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Auditory discrimination training for tinnitus treatment: the effect of different paradigms

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Abstract Acoustic deprivation, i.e. hearing loss, is responsible for a cascade of processes resulting in reorganisation of the cortex. Tinnitus mechanisms are explained by synchronization of the neural spontaneous activity and might be related to cortical re-mapping. Auditory discrimination training (ADT) has demonstrated in both animals and humans to induce tonotopical changes in the auditory pathways through neural plasticity. We hypothesize that ADT could have some effect on tinnitus perception. The objective of this study is to compare the effect on tinnitus following two paradigms of ADT. Only patients from 20 to 60 years of age were recruited. Inclusion criteria were pure tone tinnitus of mild or moderate handicap according to the Tinnitus Handicap Inventory score (<56). ADT patients were randomized in two groups: SAME (ADT in the same frequency of tinnitus pitch, 20 patients) and NONSAME (ADT in the frequency one-octave below tinnitus pitch, 21 patients). Groups of pair of tones (70% standard tones ST, 30% deviant tones ST + 0.1–0.5 kHz) were randomly mixed for 20 min/day during 1 month. Patient had to mark when the two sounds of the pair were similar or different. Control group included 26 patients from the waiting list (WLG). Patients were also divided according to the trained frequency and the deepest hearing-impaired frequency. Outcome parameters were set up according to the answer to the question "is your tinnitus better, same, or worse with the treatment?" (RESP), the tinnitus handicap inventory (THI) and the visual analogue scale from 1 to 10 on tinnitus intensity (VAS). Tinnitus improved in 42.2% of the patients (RESP). VAS and THI scores were reduced but only THI differences were statistically significant ($P = 0.003$). ADT patients improved significantly compared with WLG in RESP and THI scores ($P < 0.01$). Training frequencies one-octave below the tinnitus pitch (NONSAME) decreased significantly THI scores compared with patients trained frequencies similar to tinnitus pitch (SAME, $P = 0.035$). RESP and VAS scores decreased more in NONSAME group though differences were not significant. We did not find any differences when comparing the group training the deepest hearing-impaired frequency and the group who trained other frequencies. Auditory discrimination training significantly improved tinnitus handicap compared to a waiting list group. Those patients who trained frequencies one octave below the tinnitus pitch had better outcome than those who performed the ADT with frequencies similar to the tinnitus pitch ($P = 0.035$)

Keywords Tinnitus · Cortical reorganisation · Auditory training · Plasticity

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Introduction

The central auditory processing (CAP) can be modified after peripheral deafferentation. The tonotopic representation in the auditory cortex changes due to brain plasticity. Plasticity is the ability of the sensory system to modify its connections and adapt functionally after modifications in the acquisition of information [1]. Wide cochlear lesions (i.e. complete deafness) are more susceptible to induce cortical reorganisation, in the same way as what happens in the deafferented region of somatosensory cortex after a total limb amputation [2]: Moderate hearing loss can be enough stimuli to start these changes. Animal research has demonstrated the reorganisation of the tonotopic map in the central structures of the auditory system secondary to high frequency hearing loss (HF-HL) [3–5]. Acute exposure to an intense sound causes permanent cochlear damage, which results in cortical remapping. Noreña et al. compared a group of cats, placed in a high frequency (HF) enriched acoustic environment after a traumatizing noise, with other two groups of cats placed in a quiet and a low-frequency sound environment [6]. Cats exposed to a HF acoustic environment showed more restricted hearing loss and no plastic tonotopic map changes in primary cortex, suggesting no reorganization processes compared to the other two environments. The lack of reorganization could be interpreted as an absence of neural signs of tinnitus [7].

Other authors have associated tinnitus mechanisms with cortical reorganization [8, 9]. Mühlnickel et al. demonstrated that the cortical areas stimulated by a sound with the same frequency as the tinnitus pitch have shifted into adjacent zones of the auditory cortex. Lockwood [10] studied some patients who could voluntarily modulate their tinnitus through oral-facial movements. He demonstrated a more widespread cortical activation by pure tones through PET techniques. Using EEG-Mismatch negativity, Weisz [11] showed abnormal auditory mismatch responses in the lesion-edge regions in tinnitus patients. The source of the N_{100} dipole in the evoked magnetic field in response to tonal edge-frequency stimuli was abnormal in the tinnitus group compared to normal controls. The responses to tonal stimuli with one octave-lower frequency were also affected [12]. However, these changes were not correlated to the strength of the tinnitus, in the opposite way to Mühlnickel's findings. Some recent studies have demonstrated opposite arguments to the increase of lesion-edge areas as the neural correlate of tinnitus. If the remodeling process affects the lesion-edge frequencies, tinnitus pitch should be matched in these frequencies, but for authors like Eggermont, tinnitus pitch is more commonly matched in the deepest hearing loss frequencies [9]. His studies show an increased spontaneous firing rate, peak cross-correlation coefficient, and burst-firing activity in the areas of primary auditory cortex corresponding to the most damaged cochlear areas after acoustic trauma. Reorganisation processes related to tinnitus persistence would be more enhanced in the hearing loss areas instead of in lesion-edge frequencies. The study published by Diesch confirms that tinnitus frequency was located above the audiometric edge frequency (boundary of the hearing loss slope) and not in the edge area. He demonstrated a maximum enhanced state of excitability (steady-state auditory evoked magnetic field) of the frequency region above the audiometric edge. This area was corresponded to the one a step below tinnitus frequency [13].

Auditory rehabilitation (AR) has proved to be effective in functional changes of cortical tonotopy. An example of AR can be found in musicians. They performed better discrimination tasks in the piano trained frequencies compared to a non-musicians control group [14]. Reorganization processes were achieved using functional magnetic source imaging (single dipole model). In the study published by Recanzone, monkeys were trained to discriminate among closed frequency tones. Cortical tonotopic changes were demonstrated through electrophysiologic techniques. There was an over-representation of the trained frequencies [15]. Other examples of AR are related to the auditory abilities of the blind people after acoustic training procedures. The progressive increase of comprehension in hearing impaired patients after several months using hearing aids implies a process of brain reorganization to improve the efficacy of the auditory processing. The study performed by Noreña and Eggermont confirmed the positive effect of specific sound stimuli to avoid or increase remapping processes after noise induced hearing loss [7].

If AR has demonstrated cortical changes in patients with hearing loss, and tinnitus could be a consequence of plastic reorganisation in the auditory cortex, we can consider that AR might have some positive effect on tinnitus management [16]. The data published by Flor [17] and Herraiz [18] suggest that Auditory Discrimination Training (ADT) have a positive effect on tinnitus management, although no study to test the cortical changes in tinnitus patients after ADT has been published. The response could be related to the training location, although we still do not know what frequencies should be trained to achieve more success.

The aim of our study is to describe the effect on tinnitus of a new ADT paradigm: tinnitus frequency training versus closed to tinnitus pitch training. ADT paradigm according to the deepest hearing loss frequency will be also presented. Results will be compared with a waiting list group and other ADT protocols.

Materials and methods

This is a prospective randomized clinical trial. We have included 45 patients referred to our tinnitus clinic from January 2006 to February 2008. Forty-one patients completed the study. Only patients from 20 to 60 years of age were recruited. Older individuals could have some difficulties to perform the tasks. ADT-patients were randomly assigned in two groups: SAME (auditory discrimination training in the same frequency of tinnitus pitch, 20 patients), and NON-SAME (discrimination training around a frequency near to but not the same as the tinnitus pitch, 21 patients). A waiting list group (WLG) comprised 26 patients (who waited 1–3 months to be seen in our tinnitus clinic). Any of the WLG patients participated in the ADT protocol afterwards.

Patients were additionally analyzed according to the hearing level. The group HLSAME ($n = 22$) includes all the patients that have performed ADT training in a frequency spectrum that corresponds to the most impaired hearing frequency. The group HLNONSAME ($n = 19$) includes those patients that have performed an ADT protocol in a frequency spectrum that corresponds to the nearest frequencies to the most impaired one.

All the patients had a mild or moderate tinnitus handicap (THI < 56). We have not included severe tinnitus subjects because the associated alteration in affect/emotion, i.e. anxiety/depression, mostly present in tinnitus of the severe disabling type could not be consistent during the ADT period and it could bias the treatment response.

A complete ENT examination was performed. Tinnitus assessment protocol followed the CIBA recommendations [19] and the Tinnitus Research Initiative Consensus [20]. Psychoacoustical tinnitus characteristics (pitch, loudness, minimal masking level, and residual inhibition) were tested and re-tested to increase the reliability of the measurements. The inclusion criterion for tinnitus pitch was pure-tone tinnitus matched in the range from 3,000 to 8,000 Hz. A visual analogue scale of intensity (VAS) and a Spanish validation of the Tinnitus Handicap Inventory (THI) [21] were considered for the evaluation of tinnitus severity.

ADT consisted of a 20-min auditory discrimination task (two 10-min tracks), once per day during 30 days using a domestic MP3 device. Every track was previously recorded in the MP3 device, generated by specifically developed software. Every track showed 300 pairs of tones of 100 ms each tone. Seventy percent of the pairs corresponded to the standard tone (4, 6, or 8 kHz) while the rest 30% were the deviant one (from 4.1 to 4.5 kHz, for 4 kHz, 6.1–6.5 for 6 kHz and 8.1–8.5 for 8 kHz). Latency between the tones of each pair (around 100 ms) and between the pair of tones (around 2 sec) was randomly mixed. There were six different tracks to be used according to the protocol (day one: tracks 1–2, day two: tracks 2–3, etc.).The patient had to mark every stimulus in a notebook (S = same, D = different, when the two sounds of the pair were similar or different, respectively). Eighteen patients (group SAME) performed a 4, 6, or 8 kHz training according to their tinnitus pitch (4, 6, or 8 kHz, respectively). The remaining 22 ones (group NONSAME) trained the frequency one octave below their tinnitus pitch, except for the 4 kHz group, that performed one octave over (6 kHz) and the 3 kHz group that trained at 4 kHz.

Results were reported according to three parameters: patient's answer to the question "is your tinnitus better, same or worse since we started the treatment?" (RESP); visual analogue scale on tinnitus intensity (VAS) and tinnitus handicap inventory (THI). Data were obtained after 30 days of training. Tinnitus spectrum was measured after the treatment. Statistical study was performed using SPSS 13.0 software program. Qualitative variables were compared with χ^2 and McNemar tests, whereas quantitative variables were done with Student′s t and Wilcoxon non-parametric tests. All significance tests were two-tailed and conducted at the 5% significance level.

Results

Forty-five patients (30 men, 15 women) were included in the ADT protocol. Age average was 42 ± 11 years of age. The left ear was more commonly affected than the right one (29 vs. 11%). Tinnitus was bilateral in 53%, cephalic in 7% of the patients and it had been present for 45 ± 54 months (range 1 month–11 years). Noise-induced hearing loss and acute acoustic trauma were the most common diagnosis (31 and 29% respectively). Sixty percent matched their tinnitus at 8 kHz, 15.6% at 6 kHz, 17.8% at 4 kHz and 6.7% at 3 kHz. Table 1 shows the psychoacoustical characteristics of the tinnitus.

Duration of the tinnitus was averaged in 45.3 ± 42.4 months. All the patients presented high frequency hearing loss (descendent curves) with normal pure tone averages on speech frequencies (22.4 dBHL). Average hearing thresholds for high frequencies were 40 ± 23 dBHL for 4 kHz, 47 ± 26 dBHL for 6 kHz and 53 ± 20 for 8 kHz. Fifty-five percent of the patients matched their tinnitus at the most impaired hearing frequency. Decreased sound tolerance (DST) was referred by 32% of the cases. The number of activities affected by the sample secondary to DST was 1.7 ± 1.1 from a list of 11. Visual analogue scale for sound hypersensitivity was averaged in 3.6 ± 2.3 (range 0–10). Aural pressure and vertigo were uncommon symptoms (less than 5% of the patients). Migraines were reported by 15% of the sample and no other relevant central symptoms were found. Three patients completed our battery tests for central auditory processing disorders. Altered dichotic and signal/noise tests were found in the two of them. Magnetic resonance imaging (MRI) was performed in all the patients to rule out any retrocochlear disease.

There were four dropouts from the trial. Two patients from the SAME group did not follow our outcome program and were lost. One patient (NONSAME group) decided to give up the ADT after 15 days of training because he did not believe in its possible benefits. One patient from NONSAME group did not fill the THI questionnaire after 1 month of treatment. Therefore, 21 patients were finally included in the NONSAME group and 20 in the SAME group.

Table 1 Psychoacoustical characteristics of the tinnitus for each group

	n	Loudness (db)	PItch	MML (db)	RI	VAS	THI (%)
TOTAL	41	13 ± 12	3 kHz: 3	31 ± 21	Compl 8	5.5 ± 1.7	37 ± 20
			4 kHz: 7		Part 21		
			6 kHz: 6		Neg 8		
			8 kHz: 25		Reb 3		
WLG	26	15 ± 13	3 kHz: 1	27 ± 22	Compl 3	5.3 ± 1.4	29 ± 20
			4 kHz: 7		Part 18		
			6 kHz: 5		Neg 4		
			8 kHz: 13		Reb 1		
SAME	20	11 ± 13	4 kHz: 5	29 ± 18	Compl 4	5.8 ± 1.9	32 ± 21
			6 kHz: 3		Part 8		
			8 kHz: 12		Neg 5		
					Reb 1		
NONSAME	21	15 ± 12	3 kHz: 3	33 ± 23	Compl 4	5.4 ± 1.6	41 ± 19
			4 kHz: 2		Part 13		
			6 kHz: 3		Neg 3		
			8 kHz: 13		Reb 2		
HLSAME	22	12 ± 11	4 kHz: 2	28 ± 19	Compl 5	5.5 ± 1.6	37 ± 22
			6 kHz: 4		Part 8		
			8 kHz: 16		Neg 6		
					Reb 2		
HLNONSAME	19	14 ± 14	3 kHz: 3	35 ± 23	Compl 3	5.5 ± 1.9	38 ± 19
			4 kHz: 5		Part 13		
			6 kHz: 2		Neg 2		
			8 kHz: 9		Reb 1		

WLG waiting list group, *SAME* ADT in the same frequency as tinnitus pitch, *NONSAME* ADT in different frequency than tinnitus pitch, *HLSAME* ADT in the deepest hearing loss frequency, *HLNONSAME* ADT in different frequency than the deepest hearing loss one. *MML* Minimal masking level, *RI* Residual inhibition (*compl* Complete, *Part* partial, *Neg* negative, *Reb* rebound effect). *VAS* visual analogue scale, *THI* Tinnitus handicap level

The waiting list group (WLG) included 26 patients (12 men, 14 women). Age average was 47 ± 11.6 years. There were no significant differences between ADT and WLG groups, according to age, number of months of tinnitus persistence, initial THI and VAS scores (two-tailed *t* Student test).

ADT group evaluation

Tinnitus improved in 42.2% of the sample ($n = 41$, parameter RESP). THI mean score was statistically reduced from 37.4 to 29.9 ($P = 0.004$) and VAS decreased from 5.53 to 5.02 although this difference was not significant ($P = 0.06$, two-tailed *t* Student test). ADT efficacy did not depend on the etiology of the tinnitus. The patients performed 95% of the possible training sessions. Initial tinnitus psychoacoustical loudness, minimal masking level, duration of the tinnitus, VAS, and THI scores had no influence on ADT results.

ADT versus WLG evaluation

ADT patients improved significantly (42.2%), compared to WLG (4%), when considering the answer "my tinnitus is better" ($P = 0.000$, χ^2). THI mean score after ADT showed a statistical significant improvement (reduction in 7.42 points, $P = 0.003$) compared to waiting list group (increase of 1.46 points). VAS scores also decreased (reduction in 0.5 compared to WLG that increased in 0.04) but this difference was not significant (Fig. 1).

SAME group evaluation

Tinnitus improved in 26% of the sample (parameter RESP). THI mean score was reduced from 32.0 to 29.8 and VAS decreased from 5.79 to 5.47, although the differences were not significant).

NONSAME group evaluation

Tinnitus improved in 54% of the sample (parameter RESP). THI mean score was statistically reduced from 41.4 to 30.1 ($P = 0.000$) (two-tailed *t* Student test). VAS decreased from 5.35 to 4.69 although this difference was not significant, $P = 0.06$).

SAME versus NONSAME group comparison

When considering the answer "my tinnitus is better", a greater number of patients that followed the paradigm

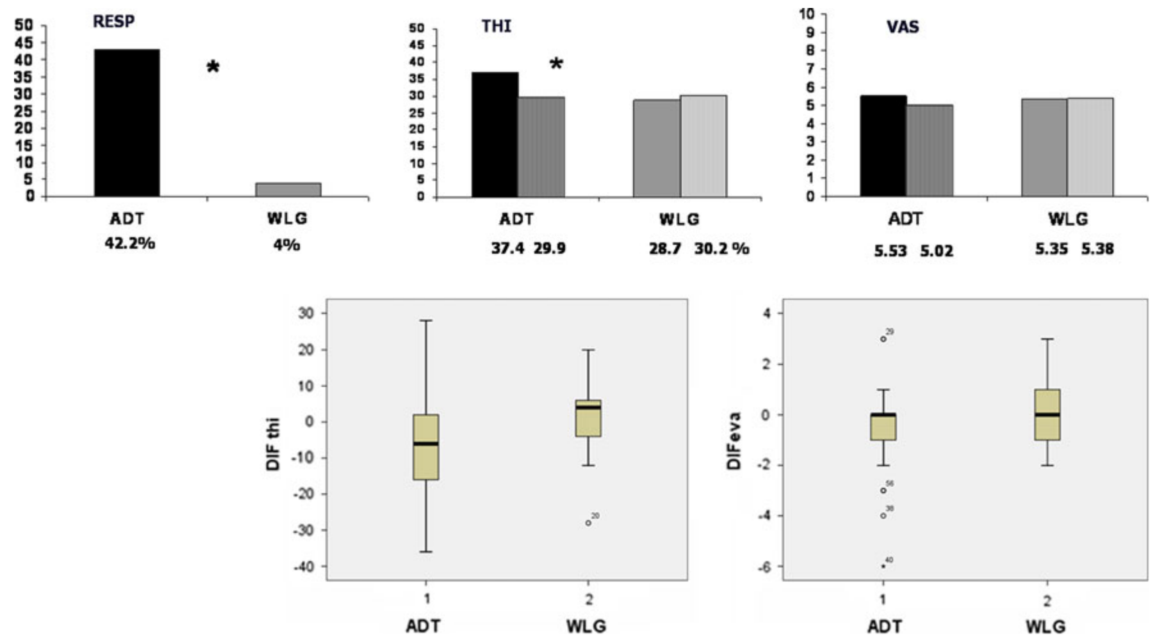

Fig. 1 Comparison between auditory discrimination training group (ADT) and waiting list group (WLG) according to the parameters RESP (response to the question *is your tinnitus better after the treatment*?, visual analogue scale (VAS), tinnitus handicap inventory (THI). DifTHI (differences in the initial THI and post-treatment THI scores), Difeva (differences in the initial VAS and post-treatment VAS scores). $*P < 0.001$

NONSAME improved compared to SAME group (54 vs. 26% respectively), although it was not statistically significant ($P = 0.07$). NONSAME VAS improvement was higher than SAME group (reduction of 0.65 vs. 0.32, respectively), statistically not significant. THI scores decreased significantly more in NONSAME patients (reduction in 11.31 and 2.11, for each group, $P = 0.035$) (Fig. 2). ANOVA test was used for regression analysis, where the dependent variable was the difference in THI scores before and after the treatment. It was significant ($P = 0.035$) and the coefficient indicated that the THI will be reduced in 9.2 points for NONSAME patients. Including more independent variables (duration of the tinnitus, initial THI and VAS) in our regression analysis showed a significant ANOVA ($P = 0.014$). The independent variable "initial THI" was significant ($P = 0.07$) meaning that high THI baseline scores predicted beneficial treatment outcome.

ADT according to hearing impairment

When considering the answer "my tinnitus is better", there was no difference between both groups HLSAME and HLNONSAME. We have not found any statistical difference when considering the improvement in THI (reduction of 7.15 for HLSAME and 7.79 for HLNONSAME) and VAS scores (reduction of 0.62 and 0.37 respectively) (Fig. 3).

Discussion

The data published by Flor [17] and Herraiz [16, 18] showed the positive effect of ADT on tinnitus management. We have demonstrated that different ADT protocols improve tinnitus severity (visual analogue scales and tinnitus handicap inventory), but there are not yet enough studies to verify which of the protocols should be more reliable and successful. If we consider Mülhnickel's theories, we should train the frequencies close to but not similar to tinnitus pitch but if we consider Eggermont's, we should train the frequencies corresponding to tinnitus pitch (maximum reorganization area). In our clinical trial, training frequencies close to the tinnitus pitch have been more effective than training frequencies equal to the tinnitus pitch (considering THI improvement). When comparing the groups according to the highest impaired hearing frequency, we have not found any difference in the results of both. The trial performed by Noreña and Eggermont demonstrated the benefits of a specific sound (HF) to avoid remapping processes after a noise induced cochlear damage. Lower sound environment did not obtain these benefits [7]. Therefore, we could insinuate that reversing the tinnitus related cortical changes emerging after auditory deprivation would need an acoustic stimulation in the same frequencies as the damaged ones [22]. Although these observations could help for the treatment design, the previous trial is based on the effects of passive exposure and the results of active auditory

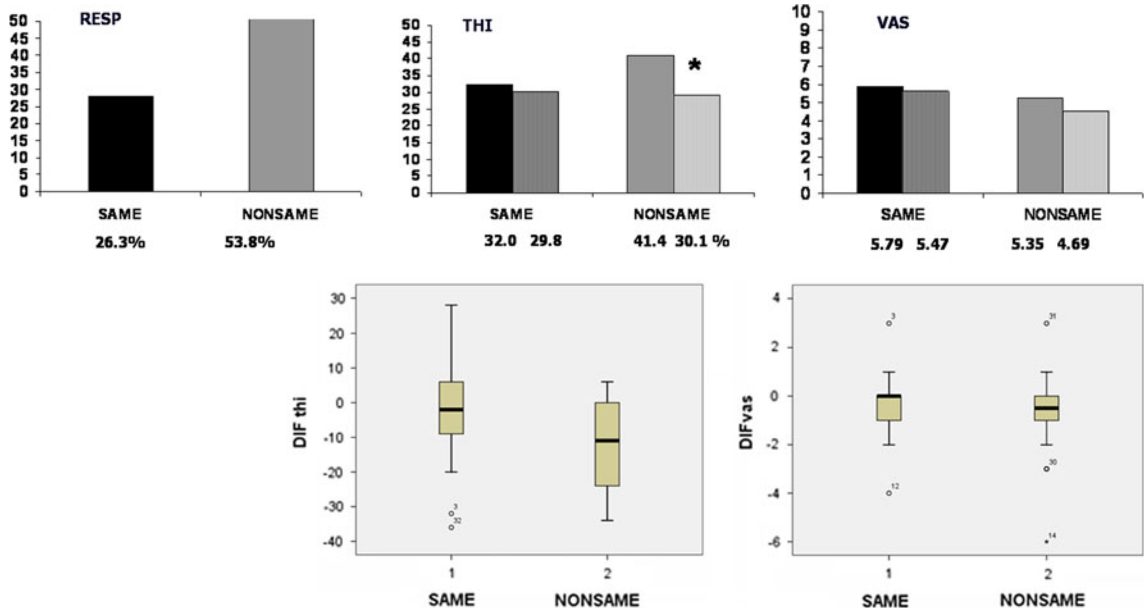

Fig. 2 Comparison between the two ADT paradigms (SAME: ADT in the same frequency as tinnitus pitch; NONSAME: ADT in different frequency than tinnitus pitch) according to the parameters RESP (response to the question *is your tinnitus better after the treatment*?, visual analogue scale (VAS), tinnitus handicap inventory (THI). DifTHI (differences in the initial THI and post-treatment THI scores), Difvas (differences in the initial VAS and post-treatment VAS scores). *$P < 0.001$

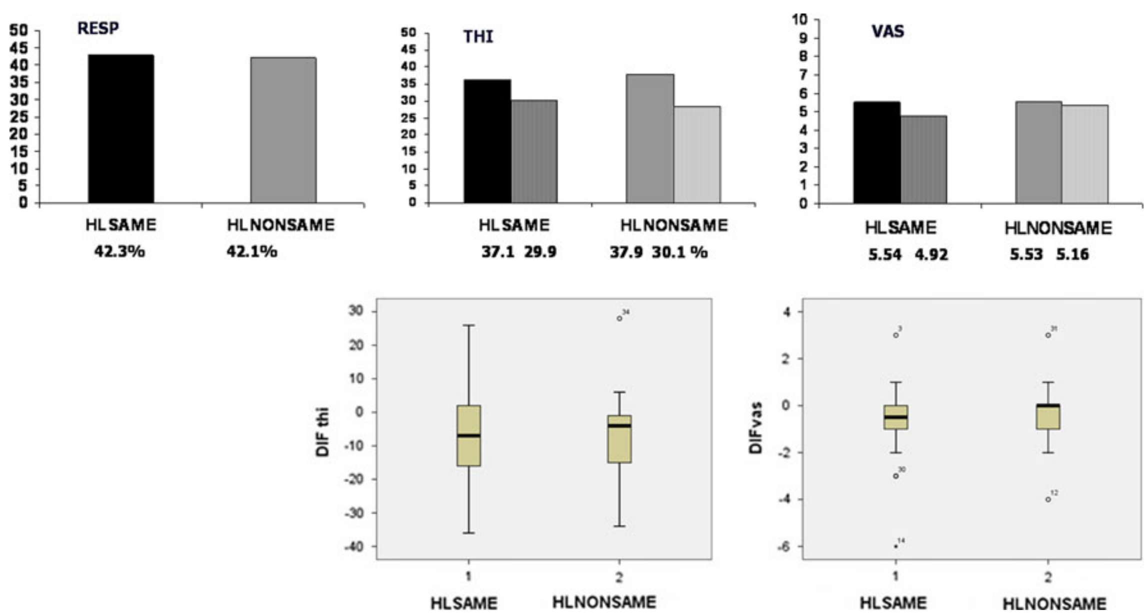

Fig. 3 Comparison between the trained frequency and the most-impaired hearing frequency (HLSAME: ADT in the deepest hearing loss frequency; HLNONSAME: ADT in different frequency than the deepest hearing loss one) according to the parameters RESP (response to the question *is your tinnitus better after the treatment*?), VAS (visual analogue scale), THI (tinnitus handicap inventory). DifTHI (differences in the initial THI and post-treatment THI scores), Difvas (differences in the initial VAS and post-treatment VAS scores). *$P < 0.001$

training may be completely different. The question remained in what exact frequency respect to the tinnitus should be trained and our study confirms the benefit of the closest but not the same frequency as the tinnitus pitch.

Attention can be an important factor involved in the efficacy of ADT. Some authors have suggested attention problems in tinnitus patients [23]. A preliminary work demonstrated tinnitus relief, considering pitch-matched loudness and minimal masking levels, after a 15-day Auditory Object Identification and Localization (AOIL) training [24]. ADT tasks act as exercises to improve the attention (discrimination of pairs of sounds). Therefore, the patient could present a relief in this cognitive situation, and therefore, tinnitus would improve as well. If attention would be the most relevant mechanism, there should not be differences between the two groups. On the other hand, it has been electrophysiologically demonstrated that these remodeling processes can take place regardless of whether acoustic targets were explicitly trained or presented as a background signal [25]. We have started to test a new ADT protocol where patients do not have to pay attention to the sounds or write which tone is being played. This exercise will rule out the role of attention and we will compare it with previous ADT protocols.

We have only included pure tone tinnitus. The tinnitogram as a subjective evaluation is susceptible of some variability in the results. We have re-tested the tinnitogram in order to avoid this variability but a bias cannot be rule out. Errors in patient selection considering the tinnitus pitch will influence the whole ADT group. Re-test the tinnitogram not only twice the same day but also different days would be more reliable. We have not tried ADT in broad or narrow band noise tinnitus, and we do not know what sound should be used or what frequencies should be trained. Some authors measure the tinnitus pitch according to a spectrum instead of a pure tonal sound. This observation could be interesting to confirm what part of the spectrum should be trained or to design specific trials according to this characteristic [26, 27].

All our patients were classified for mild or moderate tinnitus according to the Tinnitus Handicap Inventory. The effects of ADT in severe tinnitus (THI > 56) would be tested in the future.

The placebo effect in tinnitus treatment has been described to be up to 40% of the patients and this fact has to be considered in any reported results. A waiting list group is not the most appropriate control group to be considered in tinnitus trials, although it has been used widely in the literature. In this case, the type of treatment makes difficult the design of a placebo control group (both groups should listen to the sounds). In our study, the response of the “treated NONSAME group” (54%) was clearly significant over the “placebo SAME group” (26%).

Keeping the ADT discrimination tasks for more than the initial month of the study was proposed to those patients who obtained benefit from the treatment. From those ADT responders, 10.5% decided to stop ADT because they felt well enough and 31.5% asked for another extra treatment (drugs, TRT, residual inhibition therapy). Fifty-eight percent continued performing the ADT during 2 or 3 days per week, from 3 to 4 months later. Thirty-six percent of the patients from this group were lost because they did not come back to our office. Forty-five percent reported an extra improvement of their tinnitus after 3 months of ADT. The rest 28% referred no more benefit when keeping ADT after the first month.

Tinnitus retraining therapy (TRT) uses a continuous binaural sound (broadband noise generator) in order to increase habituation processes for tinnitus management. The new digital noise generators can produce a narrow band noise. It has not been demonstrated that retraining using the same frequency of the tinnitus or a narrow band sound corresponding to the hearing-impaired frequencies, is more effective than broadband noise generators. There is some scientific evidence in a virtual (non-clinical) model for better results using narrow band sounds [28]. The unsolved question is whether it would be more effective to use a passive acoustic stimulation with a continuous narrow band noise (TRT) or better results could be achieved using an active auditory stimulation protocol (ADT), training near to or the same frequencies as the tinnitus pitch.

The dynamic development of ADT protocols should improve the efficacy and success in tinnitus management. Longer and more frequent training sessions, increasing difficulty to perform the discrimination tasks and the individualisation of the frequencies trained, should bring us new paradigms that ought to work more accurately in each patient.

Conclusions

Auditory discrimination training for tinnitus treatment was superior to a waiting list control group. Those patients, who trained frequencies one octave below the tinnitus pitch, had significantly better outcome than those, who performed the ADT with frequencies similar to the tinnitus pitch. ADT has demonstrated to be an effective approach for pure-tone tinnitus pitch patients.

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