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# Implementation and Long-Term Evaluation of a Hearing Aid Supported Tinnitus Treatment Using Notched Environmental Sounds

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**ABSTRACT** Recent work has shown that sharp spectral edges in acoustic stimuli might have advantageous effects in the treatment of tonal tinnitus. In the course of this paper, we evaluate the long-term effects of spectrally notched hearing aids on the subjective tinnitus distress. By merging recent experimental work with a computational tinnitus model, we modified the commercially available behind-the-ear hearing aids so that a frequency band of 0.5 octaves, centered on the patient's individual tinnitus frequency, was blocked out. Those hearing aids employ a steep notch filter that filters environmental sounds to suppress the tinnitus-related changes in neural firing by lateral inhibition. The computational model reveals a renormalization of pathologically increased neural response reliability and synchrony in response to spectrally modified input. The target group, fitted with spectrally notched hearing aids, was matched with a comparable control group, fitted with standard hearing aids of the same type but without a notch filter. We analyze the subjective self-assessment by tinnitus questionnaires, and we monitor the objective distress correlates in auditory evoked response phase data. Both, subjective and objective results show a noticeable trend of a larger therapeutic benefit for notched hearing correction.

**INDEX TERMS** Tinnitus, notched acoustic stimulation, hearing aids, translational engineering, clinical trial.

## I. INTRODUCTION

The up-regulation of sensory gain and/or the degradation of inhibitory projections across hierarchical processing stages of the auditory pathway due to peripheral deprived frequency bands is likely to give rise to the auditory phantom percepts in tinnitus [1]. A confined damage in the peripheral auditory pathway can result in a bandlimited neural hyperactivity defined by the tonotopic organization of the auditory pathway. This hyperactivity progressively centralizes with tinnitus duration [2], [3]. Neural hyperactivity in a dysfunctional band of the peripheral auditory pathway exhibits two distinct features:

1) The bandlimited neural activity has sharp spectral edges and due to lateral inhibitory projections it 2) tends to display an increased spike timing precision. We outline this self-ordering mechanism of neural activity in section III.A. For further details we refer to [4] and [5]. This feature can be associated with competitive advantage in stimulus selection [6], [7]. Notably the allocation of attention resources is associated with a saliency coding in the neural response reliability. Neural hyperactivity alone might not be sufficient to generate a persistent tinnitus, but in conjunction with unbalanced lateral inhibition components, it might be able to evoke a salient percept, as a coherent input can effectively inhibit less coherent competing inputs via GABA mediated inhibitory interneurons [6]. Cortical top-down projections to thalamic areas, i.e., attentional feedback loops, and even to hierarchically lower stages of sensory processing,

might promote synchrony in excess of the bottom-up self-organization dynamics by a further increase of neural response reliability and cross fiber synchrony [2], [8], [9]. The pathogenic chronification of auditory phantom perceptions might be coupled to plastic processes in areas responsible for the allocation of attention resources and may thus originate in brain areas only indirectly involved in auditory processing, such as limbic structures [10]. This extrasensory influence was already demonstrated by concomitant plastic reorganization in the auditory- and the limbic system in fMRI- and animal tinnitus-model studies [11].

To counteract the neural response orchestration, we utilize artificially created spectral edges by bandstop filtering of auditory input, as previously introduced in the tailor-made notched music training (TMNMT) by Okamoto *et al.* [17]. This approach results in a reduction of tinnitus related cortical activity and tinnitus loudness. Subsequent studies evaluated the TMNMT approach for people with tonal tinnitus positively using subjective and objective criteria [18]. In TMNMT patients listen actively to their favorite music which features a notch ($>0.125$ octaves [19]) centered at their individual tinnitus frequencies. Okamoto *et al.* [17] and Stein [18] propose that the pleasant effect of the music draws attention, which in turn promotes plastic changes, reversing the aforementioned maladaptive plasticity induced by peripheral frequency deprivation.

Hand-in-hand with this plastic reorganization by cortico-limbic activity, goes the suppression of neural hyperactivity in the deprived frequency bands by lateral inhibition. The sharp spectral edges of the stimulus notch can not only reduce pathologic neural hyperactivity but could also normalize the increased spike timing precision associated with competitive advantages in stimulus selection [5], [6], [17], [18].

For the TMNMT approach, the tailor-made notch has to be adjusted to the individual tinnitus frequency and the dysfunctional frequency band in a way that the spectral edges of the notch influence the distinctive tinnitus hyperactivity by lateral information transmission in the ascending pathway. Thus the success of this approach depends most likely on a precise determination of the tinnitus spectra/tinnitus tone in clinical settings. The research group of Pantev, e.g., utilized spectrally shifting notches as placebo stimulation in the control group setting [20].

The processing of emotionally (aversively) tinged stimuli is likely to subconsciously capture attention [12]. Thus, we designed an approach to evaluate attention binding over time (long-term habituation). This methodology is based on our preliminary findings that tinnitus ties down more attention resources with increasing distress. In this context the conscious distress is related to the amount of attention allocated to the 'tinnitus percept' [13], [14]. Along this line of reasoning, we state that high-distress sufferers should exhibit pronounced deficits in their attention capacity and their ability to habituate to aversively tinged stimuli, such as their own tinnitus tone. We define a process of attention-drift, away from a not actively attended target-stimulus over repetitive stimulus presentation as long-term habituation.

In detail we assume that the behavioral response to a stimulus is an orienting reaction followed by a potential (voluntary) sustainment of attention. Every link of this attentional chain of orienting reaction, attention sustainment, habituation and dishabituation bears unique correlates in late evoked responses that can be used to quantify these behavioral responses [14], [15].

In a preliminary study we already presented the feasibility of using habituation correlates as objective indicator for the decompensation degree in high-distress tinnitus patients [16]. We utilize these morphological changes in auditory late evoked responses to quantify the therapeutic outcome of our intervention study (see also section III.D).

> *In this study we aim to transfer the results of neuro-scientific basic research to a ready for use therapeutic product and evaluate the long-term performance of a hearing-aid assisted tinnitus intervention.*

We utilize a tailor-made notch, individually adjusted to the tinnitus-frequency, in a hearing-aids amplification range and compare the results to a control group using unmodified hearing aids of the same type over a duration of six months. As outlined above we expect beneficial effects on the patient's distress level by artificially created sharp spectral edges on subjective and objective scales. Besides a potential remedial effect of notched acoustic stimulation this treatment strategy also considers the reduction of listening effort, and thus stress, by amplification of impaired frequency bands in both patient groups. The effect of stress reduction and improvement in speech comprehension has proven valuable in tinnitus management [21], [22].

## II. STUDY DESIGN AND HUMAN SUBJECT PROTOCOL

### A. NUMBER OF SUBJECTS AND RECRUITMENT

Thirty-four patients (10 females and 24 males) with a mean age of 56.55 years (SD $=$ 10.13 years) and tonal tinnitus entered the study. The subjects were recruited from a hearing rehabilitation and tinnitus center. The study was carried out in accordance with the Declaration of Helsinki (and subsequent revisions) and was approved as scientific study by the local ethics committee (Ärztekammer des Saarlandes / Medical Council of the Saarland 220/14). The clinical trial was registered at the German Clinical Trials Register (DRKS-ID: DRKS00011005).

### B. INCLUSION AND EXCLUSION CRITERIA

All patients had a subjective chronic tinnitus (duration $>$ 6 months, score of the tinnitus questionnaire TQ12 $>$ 10 [23] without temporal interruptions and a mild to moderate hearing loss. We included patients with unilateral and bilateral tinnitus percept. The exclusion criteria included histories of

**TABLE 1. General demographic and clinical characterization of target and control group, with tinnitus frequency matchings at start of the study and after 6-months of therapeutic intervention. Pure Tone Average (PTA) is defined as mean hearing level (HL) of 0.5, 1, 2 and 4 kHz. Most Comfortable Level (MCL) in dB Sound Pressure Level (SPL).**

| | **Group 1: Control** (n = 15) | **Group 2: Test** (n = 19) |
|---|---|---|
| **Gender** | 5 female, 10 male | 5 female, 14 male |
| **Tinnitus frequency t = 0 months** | 5.13 kHz (± 3.24 kHz) | 4.29 kHz (± 1.92 kHz) |
| **Tinnitus frequency t = 6 months** | 4.89 kHz (± 2.96 kHz) | 3.52 kHz (± 2.84 kHz) |
| **Mean age** | 57 years (± 10.24 years) | 56.21years (± 10.31years) |
| **Tinnitus laterality** | 9 left, 6 right | 9 left, 10 right |
| **PTA tinnitus side** | 22.5 dB HL (± 11.2 dB HL) | 25.2 dB HL (± 14.8 dB HL) |
| **MCL tinnitus frequency** | 71.9 dB SPL (± 16.7 dB SPL) | 66.1 dB SPL (± 23.0 dB SPL) |

neurological diseases such as Alzheimer's disease, Meniere syndrome, acoustic neuromas or psycho-pathologies such as attention deficit disorder. Apart from an audiometric examination using a clinical audiometer (tested frequencies: 0.25, 0.5, 0.75, 1, 1.5, 2, 3, 4, 6 and 8 kHz), the dominant frequency of the tinnitus tones was detected for each patient by a standard frequency matching procedure before ($t = 0$ months) and after ($t = 6$ months) the study. Consecutive patients were randomly associated to one of two groups (target vs. control). Please see Table 1 for a demographic and clinical characterization of the patients.

### C. CONFIDENTIALITY AND SAFETY PROTOCOLS

After a detailed explanation of the procedures, all subjects provided written informed consent for the investigation and the subsequent data analysis. Their group assignment was blinded also for data acquisition and analysis.

## III. METHODS AND PROCEDURES

### A. UNDERLYING NEUROPHYSIOLOGICAL MODEL

Lateral inhibitory networks are prevalent along the auditory pathway to orchestrate the self-organization of neural spiking to improve the perceptual contrast by accentuating spectral edges. The Dorsal Cochlear Nucleus (DCN) has a nested network of wide- and narrow-band inhibitory neurons [24]: Type IV neurons, associated with DCN fusiform and/or giant cells, in the following referred to as principal cells (P). Those P neurons respond best to broadband noise and convey auditory information to hierarchically higher processing levels. The vertical inhibitory interneurons are of type II (I2). Contrary to the P cells, those neurons respond strongly to a tonal stimulation at their characteristic frequency, but respond weakly to pure tone stimuli. The wideband inhibitory interneurons (W) receive inputs over a wide frequency band (magnitude of 3 octaves) and inhibit both P and I2 neurons to wideband stimuli. Fig. 1 illustrates the excitatory

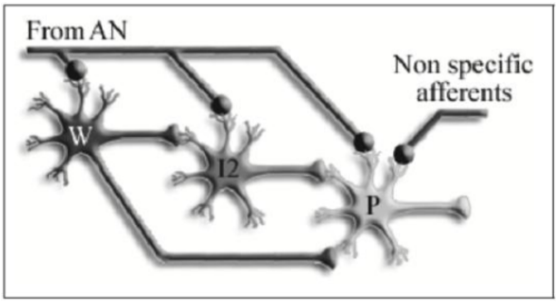


**FIGURE 1. Conceptual circuitry of a band-limited DCN channel. Principal cells (fusiform and giant cells) are labeled with P, I2 denotes inhibitory interneurons of type II. Wideband inhibition is labeled with W. Additionally the cells receive input from the auditory nerve (AN) and non-specific excitatory afferents. Inhibitory synapses have cone–shaped illustrations, excitatory synapses are depicted spherical. The non-specific afferent projections are introduced to maintain spontaneous activity in the principal cells even after cochlear ablation.**

and inhibitory connections underlying the DCN model of auditory processing.

We know from modeling and experimental research [2] that the spontaneous activity of the Auditory Nerve (AN) and subsequent nuclei is elevated in response to a cochlear hearing loss, either by homeostatic mechanisms [3] and/or cation channel imbalance (HCN; KCNQ2/3) [25]. So the tinnitus related hyperactivity can be described by a point process, simulating the tonotopic distribution of normal and elevated spontaneous activity by the time of zero-crossing of nerve action potentials. As a consequence, narrow-band hyperactivity (as in tonal tinnitus) should be emphasized by subsequent lateral inhibition networks, eliciting a phantom percept. This orchestrated neural activity might additionally become accentuated by attention networks due to subjective valance attribution [26].

In a computational model approach we simulated the self-organization of neural spiking activity across the DCN [5] in aforementioned point processes. As hypothesized, due to lateral projection fibers, the pathologically increased spontaneous neural activity gradually synchronizes and becomes more periodic. That way the neural activity along the tonotopy forms a narrow-band region of synchronized and regular spiking, bordered by tonotopic bands of suppressed spiking activity. We experimented with different notch widths in the model input, thus modulating the influence of lateral inhibitory projections and analyze the model by a coefficient of spiking variation, given by $(1/\sqrt{\lambda})$, with $\lambda$ is the mean of the underlying Poisson distribution. The results bolster the use of narrow notches with bandwidths of approximately 0.5 octaves [5].

### B. HEARING AID SETTINGS

Both study groups were fitted with commercially available hearing aids, featuring a linear spaced 48-channel polyphase filterbank with a sampling rate of 24 kHz. The hearing aids of our target group were additionally modified by a biquadratic

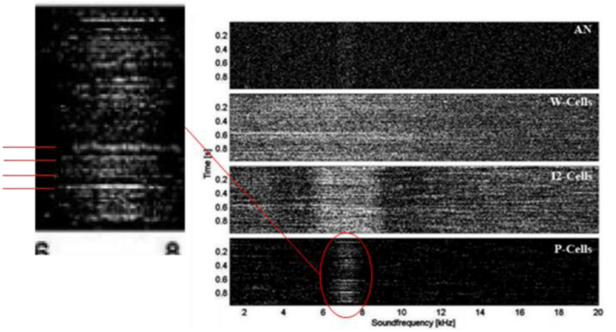


**FIGURE 2.** In-silico approximation of pathologic increased spiking synchrony and elevated response reliability as neural origin of a tinnitus percept. The stacked images depict a simulation of cell-type specific neural activity and correspond to the conceptual circuitry of the DCN, as shown in III.A. White dots represent single action potentials across a virtual tonotopy over time. Red lines emphasize the increase of neuronal orchestration (cross-fiber synchrony and response reliability). The tonotopy of the initial auditory nerve hyperactivity and spontaneous firing is preserved across every level of the DCN model.

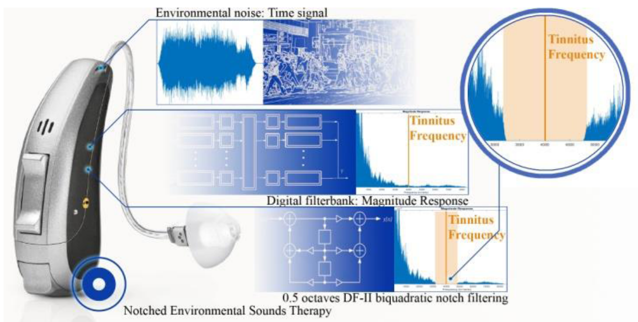


**FIGURE 3.** Descriptive illustration of the signal analysis and notched amplification in the modified hearing aids. The time-domain auditory signal was linearly mapped to the 48 hearing aid channels and additionally notch filtered to emphasize spectral contrasts to counteract the pathologic neural orchestration (see section III.A).

notch filter of 0.5 octaves bandwidth (direct form II 2$^{nd}$ order IIR).

The maximum effective attenuation was 40dB. The notch center frequency was matched to the subject's individual tinnitus frequency (see II.C) at the beginning of the study.

### C. DATA COLLECTION

#### 1) SUBJECTIVE THERAPY ASSESSMENT

For the subjective therapy assessment, the individuals completed the tinnitus questionnaire TQ52 by Goebel and Hiller [27] at the beginning of the study, after 3 and after 6 months, respectively.

#### 2) OBJECTIVE THERAPY ASSESSMENT

Neural long-term habituation (l-hab) correlates in ALR sequences have been used to quantify tinnitus distress [28]–[30]. The underlying hypothesis is that decompensated tinnitus patients suffer from a l-hab deficit, making it impossible to habituate to auditory stimulation, especially in the range of the tinnitus sound. We associate this habituation deficit to aversive attentional binding [12], [30]

#### 3) DATA ACQUISITION AND STIMULI

EEG data was collected with an integrated 24-bit EEG system (g.USBamp, g.Trigbox, g.PAH, g.tec, Austria), using a sampling frequency of 512 Hz. In [30] we found the dominant attention features in N1/P2 morphology at the alpha-theta border (7.68 Hz, see II.D). For recording we thus utilize a bandpass filter with cutoff-frequencies of 1 and 30 Hz as tradeoff between the full signal range and the removal of offset and high-frequency artifacts. The acquisition-processing program and all further post-processing were achieved using scientific computing software (Mathworks Inc., USA). Ag/AgCl electrodes (Schwarzer GmbH, Germany) were attached as follows: ipsilateral to the stimulus at the corresponding mastoid (M1 or M2), common reference at the vertex (Cz), and ground at the upper forehead. The electrode labels are according to the standard 10-20 system. Impedances were maintained below 5 kΩ in all the measurements.

The subjects were instructed to sit comfortably and to minimize movement. During the electrophysiological recording, the subjects watched a silent animal documentary on a screen positioned in front of them. Subsequently, auditory late responses (ALRs) were obtained using pure tone bursts, matched to the individual tinnitus frequency.

Each sine tone had a duration of 40 ms and a rise and fall time of 10 ms. The stimuli were presented using an interstimulus interval of 750 ms via headphones (Sennheiser, HDA200).

Before the measurement started, the stimulus intensity was adjusted to the individual's MCL, see Table 1. A total of 600 trials, i.e., the responses to individual stimuli, free from amplitude artifacts (artifacts were removed by an amplitude threshold ($\pm 50\ \mu$V) detection) were recorded in each condition. The electrophysiological recording was performed at the beginning of the study, after 3 months and after 6 months. The time for one complete experiment was approximately 30 minutes including time for preparation of the subject and electrodes placement.

### D. DATA ANALYSIS

#### 1) SUBJECTIVE DATA

We evaluated the group differences statistically by a one-way ANOVA analysis of the therapy outcome by means of TQ52 improvement. Additionally we characterized the effect size (Cohen's d) based on the group mean differences [31].

#### 2) OBJECTIVE DATA

Long-term habituation reflects the loss of automatic attention to consecutively presented uniform sounds at a comfortable loudness level which results in a decline of the (instantaneous) wavelet phase synchronization stability (WPSS) in ALR sequences [13], [29] over the experiment.

In [13] and [30], the WPSS of a set of M ALR single trials, denoted by $X = \{\chi_m \in L^2(\mathbb{R}) : m = 1, \ldots, M\}$ is defined as:

$$\Gamma_{a,b}(\chi) := \frac{1}{M}\left|\sum_{m=1}^{M} e^{i\arg((\mathcal{W}_\psi x_m)(a,b))}\right|, \qquad (1)$$

where $(W_\psi \chi_m)$ (a,b) is the continuous wavelet transform [32] of an ALR single-trial $\chi_m$ to the complex wavelet $\psi \in L^2(\mathbb{R})$, depending on the scale parameter $a$ and the shift parameter $b$. We utilize a band-filtered signal with a=40 of the 6$^{th}$ derivative of the complex Gaussian wavelet (corresponding to a pseudo frequency of 7.68Hz). For the analysis we decompose our set of ALRs $X$ in N subsets (so $X = X_1 \cup X_2 \cup X_3 \cup \ldots \cup X_N$) of J trials. In consequence we define M = JN. Using this notation, we compute:

$$\mathcal{G}_{a,b} = (\Gamma_{a,b}(\chi_n))_{n=1}^{N}, \qquad (2)$$

which is the WPSS of the individual subsets $X_N$.

Let $\alpha^{\chi}_{a,b,N} + \beta$ ($\alpha$, $\beta \in \mathbb{R}$) be a first order regression, polynomial fitted to (2). We now can quantitatively define the long-term habituation as:

$$h = \mu \min\{0, \alpha_{a,b,N}\}, \qquad (3)$$

where $\mu \in \mathbb{N}$ is a constant scaling factor. In other words $h$ is defined as the decrease of the WPSS over the duration of the experiment and consecutive stimulation, which is correlated to a decline of selective auditory attention towards the stimuli [13].

To further quantify the therapeutic effect in terms of attentional habituation towards tinnitus pitch matched acoustic stimuli. We compute a habituation gain factor l-hab gain $\tau$ by

$$\tau = \max\{0, h_{post} - h_{pre}\}, \qquad (4)$$

where $h_{post}$ and $h_{pre}$ is the long-term habituation $h$ computed before ($h_{pre}$) and after ($h_{post}$) the therapeutic intervention. Consequently, the larger the gain factor $\tau$, the more long-term habituation improves during the time-course of the study.

For this study, we utilize N=24; J =25 (i.e., M=600) and $\mu$ = 1000. The results were averaged for scale parameter a=40 and translation parameter b in [30, 70] × [60, 160] ms.

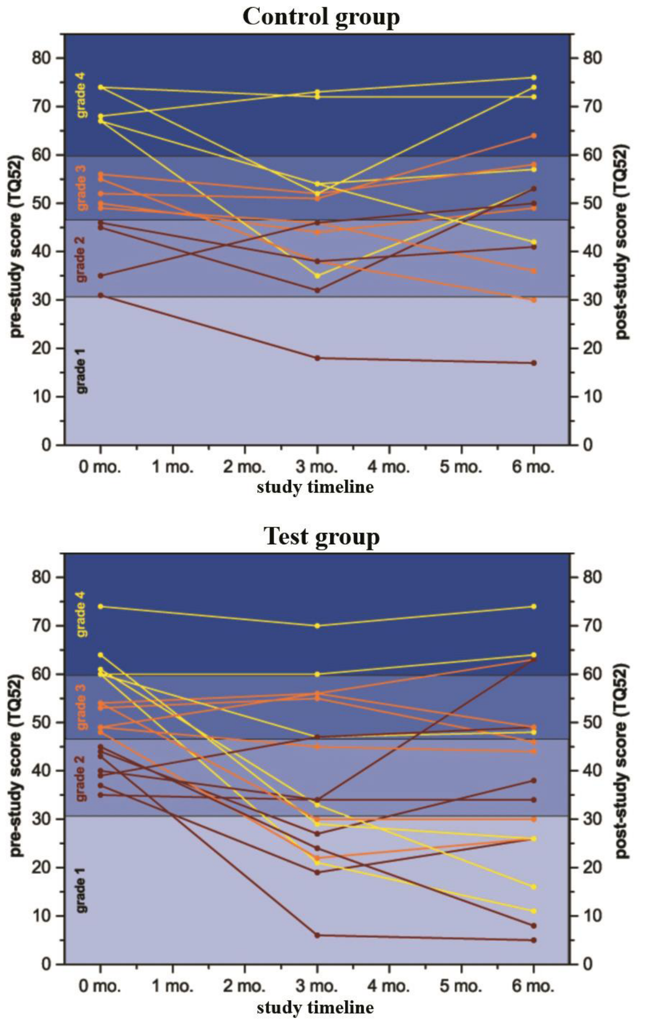


**FIGURE 4. Subjective results in terms of TQ52 score for individual patients from the control group (upper illustration) and from the target group (lower illustration). Plotted is a linear interpolation of TQ52 scores from the beginning of the therapeutic intervention, to 3 months and from 3 to 6 months post therapy start, broken down by individual TQ-distress grades. Please note the prominent improvement of grade IV patients (yellow) up to grade I in our target group.**

## IV. RESULTS AND CLINICAL OUTCOME ANALYSIS

### A. SUBJECTIVE DATA

We found a prominent improvement for the notched environmental sounds approach in Fig. 4 (lower illustration). A considerable number of patients exhibit a remarkable improvement in their TQ52 scores. Responders improve for a maximum of 49 points (min. 1), even from grade IV (decompensated) to grade I (compensated) patients. In total four patients were marked as non-responders, as their TQ-scores increased (up to 23 points). The control group (upper illustration) improved their TQ-scores for up to 23 points, ranging from grade III to the border of grades I and II.

Fig. 5 illustrates the variation in the TQ52 score due to the notched sound treatment for the control group (blue) and test group (orange). We show the mean TQ52 score before the start of the intervention as well as after three and six months respectively. The responders exhibit only a moderate improvement in terms of TQ52 score, with a maximum individual improvement of 24 points (min. 1) from grade III to lower grade II.

Whereas controls improve for a mean of 8.25 score points in the first three months time, the group trend ascends in the period from months three to six, for a net mean improvement of 3.875 score points. The target group exhibits a stronger improvement in three months time and is able to maintain this significantly reduced distress level during the entire duration of the study for a mean net gain of 12.65 score points.

Individual subjective results, as presented in Fig. 4, already show the beneficial effect of spectrally notched hearing aids in tinnitus treatment across all grades of distress. The target group improved significantly in their TQ52 scores in comparison to the patients in the control group. Although responders

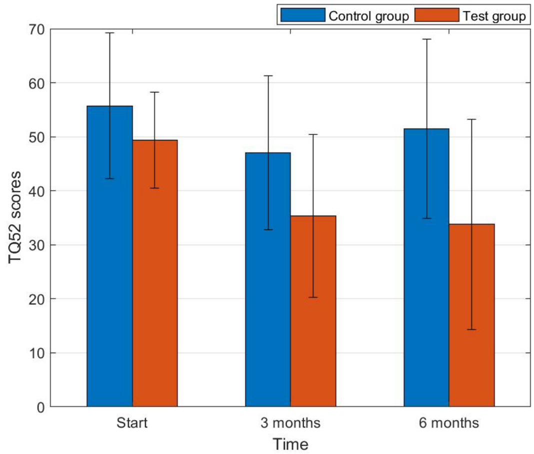


**FIGURE 5. Mean subjective results in terms of TQ52 score for control and target group over a time span of 6 months with individual values for 0, 3 and 6 months after start of the therapeutic intervention. The bar plot indicates the target group scores and standard deviations for control (blue) and test group (orange) respectively.**

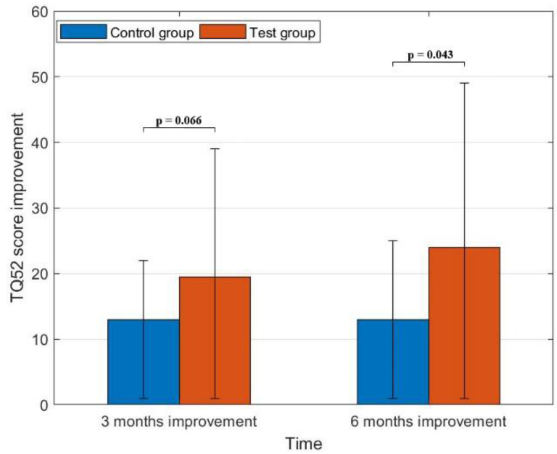


**FIGURE 6. Illustration of the TQ52 score improvements as barplots. Left side panel displays the TQ52 score improvement for responders in test (orange) and control group (blue) after three months. The p-values for the group differences are shown above the group. Right side bar plots illustrate the TQ52 score improvement for responders in both groups after six months. The p-values for the group differences are highlighted above the particular group.**

in the control group also exhibit meaningful improvements in their TQ52 score, the majority achieves only slight (to no) sustained betterment. The responders in the target group show overall larger and more persistent therapeutic effects in terms of TQ52 score.

We performed one-way ANOVA tests to check for group differences between the grouped therapy outcomes in terms of the TQ52 score improvements for responders in the target and control group over time; the p-values for the entire groups are shown in brackets. The significance threshold was set to $p < 0.05$. We only found significant group differences in the six month questionnaires. The target group exhibits a higher therapy benefit in comparison to the control group: $p = 0.043$ ($p = 0.093$). The group differences in the three month questionnaires are not significant, but trend towards an increased therapy benefit for the target group: $p = 0.066$ ($p = 0.325$).

Utilizing the "Cohen's d" effect size measure and the corresponding definition we analyzed the data for small, medium or large effect size. Normalizing the TQ52 points, the effect size is large $0.94 \pm 0.15$ (responders only; $0.89 \pm 0.14$ for all patients) for the notch effect compared to the "placebo" group with the same hearing aids but without spectral notch.

The "Cohen's d" 95% confidence interval for the six-month testing excludes "0", indicating a significant effect for $p < 0.05$.

The TQ52 score trend points to a moot sustainability of therapeutic effect in the control group. Whereas controls improve in the first three months, the group trend ascends afterwards to higher TQ scores.

The notched sound group exhibits a stronger improvement during the first three months and is able to maintain this significantly reduced distress level during the entire duration of the study. The effect size (Cohen's d) to estimate the relevance of the group mean difference is $0.94 \pm 0.15$, indicating a strong effect.

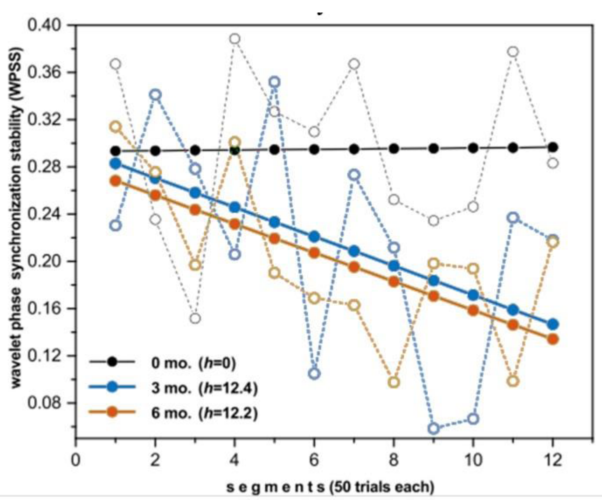


**FIGURE 7. Exemplary illustration of the habituation improvement to aversive auditory stimulation. Depicted is the loss of WPS in the course of a repetitive auditory stimulation (taken from 12 segments of 50 individual stimulations) for therapy start (0 mo) and 3 and 6 months afterwards. The l-hab values h are given in the key. The slope of the WPSS decline over the experiment is equivalent to a reduction of aversive attention binding towards the individual tinnitus tone.**

### *B. OBJECTIVE DATA*

Objective measures in terms of the l-hab value's gain factor $\tau$ mirror the subjective scoring over the duration of our study. In Fig. 7 we depict the evolution of the aversive attention binding for a single patient. Illustrated is the decrease of WPSS, i.e., the loss of attention, over the duration of our experiment for three temporal landmarks in our therapeutic approach. The steeper the decrease of WPSS, the easier the patient adapts to the aversive acoustic stimulation, meaning that the aversive attention binding towards the individual tinnitus tone becomes weaker over the time course of the notched environmental noise therapy.

Referring to the results in [17] we conducted experimental studies utilizing spectrally notched hearing aids for sharp edge effects in environmental sounds in tinnitus treatment [33]. We compared the patient's subjective self-assessment by TQ52 questionnaire with objective EEG correlates of habituation before and up to 6 months after the start of the intervention to evaluate the notched environmental sounds approach. These results reinforce our previous findings in [33] and additionally reveal a more persistent improvement of the test group compared to the control group.

Fig. 7 exemplary illustrates a linear fit to the decreasing ALR phase stability (l-hab value) over the stimulus repetition for zero, three and six months. The pre-therapy analysis (black line) shows that this particular patient showed almost no habituation to a tinnitus-tone matched acoustic stimulus. At the end of the stimulation series, the WPSS is almost as high as at the start of the experiment. Over the therapeutic intervention the aversive attention binding towards the tinnitus tone is significantly reduced. The patient shows a pronounced habituation in terms of reduced wavelet phase stability after three months and even stronger habituation to a tinnitus-matched stimulus after 6 months.

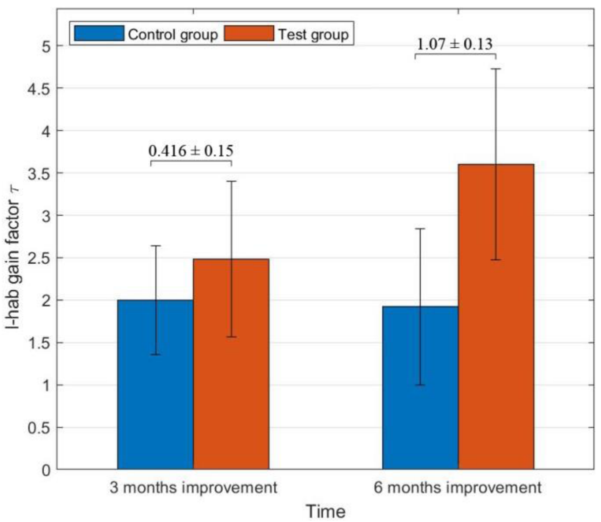


**FIGURE 8. Illustration of mean objective habituation marker development for 3 and 6 months post therapy start. The bars indicate the average habituation factor h (absolute slope of the l-hab fit) for control (blue) and target group (orange). Standard errors are given as error bars to the respective bar. Note that the variances originate in large part from ALR morphology shifts due to stimulus adaptation and can be reduced by grouping the patients according to their tinnitus frequency. The effect size (Cohen's d and standard error) for 3 and 6 month's therapy outcome is shown above each group.**

For the estimation of the habituation factor l-hab, we analyzed a series of artifact free single-sweep responses. For each patient the wavelet phase stability was calculated for consecutive blocks of single-sweep responses. The mean objective results exhibit large variances in the estimation of the long-term habituation parameter l-hab (Figs. 7 and 8).

These variances should not be mistaken for pure error estimates, but mirror inter-individual variances in tinnitus distress and habituation. Additionally morphological changes of the ALRs in response to the individual adaptation in the stimulus frequency cause a blurring in the proposed signal processing. The average l-hab gain factor for target and control group after three and six months is illustrated in Fig. 8.

The notch group exhibits stronger habituation effects to their tinnitus tone in comparison to the control group. Whereas this effect is not prominent after three months, the group-discrepancy in the ability to habituate becomes considerably larger after six months. The therapeutic gain after three months of the notched group is not only more pronounced compared to the control groups but also the analysis of the following three months show that only the test group improves further, while the habituation gain of the control group stagnates. Note, that the large standard deviation can be reduced by grouping patients according to their tinnitus frequency [16].

The large standard deviation for the objective analysis is caused by several factors:

(a) large inter-individual differences in tinnitus distress (see subjective results and standard deviations for the TQ52 scores, e.g., Fig. 5) and attention capacity, (b) variability in the hearing impairment (all the subjects rated the stimulus tone as comfortable loud but there was no hearing level adaptation) and (c) variations in the morphology of ALR components due to spectral differences in the stimulus, which was matched to the patient's individual tinnitus tone.

### *C. GENERAL DISCUSSION*

These individual changes in long-term habituation are mirrored in the mean TQ score improvement of target and control group, as illustrated in Figs. 6 and 8. Both, subjective self-assessment and objective habituation data, provide evidence for a therapeutic use of spectrally notched hearing aids as standalone treatment or as supplement to an inpatient tinnitus therapy. Spectrally notched hearing aids seem to surpass the known beneficial effects of sole hearing level correction on the individual tinnitus distress [21], [22]. Figs. 4 and 5 show a therapeutic success in both, target and control group, where our target group exhibits a more pronounced and sustained improvement in comparison to the control group.

We can interpret those results on the base of our model of tinnitus genesis and decompensation (see section III.A.):

Homeostatic plastic effects are likely to locally increase the spontaneous neuronal activity in the hierarchically lower stages of the auditory pathway in response to sensory deprivation. Contrasting the hypothetical downstream neuron in the model of Schaette and Kempter [34], modern hypotheses attribute this process to dysfunctional hyperpolarization-activated, cyclic nucleotidegated cation (HCN) and KCNQ2/3 channel configurations [25], [26].

For confined 'dead' regions in the cochlea, this pathologic hyperactivity exhibits three distinct features, associated with competitive advantages in stimulus selection: An elevated neuronal response (1) with sharp spectral edges caused by the tonotopic organization of the auditory pathway, increased spike timing precision (2) and cross fiber synchrony (3) due to lateral projection fibers [4], [35].

To analyze spike synchrony and timing we set up a numerical model of a multistage DCN lateral inhibition network, based on the conceptual circuitry of Haab *et al.* [5] and Hancock and Voigt [24]. Input to the model was a Poisson point process with increased spike rates in a confined region, simulating neuronal hyperactivity due to aforementioned homeostatic plasticity. In our simulation this simple lateral inhibition network is already sufficient to generate a narrow, well-defined band of hyperactive and precise principal neurons with a strong contrast to neighboring bands. Due to the tonotopic organization, this effect is comparable to sharp spectral edges in the acoustic environment. The hyperactive principal neurons also exhibit increased spike timing precision within the band. This is similar to the neural response to salient (high-contrast) acoustic stimuli. Both effects could be sufficient to generate a percept whose synchronous neural response which can be additionally amplified by attentional top-down processes, further boosting the competitive advantage of the stimulus in perceptual rivalry.

Please note that the effect sizes might be rather small compared to established therapy schemes which might be due to the fact that some patients had hearing aids for the first time. Thus acclimatization effects might be superimposed in some patients.

### *D. BENEFITS IN COMPARISON TO OTHER NOTCHED ACOUSTIC STIMULATION THERAPIES*

In the classic TMNM, the patient is encouraged to spend a considerable amount of time listening to their preferred music (7-21h per week), whereas in the Notched Environmental Sounds approach the therapeutic effect of spectrally modified acoustic stimulation is integrated into the patient's daily routine. We could show that an unspecific triggering of limbic or attention-guiding structures by musical conveyed content is not required to achieve a therapeutic success.

The broad and permanent availability of the hearing aid methodology offers greater independence from scheduled training sessions and grants additional degrees of freedom in the patient's therapeutic design.

Yet crucial for a therapeutic success of both intervention types certainly is a precise and robust characterization of the patient's tinnitus frequency, including potential frequency shifts during the intervention and the related (re-)adjustment of the spectral notch, which shows that there is still the need of professional therapy accompaniment.

## V. CONCLUSION

First, we could demonstrate the patient's general acceptance of spectrally notched hearing aids and a dependency of the ability to habituate to acoustic stimuli on the subjective level of distress.

Moreover we were able to collect data that hints towards a therapeutic advantage of tailored spectral notches in hearing-aid supported tinnitus treatment and that consolidates our previous findings during a six-month clinical study, comparing spectrally notched hearing aids to unmodified hearing aids of the same type.

So, secondly, we achieved the goal to transfer basic neuroscientific research into a ready-to-use therapeutic hearing aid program.

The artificial steep edges in the acoustic spectrum foster the objective reduction of EEG tinnitus correlates as well as the patient's subjective affliction assessment. Moreover the therapeutic effect in terms of a TQ score reduction appears to be more sustained compared to a stock hearing aid treatment.

Following the approach of the TMNM therapy, we did not need to create a specific listening situation to achieve a therapeutic effect with spectrally notched hearing aids. We found no adverse side effects of spectral notching in our hearing aid supported tinnitus treatment approach.

We thus conclude that the Notched Environmental Sounds Treatment approach implemented in hearing aids can be a suitable support for established tinnitus treatments. Yet we encourage a multicentric data collection in order to broaden the available data basis on the neurophysiological and neuropsychological effects of spectrally notched acoustic stimulation in tinnitus patients.

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