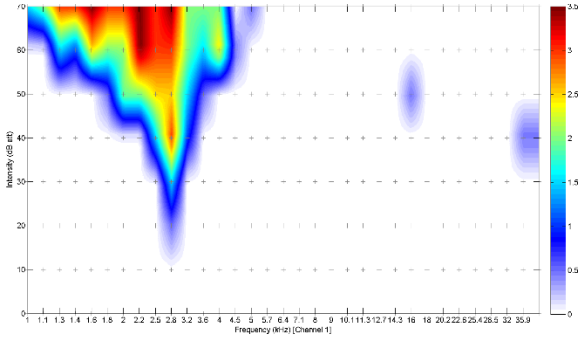


Fig.3 Example of a Frequency Response Area of an Auditory neuron from the Inferior Colliculus.

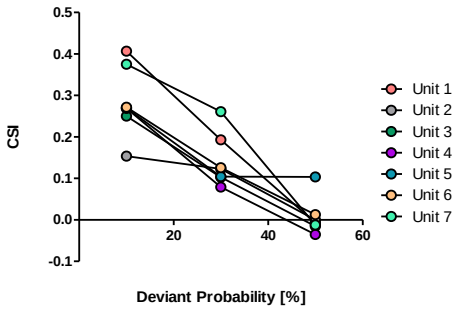


Fig.4 Common SSA Index (CSI) of the same neurons for different Deviant Probabilities.

Additionally, I had the opportunity to assist during single unit recordings in the mouse inferior colliculus together with Lorena Casado Román who was an excellent and patient teacher with a high level of knowledge.

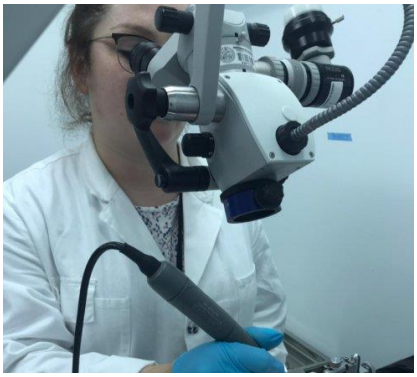
Furthermore, I had the great opportunity to participate in parts of the 'Neurobiology of Hearing' course from the University of Connecticut (UCONN) and the University of Salamanca (USAL) for graduate students in neuroscience and hearing research and upper level undergraduate students. This course provides an introduction to the auditory system and current research in auditory neuroscience with talks of leading scientist of the field, like Douglas Oliver (UCONN), Xiaoqin Wang (Hopkins) or María Dolores López García (USAL).

The CANE Lab (Cognitive and Auditory Neuroscience) in June 2019, University of Salamanca (from right to left): David Pérez González, Yuvraj Joshi, Guillermo Varela Carbajal, Christian Aedo Sánchez, Ana Belén Lao Rodríguez, Blanca Cervantes Sánchez, Lorena Casado Román, Flora Antunes, María Torres Valle, Laura Zerballos Fernández, Meike Marie Rogalla and Manuel Sánchez Malmierca. Missing member: Camilo J. Morado Díaz

For further information see https://health.uconn.edu/meds5377/.

I would like to thank Manuel Sánchez Malmierca for the opportunity to get a methodological training in his lab. I thank him for the excellent support, his trust and the nice chats we had about the future cooperation we are currently planning. I thank all the lab members for their excellent supervision, training and teaching, for being patient and always willing to help. Especially I'd like to thank Lorena Casado Román, Ana Belén Lao Rodríguez, David Pérez González and Guillermo Varela Carbajal, who have been the best supervisors I could ask for during my training stay.

Additionally, I'd like to thank the NENS for giving me this great opportunity for conducting such a fruitful training stay abroad. This experience not only helped me to develop new skills and learning new methods, it also helped me to develop personally and it gave me new insights into auditory neuroscience from a whole new perspective.



Upper left: Conducting a craniotomy. Upper right: view on the cathedral of Salamanca from the other side of the river. Third picture: me in front of the INCYL.