Research Article

Effectiveness of Clinical Trial of Tinnitus Retraining Therapy on Temporal Processing and Perceptual Judgment in Tinnitus

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Key Words

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Longitudinal study
Auditory processing
Bilateral tinnitus

Abstract

The present study evaluated the effectiveness of tinnitus retraining therapy (TRT) on certain temporal processing abilities and perceptual judgment of tinnitus. A review of literature revealed that TRT reduces the neural activity at the level of limbic and autonomic nervous system. As, the neural generators of temporal perceptual skills also lie in the cortical and sub-cortical areas of the brain, it was hypothesized in the current study that there could be an association between the two. This longitudinal study was carried out with three groups of participants. The groups included 16 participants with bilateral symmetrical tinnitus (experimental group), 10 individuals with tinnitus (placebo group), and 20 individuals with no tinnitus (control group). All the participants had normal hearing sensitivity. TRT was given to the participants of the experimental group. Temporal processing abilities, tinnitus severity, annoyance and loudness were assessed before therapy and 1, 6 and 12 months following therapy. A significant improvement in the temporal processing test scores after 12 months of therapy was noted. Therapy also resulted in reduction of tinnitus severity and tinnitus related annoyance. There was a positive association between improved temporal processing and reduced tinnitus severity and tinnitus related annoyance for the participants in the experimental group. The improvement of temporal processing skills and perceptual judgment of tinnitus after therapy indicate the effectiveness of tinnitus retraining therapy and confirm the cortical and/or sub cortical involvement in tinnitus perception.

Background

Tinnitus is the perception of sound in the absence of any external stimuli. The exact mechanism of tinnitus is still a debate; however, researchers suggest that central and peripheral auditory organs are responsible for the generation of tinnitus. Kaltenbach (2009) suggested acoustic, attention and emotional aspect, as three components behind the origin of tinnitus. The acoustic component was observed to be the perception of unwanted sound secondary to the physical damage to cochlea or higher auditory organs. These damages were reported to be discordant inner and outer hair cells (Hazell & Jastreboff, 1990; Jastreboff, 1990) or disturbed cochlear biochemistry (Sahley & Nodar, 2001). Increased spontaneous activity at the level of auditory nerve (Evans, Wilson, & Borerwe, 1981), dorsal cochlear nucleus (Brozoski, Bauer, & Caspary, 2002; Kaltenbach & Afman, 2000), inferior colliculus (Chen & Jastreboff, 1995), amygdala (Langer & Wallhäusser-Franke, 1999) and auditory cortex (Seki & Eggermont, 2003; Wallhäusser-Franke, Braun, & Langner, 1996), were also proposed as possible mechanisms for the tinnitus percept. The increased spontaneous activity is due to the imbalance between the excitatory and inhibitory synapses (Suneja, Potashner, & Benson, 1998).

The second component of tinnitus mentioned by Kaltenbach (2009) was attention, i.e., the patient's focus towards the tinnitus. Reserchers noted that people who paid more attention towards the tinnitus were found to be more annoyed than people who downgraded tinnitus to the background of their attention (Newman, Wharton, & Jacobson, 1997). Peterson and Posner (2012) highlighted the role of certain cortical and sub-cortical structures in mediating attention. They observed that affected auditory signal processing in cortical and sub-cortical structures mediated the attention away from tinnitus. However, it was secondary to the anatomical and physiological changes in the cortical, sub-cortical structures, and may have been indirectly involved for tinnitus-mediated annoyance. Annoyance resulted in a negative emotional association with tinnitus and caused functional changes in the limbic system. Thus, attention interceded the emotional component, which further was considered to arbitrate the acoustic component of tinnitus. The emotional alteration resulted in hypersensitivity towards sound and disturbed the neural synaptic synchrony that in turn magnified tinnitus percept. This was reported to create a cycle of tinnitus. This cycle of tinnitus was considerd to continue until the interference of an external component helped the patient to divert his attention away from the tinnitus. Using this idea of an external component, tinnitus retraining therapy (TRT) was suggested by Jastreboff and Jastreboff (2000). As suggested by the authors, TRT focuses on the habituation of the reactions evoked by tinnitus. There are two components of TRT, viz., counseling and sound therapy. The counseling is based on the principle of changing neural plasticity and helps in modifying the functional connections of the limbic and autonomic nervous system with the cognitive areas of the brain. Its main aim is to decrease the level of stimulation from the cortical areas to the limbic and autonomous nervous system and to retrain the brain to achieve habituation of tinnitus. The patient learns the perceptual nature of tinnitus and its cortical/sub-cortical origin. Thus, counseling gradually decreases the negative reactions associated with tinnitus and makes its perception a passive phenomenon.

The goal of sound therapy in tinnitus retraining therapy is to reduce the strength of neuronal activity related to tinnitus, and in turn, to decrease the activation of the limbic and autonomic nervous system. A low level, continuous, neutral sound increases the background neuronal activity in the auditory system. It is on the principle of gradient, where a sound appears louder and more easily detectable in the absence of any competing sound. However, with an additional sound in the auditory background, the actual sound appears soft, and the evoked neuronal activity is difficult to detect. Since, we cannot change the tinnitus related neuronal activity directly; enhancing the background neuronal activity reduces the vigor of the tinnitus perception, and thus, reduce its perceptual strength. Another important function of the low-level sound stimulation is to divert the attention away from the tinnitus. Since, the human brain has a tendency to adapt to the stimuli quickly, the continuous background noise gets adapted in the auditory system to divert the attention from the sound perception.

Studies have shown the success of TRT in the management of tinnitus. In a longitudinal clinical trial on military veterans having clinically significant tinnitus, Henry et al. (2006) found a significant reduction in the tinnitus percept using TRT for 18 months. They also noted that TRT was more effective in individuals with severe tinnitus. Herriaz et al. (2005) also reported improved tinnitus in 82% of the 158 individuals after 12 months of TRT. Better improvement was seen in patients with hearing loss (Bartnik, Fabijańska, & Rogowski, 2001). Wang et al. (2002) reported 88% improvement in the tinnitus perception after 12 months of TRT. Apart from these studies, many other researchers demonstrated the benefit of TRT in the reduction of tinnitus perception (Ariizumi, Hatanaka, & Kitamura, 2010; Bauer & Brozoski, 2011; Beriat et al., 2011; Inagaki et al., 2014; Korres et al., 2010). These results indicate that TRT is a very effective approach in the treatment of tinnitus.

A potential confounding factor in all the available research studies is the method of evaluating the efficacy of treatment. Most studies have used questioners, inventories or subjective scale of measurement to assess the effectiveness of TRT (Ariizumi et al., 2010; Baracca et al., 2007; Bauer & Brozoski, 2011; Inagaki et al., 2014). However, these methods are difficult to control and highly affected by the participant, examiner and other related bias. Thus, the validity of these measures are questionable (Clark & Watson, 1995). This poses a potential limitation to the available literature. In light of such situation, tests that are more systematic are required to evaluate the effectiveness of TRT.

Lack of objective procedures to evaluate the presence or severity of tinnitus has resulted in having to rely on the psychoacoustic measures. Psychoacoustic testing comprises of a battery of tests to assess processing of frequency, intensity and temporal parameters of sound in the auditory system (Bellis, 2011). Temporal processing is the ability of the auditory system to process the time related changes in the incoming signal. Previous studies have shown that the temporal processing abilities are affected in individuals with tinnitus (Fournier & Hébert, 2013; Jain & Dwarkanath, 2016; Gilani et al., 2013; Sanches, Samelli, Nishiyama, Sanchez, & Carvallo, 2010; Turner et al., 2006). Jain and Dwarkanath (2016) administered a series of temporal processing tests in 22 unilateral tinnitus participants and 16 bilateral tinnitus participants. The temporal processing was assessed using various measures including gap in noise test, amplitude modulation detection test, duration pattern test, duration discrimination test and backward masking test. Their results revealed significantly poorer temporal processing abilities in individuals with tinnitus, with severity being more for those with bilateral tinnitus. These studies have shown that temporal processing assessment is a reliable measure to assess the tinnitus. Hence, the aim of the present study was to measure the effectiveness of clinical trial of TRT for 12 months using a series of temporal processing tests including gap in noise test, temporal modulation transfer function, duration pattern test, duration discrimination test, and backward masking test, on individuals with bilateral symmetrical tinnitus.

Material and Methods

Participants

A longitudinal study design using a randomized experimental clinical trial was employed for the present study. A total of 46 participants with normal hearing sensitivity participated in the study. The participants were divided into three groups, viz., an experimental group of 16 tinnitus individuals (TI), a placebo group of 10 tinnitus individuals (PI) and a control group of 20 individuals with no tinnitus (NI). The participants in TI and PI group characterized their tinnitus as continuous, non-pulsatile perception of the sound in the absence of any external stimuli in both the ears, at least from last 6 months or more. Among them, TI received tinnitus retraining therapy for twelve months, whereas PI never received tinnitus retraining therapy or any other form of tinnitus rehabilitation. The evaluation of tinnitus and other psychoacoustic measures were carried out four times during the course of therapy in TI participants, i.e. at baseline (before starting the retraining therapy), one month, six months and twelve months after therapy. Only those participants who attended the therapy continuously and were available for tinnitus evaluation at each time interval were considered for the study. For PI and NI, no therapy was given; however, the measurements were done at the same time interval as mentioned for TI. The severity of tinnitus was measured using tinnitus handicap inventory in Kannada (Zacharia, Naik, Sada, Kuniyil, & Dwarakanath, 2012) and the participants having mild to severe tinnitus were only considered for the study. All tinnitus participants had bilateral symmetrical percept of tinnitus. The hearing sensitivity for pure tones (within the frequency range of 250 Hz to 14 kHz) and speech was within normal limits. The PTA was less than/equal to 15 dB and SRT + 10 dB of PTA (average of 500, 1kHz and 2kHz thresholds) and the thresholds at individual frequencies not more 20 dB till 8 kHz, 20 dB for 10 kHz and 30 dB for 12 and 14 kHz, were considered (Figure 1). Structured interview revealed that none of the participant had conductive pathology, speech, language, neurological or psychological disorder including excessive stress and depression. The participants were minimally anxious at the time of testing, as measured using Hamilton Anxiety Rating Scale (Hamilton, 1959). Table 1 shows the detailed tinnitus characteristic of each participant.

Tests

The participants matched the pitch and loudness of tinnitus to confirm the symmetry of tinnitus. For pitch matching, participants heard a pure tone and a broadband noise and stated whether his/her tinnitus is more like a tone or noise. Nine TI participants reported tonal perception of tinnitus and seven reported noisy perception of tinnitus. Similarly, seven PI participants reported tonal tinnitus and rest three-reported noisy tinnitus. For participants with tonal tinnitus perception, the pure tone frequency was narrowed down first in octave bands, and further in 1 Hz steps to match the tinnitus as closely as possible, using the audiometer. The participants with the noisy perception of tinnitus also followed the same procedure, where the broadband frequency tapered to the narrow band frequency region, to match the tinnitus as closely as possible. For loudness matching, the intensity of pure tone or narrow band noise was increased or decreased in such a way that the loudness of the sound matches as closely as possible to the tinnitus loudness. The loudness matching was at the perceived tinnitus pitch only.

Following this, temporal processing assessment

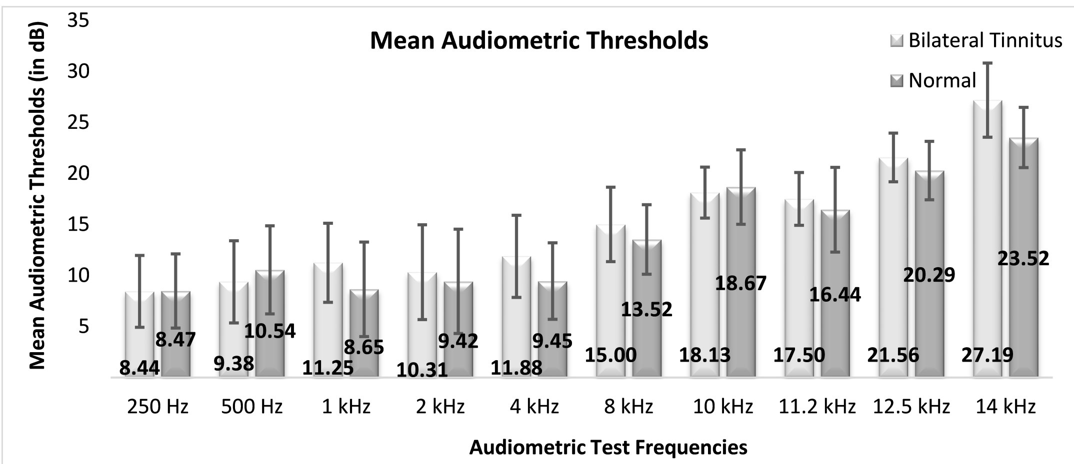

Figure 1: Mean hearing thresholds (in dB HL) for participants having bilateral tinnitus and normal hearing across regular octaves and extended high frequencies. The error bar represents standard deviation.

Table 1: Demographic data and detailed tinnitus characteristics of TI and PI

S. No.	Participant I.D.[a]	Age (years)/ Sex	Severity of Tinnitus[b]	PTA (R)	PTA (L)	Tinnitus characteristics[c]	Duration of tinnitus (months)	Annoyance level[d]
1.	TA	41/F	Severe	13.3	15	Ringing	15 months	Very
2.	TB	42/F	Mild	13.3	11.6	Buzzing	18 months	Mild
3.	TC	40/M	Severe	11.6	11.6	Hissing	17 months	Moderate
4.	TD	28/F	Moderate	10	8.3	Ringing	16 months	Moderate
5.	TE	33/M	Moderate	11.6	10	Roaring	12 months	Mild
6.	TF	31/F	Moderate	13.3	13.3	Buzzing	7 months	Moderate
7.	TG	49/F	Severe	11.6	15	Ringing	6 months	Very
8.	TH	50/M	Moderate	11.6	13.3	Roaring	6 months	Moderate
9.	TI	50/M	Moderate	13.3	8.3	Buzzing	14 months	Mild
10.	TJ	35/M	Severe	13.1	11.6	Whistling	12 months	Moderate
11.	TK	36/F	Severe	10	11.3	Ringing	23 months	Very
12.	TL	34/F	Severe	15	13.3	Ringing	13 months	Moderate
13.	TM	32/M	Moderate	13.3	11.6	Whistling	17 months	Very
14.	TN	29/M	Severe	15	15	Buzzing	8 months	Moderate
15.	TO	43/M	Severe	13.3	15	Ringing	11 months	Very
16.	TP	39/F	Severe	15	11.6	Roaring	16 months	Very
17.	PA	37/M	Moderate	11.6	15	Whistling	14 months	Moderate
18.	PB	36/M	Moderate	13.3	15	Buzzing	13 months	Moderate
19.	PC	34/F	Mild	15	15	Buzzing	14 months	Mild
20.	PD	35/M	Moderate	15	13.3	Whistling	12 months	Very
21.	PE	28/F	Severe	11.6	10	Roaring	8 months	Very
22.	PF	27/M	Moderate	10	11.6	Roaring	7 months	Very
23.	PG	26/F	Severe	13.3	15	Ringing	11 months	Moderate
24.	PH	39/F	Severe	13.3	13.3	Ringing	11 months	Very
25.	PI	31/M	Severe	11.6	15	Ringing	9 months	Very
26.	PJ	33/M	Moderate	10	11.6	Ringing	8 months	Mild

[a] *T = Tinnitus (Experimental) Group; P = Tinnitus (Placebo) Group*
[b] *Severity of tinnitus based on tinnitus handicap index (Kannada version)*
[c] *Tinnitus characteristics as reported by participants in both the ears*
[d] *Annoyance level measured on a 7-point scale*

was done using gap in noise test (GIN), temporal modulation transfer function (TMTF), duration pattern test (DPT), duration discrimination test (DDT) and backward masking test (BM). The complete test battery except DPT was done using maximum likelihood procedure [MLP, a MATLAB toolbox for psychoacoustic experiments; (Grassi & Soranzo, 2009)] routed via the audiometer. In MLP, the psychometric function of large set of participants was derived and their response for each trial was noted. The likelihood of responses was then arrived and a psychometric function was drawn. The psychometric function that gives the highest likelihood was used to decide the stimulus presented in the next trial, in a 3-alternative adaptive forced choice method. Each trial consisted of three blocks, wherein, two blocks had the standard stimulus and the other block chosen randomly had the variable stimulus. The stimulus for all the tests was presented binaurally at 75 dB SPL (average most comfortable loudness level), in a standardized acoustically treated double room audiometry setup. The tests were administered binaurally as no significant ear effect was observed in the previous study (Jain & Dwarkanath, 2016). The entire set of test administration required approximately 1-1.5 hour for each participant, and took place in a single sitting, with 2-3 breaks of 5 min each. The institution's ethical board approved the study and written informed consent was taken from each participant prior to the evaluation.

Tinnitus Retraining Therapy

TRT (Jastreboff & Jastreboff, 2000), comprised of counseling and sound therapy sessions. Initially, 3-4 counseling session (80-90 minutes each) was given by a qualified audiologist, who was practicing TRT from last five years by employing the procedures suggested in the literature. The directive intensive counseling aimed to explain the anatomy

Table 2: Significance of difference in scores for various psychoacoustic tests across groups as a function of trials.

Tests	Between Group Comparison	Baseline		PT1		PT2		PT3	
		M.D	p	M.D	p	M.D	p	M.D	p
GIN	TI vs PI	1.02	0.13	0.84	0.16	-1.33	0.03*	-1.08	0.59
	TI vs NI	5.51	0.00*	5.07	0.00*	3.15	0.00*	1.57	0.08
	PI vs NI	4.49	0.00*	4.23	0.00*	4.48	0.00*	2.65	0.00*
TMTF (8 Hz)	TI vs PI	1.25	0.27	1.27	0.27	3.21	0.00*	3.17	0.01*
	TI vs NI	6.68	0.00*	7.14	0.00*	8.47	0.00*	6.52	0.00
	PI vs NI	5.42	0.00*	5.87	0.00*	5.26	0.00*	3.35	0.00*
TMTF (60 Hz)	TI vs PI	1.09	0.10	1.31	0.12	2.23	0.00*	2.29	0.02*
	TI vs NI	4.90	0.00*	5.38	0.00*	6.42	0.00*	4.72	0.00*
	PI vs NI	3.80	0.00*	4.06	0.00*	4.18	0.00*	2.43	0.01*
TMTF (200 Hz)	TI vs PI	0.27	1.00	0.31	0.84	3.47	0.00*	1.24	0.03*
	TI vs NI	3.03	0.00*	3.45	0.00*	3.47	0.00*	2.93	0.00*
	PI vs NI	2.76	0.00*	3.13	0.00*	2.44	0.00*	1.68	0.00*
DPT	TI vs PI	-1.23	0.46						
	TI vs NI	-1.58	0.09	Testing was not done					
	PI vs NI	-0.35	1.00						
DDT	TI vs PI	45.14	0.06	34.39	0.11	-40.55	0.11	-26.94	0.91
	TI vs NI	146.56	0.00*	143.01	0.00*	71.73	0.00*	32.58	0.41
	PI vs NI	101.41	0.00*	108.61	0.00*	112.28	0.00*	59.52	0.06
BM	TI vs PI	3.68	0.30	3.92	0.22	28.21	0.00*	10.88	0.01*
	TI vs NI	21.06	0.00*	21.03	0.00*	28.21	0.00*	19.25	0.00*
	PI vs NI	17.37	0.00*	17.11	0.00*	15.83	0.00*	8.37	0.05*

M.D = mean difference

Digits in bold are significant to 95% confidence interval

Table 3: Significance of difference in scores for various psychoacoustic tests across groups as a function of trials.

Test	Group	B vs P1		B vs P2		B vs P3		P1 vs P2		P1 vs P3		P2 vs P3	
		MD	p	MD	p	MD	p	MD	p	MD	p	MD	p
GIN	TI	0.29	0.20	2.60	**0.00**	3.03	**0.00**	2.31	**0.00**	2.74	**0.00**	0.42	1.00
	PI	0.24	1.00	0.01	1.00	0.59	1.00	0.26	1.00	0.34	1.00	0.61	1.00
	NI	0.14	0.44	0.24	0.25	0.15	1.00	0.39	0.05	0.00	1.00	0.39	0.03
TMTF (8Hz)	TI	0.28	0.10	1.67	**0.00**	1.85	**0.00**	1.38	**0.00**	1.56	**0.00**	0.17	0.12
	PI	1.23	0.14	0.43	1.00	1.14	0.31	0.80	1.00	0.08	1.00	0.71	1.00
	NI	0.17	1.00	0.12	1.00	0.31	1.00	0.05	1.00	0.13	1.00	0.19	1.00
TMTF (60Hz)	TI	0.19	0.05	1.26	**0.00**	1.43	**0.00**	0.93	**0.00**	1.24	**0.00**	0.31	0.11
	PI	0.40	1.00	0.43	1.00	0.11	1.00	0.02	1.00	0.52	1.00	0.55	1.00
	NI	0.29	1.00	0.39	0.32	0.55	0.56	0.10	1.00	0.26	0.99	0.16	1.00
TMTF (200Hz)	TI	0.15	0.08	0.35	0.59	0.66	**0.00**	0.19	1.00	0.50	**0.00**	0.31	0.11
	PI	0.71	0.08	0.12	1.00	0.88	0.54	0.58	0.70	0.17	1.00	0.75	0.74
	NI	0.25	1.00	0.08	1.00	0.19	1.00	0.17	1.00	0.06	1.00	0.11	1.00
DDT	TI	10.22	0.06	74.37	**0.00**	78.74	**0.00**	64.1	**0.00**	68.5	**0.00**	4.37	0.29
	PI	1.45	0.10	18.06	1.00	41.2	0.92	23.4	0.86	0.26	1.00	23.2	0.52
	NI	6.67	1.00	0.45	1.00	4.14	1.00	7.13	1.00	10.81	0.52	3.68	1.00
BM	TI	0.70	1.00	0.86	0.80	3.24	0.06	6.16	**0.00**	6.53	**0.00**	0.37	0.05
	PI	2.32	1.00	2.20	1.00	2.17	1.00	0.12	1.00	0.15	1.00	0.03	1.00
	NI	0.73	1.00	0.28	1.00	0.25	1.00	1.01	1.00	0.47	1.00	0.53	1.00

**Significant at 95% confidence interval.*

M.D = mean difference

and physiology of the auditory system, possible mechanism behind the tinnitus perception, negative behaviors associated with tinnitus and misconceptions about tinnitus. The counselor highlighted the role of limbic and autonomic nervous system in the generation of tinnitus, subconscious processing of auditory stimuli, filtering and blocking of auditory stimuli from reaching consciousness and measures to divert the attention from the tinnitus. Following this, sound therapy sessions were provided. During sound therapy sessions, a white noise was presented to each participant at the level slightly (approximately 5 dB) below the tinnitus loudness for an average of four therapy session per client (a minimum of three and maximum of six sessions were provided). The sound therapy was provided via a laptop equipped with supra-aural headphones monitored for the output using standardized sound level meter (B & K 2238, Mediator).

Procedure

Once the participants got adjusted to the background stimuli, the sound file was transferred to their respective mobile phones and they were instructed to hear to the sound as long as they can, using the headphones equipped with the mobile. A sound level meter monitored the output of the mobile phones and matched it with the output of the laptop. Each participant maintained a daily diary to enter the duration of sound therapy. The participant manipulated the output of the noise each day, to match their tinnitus. This is based on the assumption that tinnitus fluctuates during the course of treatment, which leads to changes in the tinnitus loudness over time. During the first month of therapy, participants came once a week to clinic to ensure that the instructions are followed and it also involved a brief counseling session of approximately 45 minutes. Thereafter, the participants followed-up once in a month for successive twelve months to guarantee that they were following the sound therapy. Counseling was given in each follow-up session. All the temporal processing tests were repeated after first, sixth and twelfth month of therapy for all the participants. The scores for each specific test was compared across four trials, i.e., baseline, 1 month post-therapy (PT1), 6 months post-therapy (PT2) and 12 months post-therapy (PT3). The temporal processing assessment was also done for P1 and N1 group at the same interval, but they did not received any TRT.

Results

The Shapiro-Wilk test revealed that the data was normally distributed; hence, parametric statistics was done to assess the significance of difference for various psychoacoustic tests across trials and groups. The one way ANOVA estimated the difference in scores, for various psychoacoustic tests for each trial among groups. As expected, there was a significant group effect for all the test scores, measured at baseline, except DPT. No significant difference was seen between TI and PI for any test measured at baseline (Table 2). These results ensured that the psychoacoustic abilities at baseline were similar within tinnitus individuals (TI and PI). Repeated measure ANCOVA estimated the significance of TRT on the psychoacoustic abilities for TI. The scores at four trials (from baseline to PT3) were ‘within subject variables’ and the group distribution, as ‘between subject factors’, with the severity of tinnitus as ‘covariate’. Bonferroni’s corrections for multiple comparison was done to compare the results across trials. The results are categorized with respect to each test in the following section. Further, the effect of TRT on the subjective perception of tinnitus and the relationship between tinnitus annoyance with THI scores and loudness was established.

Gap in Noise Test

The graph 2a represents the mean GIN scores for TI, PI and NI across four trials (i.e. baseline, PT1, PT2 and PT3). The reduction in the mean scores of GIN from baseline to PT3 for TI could be attributed to the effect of TRT. There was no change in the GIN scores, from baseline to PT3 among PI, indicating that aftermath trials or time duration has no significant effect on the temporal resolution abilities in individuals with tinnitus (Table 3). Minimal change in the threshold for PI and NI across trials ruled out the practice effect influencing scores. The data violated the assumption of sphericity (Mauchly’s $W = 0.303$; $\varepsilon = 0.628$; $p<0.01$), and Greenhouse-Geisser correction was employed. Tests for within subject effect revealed a significant trial effect [F (3, 99) = 5.15; $p<0.05$, partial $\eta^2 = 0.702$] and a significant interaction effect for trials across groups [F (3, 99) = 4.54; p¡0.05, partial ? 2 = 0.519] as represented in Table 4. However, no effect of severity across trials was seen [F (3, 99) = 2.06; $p>0.05$]. Pair-wise comparison across trails within TI indicated significant change in the mean GIN scores between baseline and PT2; baseline and PT3; PT1 and PT2 (Table 3).

Temporal Modulation Transfer Function Test

The TMTF scores at the modulation frequency of 8 Hz, 60 Hz and 200 Hz was measured as a function of groups and trials (Figure 2b, c and d). An improvement was seen in performance for TI from baseline to PT3. The performance did not change markedly for PI and NI across trials. The results for TMTF at all modulation frequencies revealed a significant effect of TRT as the scores improved markedly from baseline to PT3 as represented in Table 4. The effect size was also calculated and tabulated in table 4, where more than 50% of variance in the TMTF scores was attributed to the tinni-

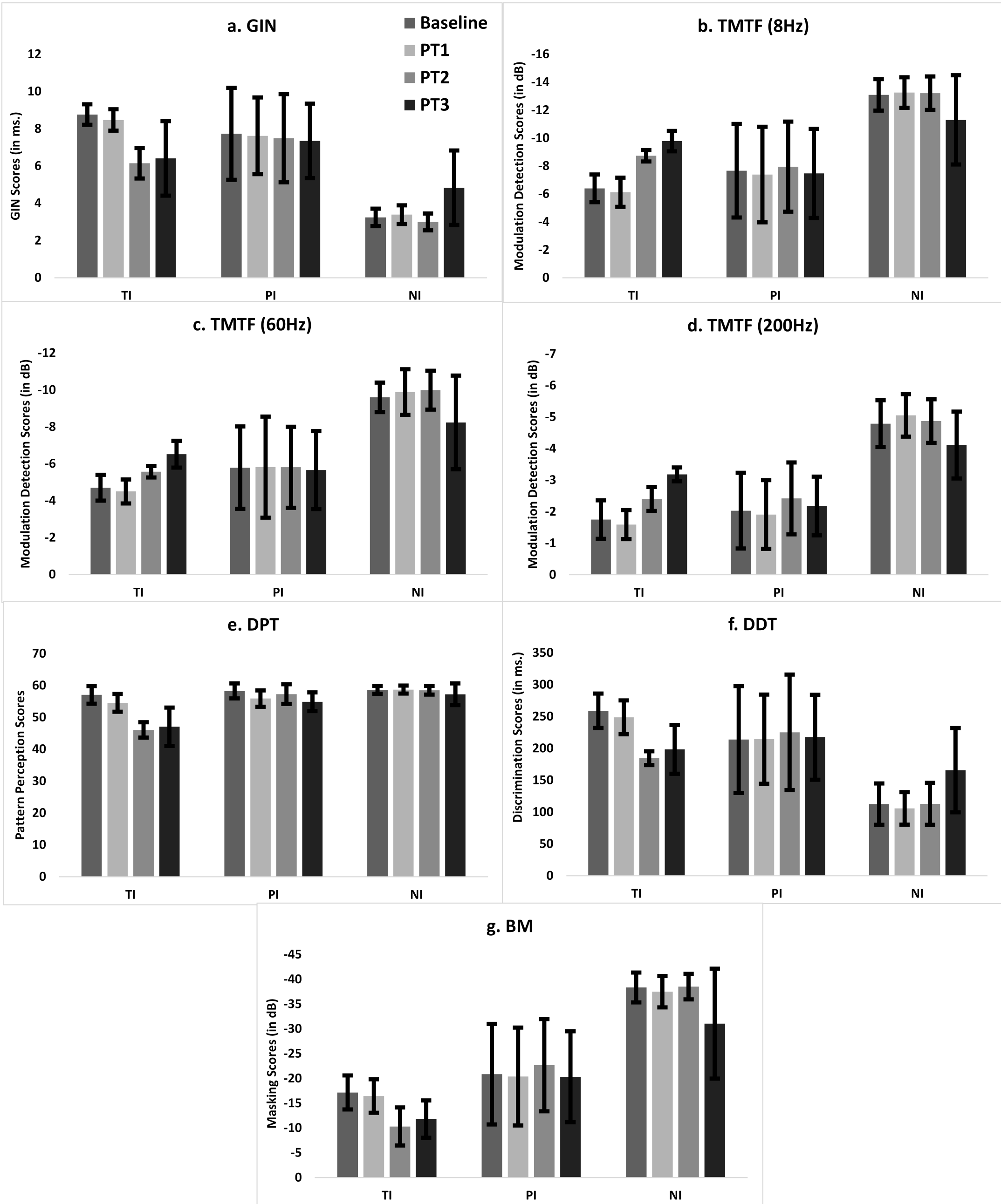

Figure 2: Mean scores for the temporal processing tests across trials for the three groups [group with tinnitus (TI), placebo goup (PI) and group with no tinnitus (NI)]. The error bar represents standard deviation.

tus retraining therapy. Further, severity of tinnitus also had no significant effect on the mean scores. Pair-wise comparison among TI revealed significant improvement in the mean scores for 8 Hz and 60 Hz modulation frequency from baseline to PT2; PT1 to PT2. From baseline to PT3 and PT1 to PT3, the significant improvement in scores was noted for all the modulation frequencies (Table 3).

Duration Pattern Test

The mean DPT scores as a function of the group across trials is shown in figure 2e. The tinnitus had minimal effect on the scores of DPT. The scores were similar for all the three groups at baseline (Table 2). These results indicate that duration pattern perception is independent of tinnitus, and hence further analysis was not done.

Duration Discrimination Test

The mean DDT scores for TI, PI and NI across trials is plotted in figure 2f. The mean scores gradually improved with time for TI. No significant difference in the mean scores between TI and PI, but the scores of TI and NI, PI and NI were significantly different, at baseline (Table 2). These results indicate that temporal discrimination is impaired in tinnitus individuals. The number of trials had minimal effect on the scores of DDT for PI and NI. However, for TI, the scores improved significantly from baseline to PT3 [$F\ (3, 99) = 4.19$; $p<0.05$, partial $\eta^2 =$

0.627]. The interaction of trials and the group also revealed a significant difference [F (3, 99) = 3.31; p<0.05, partial η^2 = 0.353], but no such threshold difference across trials was observed with respect to the severity of tinnitus [F (3, 99) = 0.96; p>0.05] as tabulated in Table 4. Bonferroni's comparison revealed significantly different DDT scores between baseline and PT2; baseline and PT3; PT1 and PT2; PT1 and PT3, but not between baseline and PT1; PT2 and PT3 (Table 3).

Backward Masking

Figure 2g shows the mean BM scores as a function of groups and trials. As evident, the mean scores for TI improved from baseline to PT3; however, the change was not statistically significant [F (3, 99) = 0.34; p>0.05] (Table 4). Similarly, no improvement was seen for PI and NI. The mean scores were significantly different between TI and PI; TI and NI at baseline (Table 2), but overall no significant difference in the mean scores for interaction between trials and group [F (3, 99) = 1.84; p>0.05]; trials and severity [F (3, 99) = 0.96; p>0.05] was noted (Table 4).

Effect of TRT on the Subjective Perception of Tinnitus

Tinnitus Severity Table 5 shows the comparative scores between the severity of tinnitus at the baseline and PT3 using THI-K. The severity of perceived tinnitus reduced with continuous therapy, as the post therapy scores were better than the pre therapy scores. TRT had a more pronounced effect on individuals with severe tinnitus than those with mild-moderate tinnitus. As evident from the table 5, the severity of tinnitus in participant TJ and TN reduced from severe to mild level, for participants TA, TC, TG, TK, TL, TO and TP improved from severe to moderate level, and for participants TE, TF, TH, TM, and TI the severity reduced from moderate to mild degree. For participant TB and TD the severity did not vary, but the scores reduced. In two-factor repeated measures ANOVA, the baseline and PT3 scores were considered as the within subject variables and severity of tinnitus was considered as between subject factor. The results revealed a significant effect of therapy [F (1, 13) = 33.41; p<0.05, partial ?2 = 0.535] on the severity of tinnitus. On the other hand, individuals in the placebo group showed no change in the tinnitus severity with trials. The only exception to this was participant PG who reported a change in the severity of tinnitus from severe to moderate with time.

Tinnitus Loudness The Table 5 shows the comparative score between the loudness of tinnitus measured at baseline and PT3. There was an average of 5.5 dB decrease in the loudness perception. Except for participant TD and TK, the tinnitus loudness reduced in rest fourteen participants. These two subjects showed minimal change in tinnitus loudness perception. These results were statistically analyzed and a significant effect of TRT on the loudness perception thresholds [F (1, 13) = 25.764; p<0.05, partial η^2 = 0.725] was noted. On the other hand, the interaction between tinnitus severity and loudness perception scores revealed no statistically significant effect [F (1, 13) = 0.104; p>0.05]. The difference is attributed to the effect of TRT as no change in the tinnitus loudness perception was seen in the placebo group with respect to trials, indicating that practice has minimal effect on tinnitus loudness perception.

Tinnitus Related Annoyance The effect of TRT was also evident on the perceived annoyance level of tinnitus as administered using a 7-point Tinnitus Annoyance Scale (Henry, Rheinsburg, & Zaugg, 2004) ranging from no annoyance ('0') to worst possible annoyance ('6'), the scores of which are tabulated in table 5 (for baseline and PT3). The participants reported that the tinnitus is less bothersome to them and most of them were satisfied with the therapy. Nevertheless, none of the participant stated that they are not at all annoyed with their tinnitus. Even participant TB who had mild annoyance due to tinnitus, reported that though the tinnitus severity reduced after therapy, the participant was still annoyed because of tinnitus to a certain extent. For the remaining participants, the tinnitus was annoying to a convincing level. Participants TD and TH even reported that immediately after training, the tinnitus was more annoying, but with the course of therapy, the tinnitus was comparatively less irksome. Repeated measures ANOVA estimated the significance of differences between baseline and PT3 annoyance scores and the results indicated a significant effect of TRT in reducing tinnitus related annoyance [F (1, 13) = 14.130; p<0.05, partial η^2 = 0.652]. Once again, no significant effect of tinnitus severity on the annoyance related to tinnitus was observed [F (1, 13) = 0.355; p>0.05].

To estimate the relationship between the three subjective variables a multinomial logistic regression was carried out. The annoyance scores were 'dependent variables', and the THI and loudness scores were 'factors'. The baseline scores, PT3 scores, and the severity of tinnitus were 'covariates'. The model fitting information with non-significant likelihood ratio (p = 0.659) indicated that the model fits the data well. The likelihood ratio test indicated that neither THI scores, nor loudness scores were significantly different from the annoyance scores (p = 0.999 & 0.996, respectively). These results show that the change in annoyance scores could be due to the change in THI and loudness scores.

Table 4: The results of repeated measures ANCOVA indicating the significance of differences across trials, trials as a function of the group, and across trials as a function of severity

Tests	Trials			Trials*Group			Trials*Severity	
	F	p	Partial η^2	F	p	Partial η^2	F	p
GIN	5.150	0.023*	0.702	4.548	0.006*	0.519	2.061	0.168
TMTF 8Hz	5.743	0.009*	0.621	1.363	0.260	-	1.339	0.279
TMTF 60Hz	3.829	0.048*	0.686	0.706	0.562	-	0.047	0.918
TMTF 200Hz	1.840	0.036*	0.512	1.491	0.212	-	0.619	0.501
DDT	4.193	0.036*	0.627	3.314	0.020*	0.353	0.854	0.416
BM	0.343	0.794	-	1.841	0.144	-	0.969	0.393

*Note: *Significant at 95% confidence interval.*

Discussion

The present study aimed to evaluate the long-term effect of TRT using temporal processing tests in tinnitus individuals with normal hearing sensitivity. The findings clearly indicate that the temporal processing abilities improves following therapy. Since, Pawel and Margaret Jastreboff proposed the tinnitus retraining therapy in the late 1990's (Jastreboff & Jastreboff, 2000), numerous researchers have reported the effectiveness of tinnitus following TRT. A brief review of literature revealed that approximately 18-19 studies in the past addressed the benefit. All these studies have either used patients self-reported improvement in tinnitus, tinnitus handicap inventories, tinnitus handicap questioner, visual analog scale, or other procedures to evaluate the efficacy of TRT, details of which is tabulated in table 6. However, the clinical validity of such measures alone are questionable (Clark & Watson, 1995). Thus, a more systematic approach to measure the efficacy carved the need of the present study. Since, previous research revealed that temporal processing abilities are affected in the individuals with tinnitus (Jain & Dwarkanath, 2016), the same temporal measures along with tinnitus handicap inventory and annoyance scale were used to evaluate the effectiveness of TRT. The results of the current study indicate that the scores for the temporal processing tests improved significantly after twelve months of therapy except for DPT and BM. Despite such exceptions, other test findings provide reasonable evidence to establish an association.

The strength of the present study lies in both subject and test selection process. The participants were having bilateral symmetrical tinnitus. In the previous study, Jain and Dwarkanath (2016) discussed that the origin of bilateral tinnitus is possibly because of the involvement of cortical and sub-cortical structures. The generation of unilateral and bilateral tinnitus is different, thus it is reasonable to assume that asymmetrical tinnitus may have differential processing in the auditory system that might affect the therapeutic outcome. Further, symmetrical tinnitus also represent the homogeneity among the participants. The inclusion of placebo control group ruled out the effect of time on temporal processing abilities and effect of practice was controlled using the control participants.

All the participants in the present study had normal hearing sensitivity. Temporal processing abilities are affected in individuals with hearing loss in the conventional frequency range (Bacon, Opie, & Montoya, 1998; Leigh-Paffenroth & Elangovan, 2011; Moore, Peters, & Glasberg, 1992) as well as in the extended high frequency region (Ramos & Pereira, 2005). It was also observed that the hearing sensitivity beyond 8000 Hz provide more information regarding the generation of tinnitus (Fabijańska et al., 2012; Yildirim, Berkiten, Kuzdere, & Ugras, 2010). The findings for high frequency audiometry pointed towards comparable hearing sensitivity between participants with tinnitus and control group. Hence, the role of high frequency hearing loss resulting in affected temporal processing test scores was controlled.

Along with hearing sensitivity, anxiety due to tinnitus was also controlled among participants. The exact relationship between anxiety and tinnitus is unknown, but some researchers highlight the anxiety as a symptom of tinnitus (Halford & Anderson, 1991; Stephens & Hallam, 1985) while other focus on the role of anxiety in tinnitus percept (Erlandsson & Archer, 1994). Puel and Guitton (2007) stated that anxiety does not produce tinnitus, but it exaggerate the perception of tinnitus. Thus, although the exact relationship between tinnitus and anxiety is unknown, anxiety and tinnitus are related in some or the other ways. In the present study, the anxiety was measured using Hamilton rating scale (Hamilton, 1959). On a five point rating scale, the individual?s experiences were noted for 12/14 physiological and psychological conditions related to the severity of anxiety. Ex-

Table 5: The comparison between pre therapy (baseline) and post therapy (PT3) THI scores, perceived loudness level and perceived annoyance level

Participant I.D.	Baseline scores[a]	PT3 scores[a]	Baseline severity level[b]	PT3 severity level[b]	Baseline perceived loudness[c]	PT3 perceived loudness[c]	Baseline annoy-ance level[d]	PT3 an-noyance level[d]
TA	60	52	Severe	Moderate	27 dB	23 dB	4	2
TB	34	22	Mild	Mild	25 dB	20 dB	2	1
TC	64	40	Severe	Moderate	28 dB	20 dB	3	2
TD	56	44	Moderate	Moderate	23 dB	21 dB	3	3
TE	40	34	Moderate	Mild	30 dB	26 dB	2	1
TF	50	34	Moderate	Mild	29 dB	25 dB	3	2
TG	62	54	Severe	Moderate	31 dB	25 dB	4	2
TH	46	32	Moderate	Mild	23 dB	19 dB	3	1
TI	50	36	Moderate	Mild	29 dB	21 dB	2	2
TJ	60	36	Severe	Mild	27 dB	18 dB	3	1
TK	62	48	Severe	Moderate	27 dB	26 dB	4	2
TL	70	54	Severe	Moderate	28 dB	23 dB	3	3
TM	52	34	Moderate	Mild	25 dB	16 dB	4	2
TN	60	54	Severe	Mild	28 dB	18 dB	3	2
TO	58	50	Severe	Moderate	30 dB	25 dB	4	3
TP	66	52	Severe	Moderate	28 dB	24 dB	4	3

[a] *Scores calculated using tinnitus handicap inventory in Kannada (THI-K)*
[b] *Severity of tinnitus estimated as per THI-K scoring*
[c] *Values mentioned in terms of audiometric intensity units (dB HL)*
[d] *Perceived annoyance level as reported by the participants on 7 point tinnitus annoyance scale*

cept for question no. 4 and 8 in the rating scale, all the participants reported that the behavior was absent (0), or mild (1). Question 4 enquires about ?insomnia?, where the participant had to report any difficulty in sleeping or waking. Most of the participants in the tinnitus group reported disturbed sleep, and stated that the perception of tinnitus increases at night. This is a common problem associated with tinnitus and attributed to the increased neuronal activity in the auditory pathway as auditory system continuously monitor the sound environment during sleep (Jastreboff & Hazell, 2004). Hence, disturbed sleep was not associated with the anxiety rating. Similarly, for question no. 8, the information related to somatic (sensory) behavior was a self-reported measure of tinnitus severity. No participant reported blurring of vision, feeling of weakness and pricking sensation, but all reported perception of tinnitus. Thus, these two conditions were excluded. The remaining twelve conditions were scored, but not categorized according to the severity of anxiety, as the two conditions were removed. Nonetheless, all participants scored ‘1’ or less for all twelve conditions, before measuring the temporal processing skills. However, for some trials, few participants were anxious during the testing session. They were counseled to be relaxed, and testing was carried out on the day or two following it, after re-administering the anxiety, and ensuring that the subjects were less anxious.

It is also worthy to note that the temporal processing tests used in the present study are sensitive to measure the physiological changes in the auditory system. Pickles (1988) and Moore (1997) found that the inferior colliculus as well as the medial geniculate body play a major role in auditory temporal perception in normal hearing individuals. The inferior colliculus (Rees & M?ller, 1983) and medial geniculate body (Rouiller, de Ribaupierre, Toros-Morel, & de Ribaupierre, 1981) play a vital role in modulation detection, an important parameter of temporal resolution. Similarly, Brosch, Schulz and Scheich (1998) suggested the neural correlate of backward masking is in the cortical and sub-cortical regions of the brain. Other studies also revealed the involvement of insula in the pattern perception (Bamiou et al., 2006) and gap detection procedures (Bamiou et al., 2006; Efron, Yund, Nichols, & Crandall, 1985; Musiek et al., 2005). Colavita, Szeligo, and Zimmer, 1974) reported that the pattern perception ability is normal only when insular-temporal cortex is intact. According to them, ablation of insular-temporal cortex in cats affects the ability to order three stimuli based on duration. However, in humans, the duration pattern is less sensitive to differentiate between normal and abnormal processing because of easiness of the task. The result for DPT is dis-similar to that obtained in the previous study (Jain & Dwarkanath, 2016). This pose a serious question on the test

*Table 6: Summary of the research literature indicating the measures used to evaluate the long-term effect of TRT**

S. No.	Authors	Year	'n'	Duration of TRT	Measures of Evaluation
1.	Inagaki, Oishi, Kanzaki, et al.	2014	33	2 years	THI
2.	Kim, Chung, Jung & Suh	2014	38	9 weeks	THI; VASI
3.	Beriat, Ezerarslan, Akmansu et al.	2011	91	1 year	THI; VASI; AP
4.	Bauer & Brozoski	2011	21	18 months	THI; BDI
5.	Ariizumi, Hatanaka & Kitamura	2010	270	18 months	PLM; PA
6.	Korres, Mountricha, Balatsouras, Maroudias, Riga & Xenelis	2010	63	1 year	THI; VASI
7.	Forti, Costanzo, Crocetti, Pignataro, Del Bo & Ambrosetti	2009	45	18 months	THI
8.	Herraiz, Hernandez, Toledano & Aparicio	2007	137	1 year	THI;VASI; PSE
9.	Maderia, Montmirail, Decat & Gersdorff	2007	46	1 year	PSE
10.	Baracca, Forti, Crocetti et al.	2007	51	18 months	PSE; THQ
11.	Londero, Peignard, Malinvaud, Avan & Bonfils	2006	96	1 year	THQ
12.	Caffier, Haupt, Scherer & Mazurek	2006	70	2 years	THQ ; TSQ ; VASI
13.	Mazurek, Fischer, Haupt, Georgiewa, Reisshauer & Klapp	2006	92	1 year	THQ; PLM; SECDI
14.	Henry, Schechter, Zaugg et al.	2006	123	18 months	THI; THQ; TSQ
15.	Suchova	2005	55	6 months	PSE
16.	Herraiz, Hernandez, Plaza & de los Santos	2005	158	1 year	THI; VASI
17.	Berry, Gold, Frederick, Gray & Staecker	2002	32	6 months	THI; PSE
18.	Wang, Jiang, Yang & Han	2002	117	1 year	PSE
19.	Bartnik, Fabijanska & Rogowski	2001	68	2 years	THQ

**Source: Pub Med (http://www.ncbi.nlm.nih.gov/pubmed/)*
THI = Tinnitus Handicap Inventory; VASI = Visual Analog Scale of Intensity; AP = Audiological Parameters; BDI = Beck's Dépression Inventory; PLM = Psychoacoustic Loudness Measures; PA = Patient's Attitude; PSE = Patient's Self Evaluation; THQ = Tinnitus Handicap Questioneer; TSQ = Tinnitus Severity Questionnaire; SECDI = Scale of Emotional and Cognitive Distress and Intrusiveness.

retest reliability of DPT, as the stimuli and participants were same. Minimal change in the BM scores across trials could be attributed to the task difficulty.

The findings of the present study provide an insight to the generation of tinnitus. The anatomical or the physiological changes may occur in the central auditory system after long-term training. These effects are not defined after short-term therapy. The significant changes were observed only after six or twelve months of therapy (PT2 or PT3) but not after one month of therapy (PT1). Thus, training changes the neural plasticity. Researchers (Gaser & Schlaug, 2003; Pantev et al., 1998; Pantev, Engelien, Candia, & Elbert, 2001; Peretz & Zatorre, 2005) showed that long term musical training result in the structural and the functional changes in the auditory system, in turn, leads to the changes in the processing of the auditory stimuli. Other findings (Trainor, Shahin, & Roberts, 2009) even focused on cortical changes as well as subcortical and lower brainstem changes (Kraus, Skoe, Parbery-Clark, & Ashley, 2009; Krishnan, Gandour, Bidelman, & Swaminathan, 2009) after long term training. Apart from neuroanatomical and neurophysiological changes, evidences even suggest neurochemical changes in the auditory nervous system following sound therapy. The release of the nitric oxide in the auditory system results in the relaxation induced by continuous low level soothing sound (Salamon, Kim, Beaulieu, & Stefano, 2003). This may be a possible reason of reduced annoyance in tinnitus individuals after sound therapy.

The most important outcome of this study is that it confirms the involvement of central auditory system in the generation of tinnitus. In absence of any peripheral pathology, the temporal processing tests employed in the present study are highly sensitive to the structural and functional changes in the sub-cortical and cortical structures (Chermak & Musiek, 1997; Freigang et al., 2011; Ludwig et al., 2014). The reduced scores on these tests in individuals with tinnitus clearly indicate certain sub-cortical or cortical involvement in tinnitus (Jain & Dwarkanath, 2016). These observations were further confirmed by measuring the effectiveness of TRT in the reduction of perceived tinnitus. According to Jastreboff and Jasterboff (2000) TRT induces changes in the neuronal activity of the auditory system, which are responsible for the generation of tinnitus. These changes are speculated to activate the sub-cortical and cortical regions. The outcome of this varied activation is measured indirectly in the present study, with temporal processing tests. As evident from the results, the temporal processing ability improved after twelve months of tinnitus retraining therapy, evidence to establish an association between TRT and temporal processing skills. Thus, it may be justifiable to comment that sub-cortical and cortical regions in the brain are involved in the tinnitus percept, at least in individuals with bilateral tinnitus with normal peripheral hearing sensitivity.

The participant's self-reported improvement in tinnitus perception and improved scores on THI-K, subjective loudness matching and annoyance rating scales, strengthened the psychoacoustic test findings. A range of studies have reported the benefit of TRT in reducing tinnitus percept as measured using THI, psychoacoustic measurement of loudness and annoyance rating (Table 6 for detail description). Hence, the psychoacoustic measures along with a subjective rating of tinnitus clearly indicate an association between temporal processing and TRT.

Another important finding of the present study is in terms of the brain's ability to adapt to the changes irrespective of the age and gender. This neural plasticity is very important, especially in pathological conditions. Previous research literature reported changes in neural plasticity with musical stimuli, but this study is first of its type to demonstrate the neural plasticity following sound exposure, and with sufficient empirical evidences to rationalize the statement. However, assessment procedures, including radiological evaluation should be administered to objectively confirm the findings. Future research may aim to perform radiological evaluations to objectively assess the benefit of TRT.

Conclusions

The findings of the present study conclude a significant effect of TRT in reduction of tinnitus perception. This finding adds on to the available literature, but a novel in its method of measurement. The study also highlights the association of sub-cortical and cortical structures in the perception of tinnitus and hence, supports the view of the central involvement in the generation of tinnitus.

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