Auditory Alpha Entrainment for Tinnitus Relief - STSM Report

1 Purpose of mission

The primary goal of the STSM was to test different amplitude modulated (AM) sounds for EEG (electroencephalography) alpha entrainment aiming at tinnitus relief in different subgroups of tinnitus sufferers. For this purpose, different carrier sounds (i.e., pure tones at different frequencies, noise types and music) were sinusoidally amplitude modulated with 10 Hz or individual alpha frequency and presented continuously to the participants. The outcome measures were primarily individual psychometric measures, testing efficacy in tinnitus suppression and perceptual valence of the sounds, and secondarily pilot EEG recordings, testing possible neural underpinnings of the effects. Furthermore different study and intervention designs were sketched and evaluated to further systematically test the feasibility of the approach in future two-center collaboration. The main output of this mission was to establish a lab setting with audio equipment for stimulation and parallel EEG recording. Beyond that, a joint supervision of a doctoral student by the host and the guest also emerges out of these efforts. Noteworthy, in contrast to the last STSM of the guest, the focus was *not* set on data collection and/or finished analysis.

2 Description of the work carried out during a mission

In preparation and in parallel to actual testing on participants, a computer was set up with audio tools, Matlab and a respective pipeline to generate individual stimuli while integrating them into the experimental routine (e.g., presentation software). Furthermore, a doctoral student was introduced to the theory and handling of the stimuli, handling and management of audiometry and auditory stimulation, as well as EEG recording equipment. Respective guidelines and working instructions were created for the ongoing standardization purposes.

8 patients indicating tonal tinnitus (2 females) were recruited out of the pool of the Interdisciplinary Tinnitus Clinic in Regensburg. The focus was there set on a specific subgroup, namely patients with a permanent single frequency tonal tinnitus. In an initial session, participants were undergoing tinnitus matching with a custom-tailored MAX patch to primarily establish the pitch frequency and laterality of the tonal tinnitus (see Table 1). Following that, the participants were presented 6 different auditory stimuli, produced with custom Matlab scripts, in a randomized sequence for 3 minutes each approx. 50 dB above sen-

sation level. 4 out of the 6 stimuli were amplitude modulated whereas 2 sounds served as control stimuli (pink noise and 250 Hz pure tone (sine)). The AM sounds were all sinusoidally modulated (100% modulation depth) with 10 Hz applied on different carriers: 1) 108 Hz pure tone 2) pure tone at the tinnitus frequency as established by the matching 3) 250 Hz saw waveform 4) a pop song with a modulated frequency band approximately an octave around the tinnitus frequency. At baseline and after each block the participants filled in a custom questionnaire which consisted of two visual analog scales (VAS) for tinnitus loudness and time aware of tinnitus in percent. Furthermore a health change item was used to assess general change in tinnitus conditions (-3 indication much worse and +3 much better). At the end of these 6 stimuli series, participants were able to choose their favorite most effective stimulus to listen to for an additional 6 minutes after a break.

After evaluating the data and condensing the experience of the behavioral phase to a more concrete design suitable for EEG recording, a single male participant was invited to participate in two further sessions with concurrent EEG recordings. In contrast to the behavioral session, only 4 stimuli were presented but for 6 minutes each (Carriers: 108 Hz 1) sine and 2) saw, 3) sine at tinnitus frequency. AM: individual alpha frequency (8.7 Hz) in first and 10 Hz in the second EEG session. 4) Control: Continuous white noise in first session, continuous pure tone at tinnitus frequency in second session). The EEG recording continued after the 6 minute stimulation and the participant was asked to press a button when his tinnitus reached baseline loudness again. The time between end of stimulation and button press equals the measure for the duration of tinnitus suppression.

3 Description of the main results obtained

As introduced, the primary goal of this partly exploratory and partly case study was to establish proper experimental designs for future data collection. Nevertheless the most important data is presented and discussed, namely the outcome of the initial behavioral session with the 8 participants (Table 1) and the time of tinnitus suppression of the different stimuli in the last single participant session (in text below).

The matching procedure showed that 2 participants invited did not conclusively exhibit tonal tinnitus or the center frequency of any other type could not be determined (see Table 1). When looking at the change items, a superiority of the AM sounds compared to the control sounds seems plausible. Furthermore, the 6 minute stimulation with the preferred stimulus had overall larger effects. The x in the last column are indicative of a subjective efficacy (self-report) of the AM approach with large X indicating a large effect and spontaneously expressed interest in continued use. Looking at efficacy of the different carrier sounds, the tinnitus frequency shows best results (Table 1, second last and last column).

In the single participant session with the key press paradigm, the control stimulus was changed to a pure tone in tinnitus frequency suppressing tinnitus completely for 1:00 (in contrast to a 7 second suppression with a white noise control stimulus in the second last session). The low frequency AM stimuli showed less suppression duration (0:45 for sine, 0:48 for saw) whereas the carrier

at the tinnitus frequency was able to suppress the tinnitus for 2:45 and after immediate subsequent stimulation the suppression was prolonged to 3:05.

Interpreting this preliminary data alongside some preliminary data gathered before the STSM, it remains unclear 1) if entrainment and subsequent increase in alpha EEG band power suppresses tinnitus (especially in the case of low frequency carriers) or 2) if it is a mere effect of (residual) inhibition or 3) a mixture of both. As the data, while still having only limited interpretational value with the current low number of cases, both on a behavioral (see Table 1) and neurophysiological level (see Figure 1) is indicative of either or both interpretations. The effects have to be further disentangled as the primary aim of the approach still is the normalization of the alpha band via the auditory modality and possible, related subsequent suppression of the tinnitus percept and/or suffering. The EEG data show an increase in the stimulated alpha frequency around 10 Hz which persists for minutes after stimulation (Figure 1. Preliminary data is shown here as single subject data of the STSM was deemed inferior for the general illustrative purpose here). Furthermore, the single participant behavioral data shows that the unmodulated carrier sound at the tinnitus frequency (being the optimal control stimulus) is only capable of suppressing the tinnitus sound for 1:00 whereas the AM version suppresses it for up to 3:05, which is in line with the overall impression that AM sounds are favorable both in efficacy and valence.

4 Future collaboration with the host institution

As indicated above, the establishment of a collaboration was one of the main goals of the mission with efforts coordinated and procedures standardized. Serendipitously, identical EEG systems are used in the centers of Regensburg and Zurich enabling the gathering of highly comparable common data across centres. The guest site will start measurements in December while the host site plans to continue the project starting February. Furthermore, mobile long-term stimulation with respective longitudinal experimental procedures are also planned.

5 Foreseen publications/articles resulting from a mission

It is planned to publish an article after the next iteration of the project with a fitting sample size.

6 Confirmation by the host institution

Attached to the email with this report.

7 Other comments

We would like to thank for the opportunity to undertake this mission and look forward to the continuation of the project.

		measure of subjective change							efficacy
		control		AM					
		pink noise	250 Hz sine	250 Hz saw	music	tinnitus frq	108 Hz sine	**favorite (6 min)**	
ID	tinnitus characteristics	A	B	C	D	E	F	**Z**	
1	2 pure tones (4.3 and 6.8 kHz), left	2	0	0	1	1	1	**1**	
2	noise, bilateral	0	0	0	0	0	0	**0**	
3	pure tone, 4.5 kHz, right	0	0	0	0	0	0	**0**	
4	pure tone, 4 kHz, left	0	0	0	0	0	-1	**1**	X
5	buzzing sound, left	1	0	0	0	1	0	**1**	x
6	8 kHz, left>right	-1	0	0	1	1	0	**1**	x
7	pure tone (incl. noise), 4.5 kHz, bilateral	-1	-1	-1	0	-1	0	**/**	
8	pure tone, 4.6 kHz, left	0	0	2	1	2	1	**3**	X

Table 1: Stimulation Results: Behavioral Data. *Change in tinnitus after stimulation on a scale from -3 "much worse" to 3 "much better". Chosen favorite stimulus is color-coded to the stimulus types in the second last column. 4 out of 8 participants had short-term suppression of tinnitus with AM sounds (3 with carrier in tinnitus frequency and 1 with 108 Hz carrier) and are indicated with an x. Participant 7 was a dropout due to averse reactions to the stimuli and participant 1 favored the control pink noise masking sound. Participant 2 did not have tonal but intermittent noise-like tinnitus whereas participant 3, while meeting the criteria of tonal tinnitus, did not respond to the AM stimuli as the only participant of the selected subgroup. In conclusion and in line with similar results of preliminary data at the home institute (n=4), the approach seems to be able to suppress tinnitus perception for a short time after stimulation.*

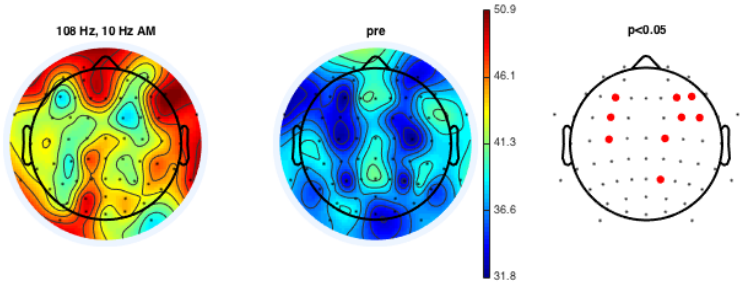

Figure 1: Stimulation Results: Preliminary EEG data of 108 Hz AM stimulation. *1 minute after 5 minutes of diotic stimulation at 70 dB participants (n=3) showed increased 10 Hz band activity over fronto-temporal electrodes ($p < 0.05$). Tinnitus was subjectively suppressed in 2 out of 3 cases. The results could be, carefully interpreted, related to the behavioral results of Table 1 with enhanced alpha activity playing a role in tinnitus suppression.*