

Customized notched music training reduces tinnitus loudness

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Chronic tinnitus is a symptom with high prevalence. There is evidence that the tinnitus perception is related to unfavorable cortical plastic changes. In our recent study we have developed and evaluated a customized music training strategy that appears capable of both reducing cortical tinnitus related neuronal activity and alleviating subjective tinnitus perception. We hypothesize that the regular and enjoyable music training reverses unprofitable cortical reorganization to a certain degree by means of the focused strengthening of auditory inhibitory neuronal networks.

Subjective tinnitus is one of the most prevalent symptoms of hearing disorders in industrialized countries.^{1,2} Chronic tinnitus can severely worsen a patient's quality of life.³ The tinnitus perception arises in auditory cortex, and tinnitus generation and maintenance have been associated with maladaptive auditory cortex reorganization.³⁻⁵ Maladaptive cortical plasticity has been shown to be reversible by behavioral training.^{6,7}

In our recent study, we developed and evaluated a customized music training procedure that aims at the reduction of subjective tinnitus loudness in normal-hearing humans suffering from chronic, tonal tinnitus.⁸ The training was intended to reverse maladaptive plastic processes in auditory cortex supposedly contributing to the tinnitus perception. For the training, the patients selected their favorite music. The frequency spectrum of the music was modified for each patient individually by means of digitally filtering out the frequency band of one octave width centered at the individual tinnitus frequency (i.e.,

the frequency that sounds like the tinnitus). The patients were instructed to listen to their customized music regularly with pleasure.

The results of our training evaluation study⁸ demonstrated that those patients who had listened to their pleasant customized music (target group, N = 8) daily for approximately 2 hours over the course of 12 months experienced significantly reduced subjective tinnitus loudness ($F(1,7) = 26.1$, $p = 0.001$). Moreover, subjective tinnitus annoyance ($F(1,7) = 13.0$, $p = 0.009$) as well as experienced handicapping by the tinnitus ($F(1,7) = 15.1$, $p = 0.006$) decreased significantly. In contrast, matched patients who had instead listened to pleasant placebo music (placebo group, N = 8) did not experience any significant changes in these variables over time (loudness: $F(1,7) = 0.4$, $p = 0.54$; annoyance: $F(1,7) = 0.19$, $p = 0.68$; handicapping: $F(1,7) = 0.17$, $p = 0.69$). The same holds true for matched patients who did not perform any tinnitus treatment (loudness: $F(1,6) = 0.9$, $p = 0.38$; annoyance: $F(1,6) = 0.14$, $p = 0.72$; handicapping: $F(1,6) = 0$, $p = 0.85$) throughout this time period (monitoring group, N = 7) (**Fig. 1**).

In order to complement and corroborate the subjective change measurements with neurophysiological data, we additionally measured tinnitus related evoked neuronal activity change by means of magnetoencephalography (MEG). We used auditory stimuli corresponding to the individual tinnitus frequency to target neuronal populations in both primary and non-primary auditory cortices (**Fig. 2**) that would contribute to the tinnitus perception. After 12 months of training, tinnitus related neuronal activity was significantly

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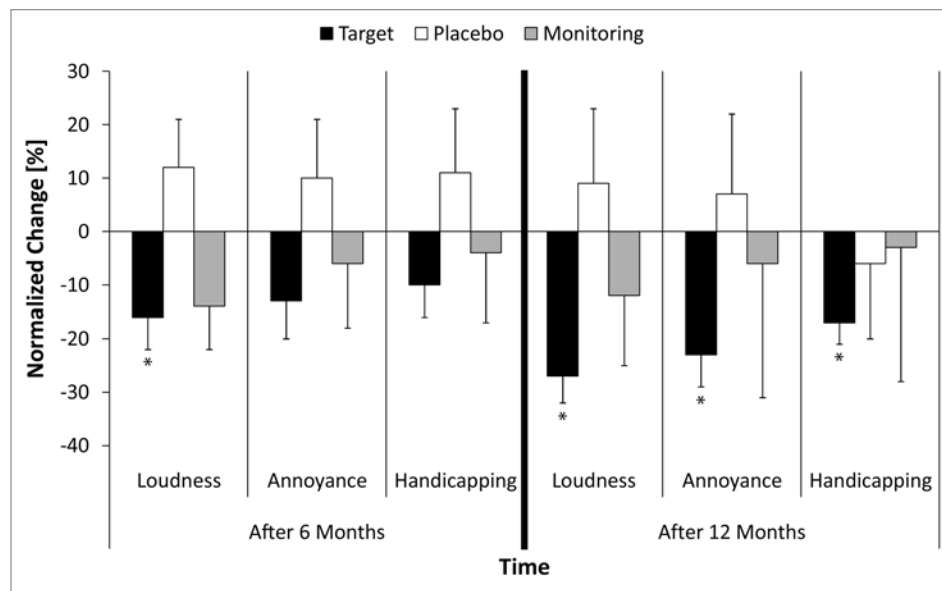


Figure 1. Tinnitus perception change over the course of the training. The bars denote average changes in percent relative to baseline; the error bars denote the standard errors of the means. Negative values reflect improvement, positive values reflect impairment. Subjective tinnitus loudness, subjective tinnitus annoyance, and experienced handicapping by the tinnitus were measured with visual analogue scales. Groups (Target, Placebo and Monitoring) are coded by grayscale (black, white and gray). Significant changes from baseline are marked with asterisks.

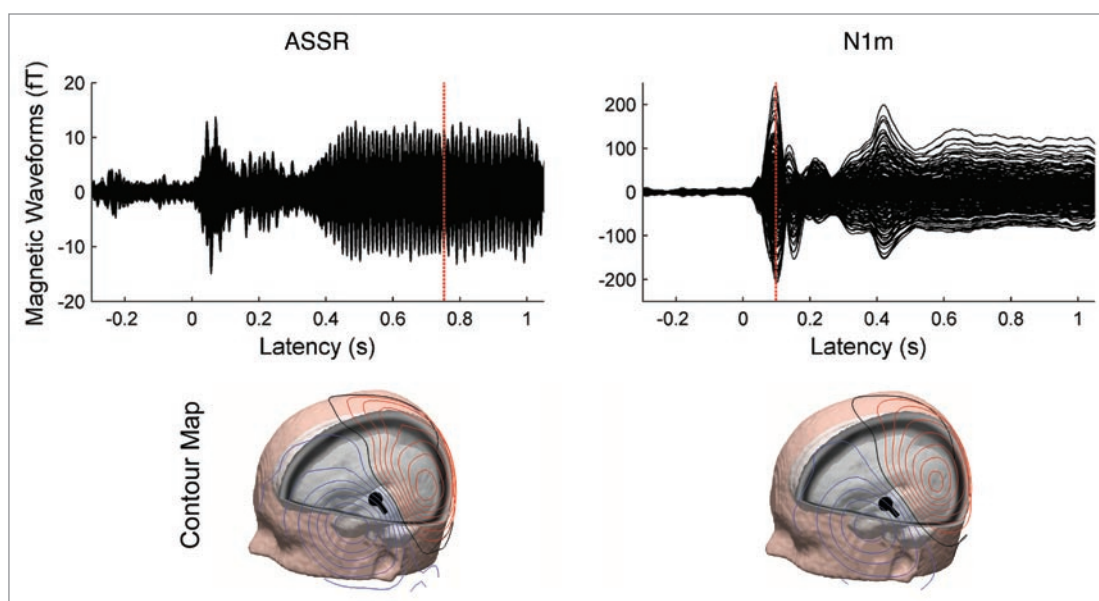


Figure 2. Examples of measured auditory evoked magnetic fields and estimated underlying sources. Top: Examples of averaged measured auditory evoked steady-state response (ASSR, originating from primary auditory cortex) and N1m response (originating from non-primary auditory cortex). Bottom: Measured contour maps and estimated dipolar sources corresponding to the responses shown in the top.

reduced in the target group (ASSR: $F(1,7) = 5.9$, $p = 0.045$; N1m: $F(1,7) = 24.6$, $p = 0.002$), but did not significantly change in the placebo (ASSR: $F(1,7) = 0.3$, $p = 0.48$; N1m: $F(1,7) = 2.2$, $p = 0.18$) and monitoring groups (ASSR: $F(1,6) = 0.0$, $p = 0.95$; N1m: $F(1,6) = 0.0$, $p = 0.85$) (Fig. 3). Source modeling revealed that the

activity measured was indeed generated in auditory cortical structures (Fig. 3).

Interestingly, there was a significant linear relationship ($r = 0.69$, $p = 0.003$) between tinnitus loudness change on the one hand and evoked neuronal activity change in primary auditory cortex on the other hand at the individual level: patients

in whom the tinnitus became less loud exhibited reduced tinnitus related primary auditory cortex activity, and patients in whom the loudness had not changed or had increased exhibited the corresponding change in tinnitus related primary auditory cortex activity.

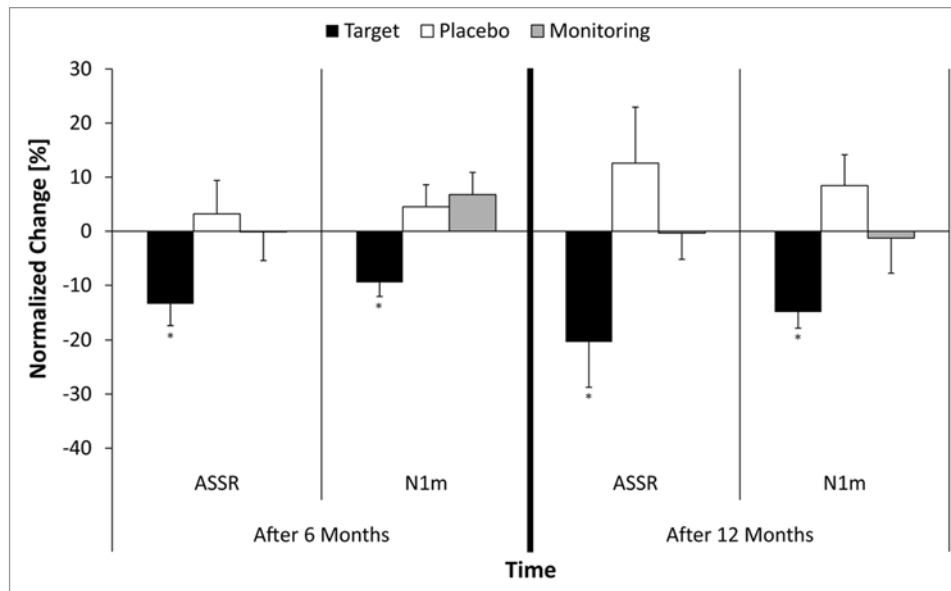


Figure 3. Tinnitus related auditory evoked field change over the course of the training. Negative values reflect reduction, positive values reflect increment. Auditory steady-state (ASSR) and N1m responses were recorded by means of magnetoencephalography (MEG) (arrangement according to Fig. 1).

Magnetoencephalography⁹ is a beneficial tool to noninvasively study the neurophysiological basis of tinnitus in humans,¹⁰⁻¹² and to neurophysiologically evaluate tinnitus treatment outcomes.⁸ Neuronal activity measured with MEG reflects rather large populations of cortical neurons. Hence, conclusions regarding underlying neuronal mechanisms have to be drawn cautiously. However, the reduction of an evoked signal over time can basically mean three things: (i) The neuronal population representing the stimulus became smaller, (ii) the neuronal population representing the stimulus fired less synchronously, or (iii) a combination of both.

The observed reductions in tinnitus loudness, annoyance and handicapping as well as the reductions in evoked neural activity appear cumulative, indicating a long-term neuroplastic effect. There is evidence in humans that tinnitus is associated with a relative excitatory-inhibitory cortical neural network dysbalance, at the expense of the inhibitory system.¹³ This loss of inhibition may lead to hyperactivity and/or spontaneous hypersynchrony of a certain cortical neuronal population, which would eventually contribute to the tinnitus perception.¹² By means of our customized music modification, we intended to “re-attract” lateral inhibition to these

neurons in order to reverse their maladaptive hyperactivity and/or hypersynchrony. It might be a consequence of this induced reversion that the tinnitus related auditory cortex activity of the target group patients decreased, and that their tinnitus became less loud (and possibly therefore less annoying and less handicapping).

The customization of the training in several aspects may be an important factor. The customization of the frequency spectrum of an acoustic stimulus in order to reverse maladaptive cortical plasticity is one thing. However, there is evidence that cortical plasticity benefits from focused attention and enjoyment.¹⁴ Therefore, it should be advantageous to motivate the brain to process the tailored acoustic input as actively and pleasurably as possible. Thus, we intentionally used music (and not broadband “noise”, which the brain would probably attempt to “get rid of” or filter out) as auditory stimulus, because music can contain meaning, it can absorb attention, and it can elicit positive emotions.¹⁵ Crucially, pleasant music can initiate the release of dopamine,^{16,17} which evidently promotes cortical plasticity. In order to maximize the probability that the tailored training music indeed would have the designated effect, we gave the patients the opportunity to choose their favor-

ite music, enabling them to listen with pleasure for a longer period of time.

The future challenge will be to provide a similar training approach for tinnitus patients with hearing loss, and to identify and consider variables that would further increase the effectivity of the training.

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