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Neural markers associated with improved tinnitus perception after tinnitus retraining therapy

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ABSTRACT

Objective: Tinnitus retraining therapy (TRT) has been widely used in tinnitus management. However, its efficacy is often assessed through subjective methods. Here, we aimed to assess potential neural changes following TRT using mismatch negativity (MMN).

Design: Chronic tinnitus (>6 months) patients participated in a six-month TRT program. We collected tinnitus psychoacoustic features and gathered the tinnitus handicap inventory (THI) before and after TRT. We also used a multi-featured paradigm, including frequency, intensity, duration, location and silent gap deviants, to elicit MMN response before and after TRT. Data were analyzed retrospectively.

Study sample: The study involved 26 chronic tinnitus patients.

Results: Post-TRT measurements showed that MMN amplitudes significantly increased for all deviant conditions ($p \leq .03$). However, we did not find a significant difference in MMN latencies for all deviant conditions ($p \geq .13$). The THI scores of the patients significantly decreased following the TRT program ($p < 0.001$). Our results reveal improved subjective tinnitus perception following the TRT program.

Conclusion: These findings indicate that TRT might be a viable alternative in tinnitus management. The greater MMN amplitudes and improved subjective tinnitus perception raise the possibility that MMN can be a useful tool in tinnitus research and tinnitus patient follow-up.

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Tinnitus; tinnitus therapy; mismatch negativity; tinnitus management; tinnitus treatment

Introduction

Tinnitus is a phantom sound perception that affects approximately 15% of the population (Shargorodsky, Curhan, and Farwell 2010). Despite extensive research focusing on the underlying mechanisms and effective treatments for tinnitus, its exact pathophysiology and remedy remain unclear. Recently, the predictive coding framework has been suggested as an explanatory model for understanding the causes of tinnitus (De Ridder, Vanneste, and Freeman 2014; Sedley et al. 2016).

According to predictive coding theory, the brain aims to minimise sensory uncertainty and it generates predictions based on prior sensory experiences, comparing these predictions to incoming sensory input across multiple hierarchical levels (Friston 2010). The difference between the actual stimulus (i.e. bottom-up) and the prediction (i.e. top-down) leads to prediction errors (Sedley et al. 2016). In a healthy central auditory system, there is a negligible amount of prediction error in the absence of a stimulus (i.e. silence) due to spontaneous activity, which is not perceived as a sound (Hullfish, Sedley, and Vanneste 2019). However, increased spontaneous activity resulting from peripheral deafferentation in the ascending auditory system may generate prediction error and be perceived as a tinnitus signal (Hullfish, Sedley, and Vanneste 2019; Sedley et al. 2019).

The predictive coding framework has been reported as one of the mechanisms underlying mismatch negativity (MMN) (Garrido et al. 2009; Wacongne, Changeux, and Dehaene 2012). MMN is an event-related potential elicited by rare deviant stimuli embedded within a regular pattern of standard stimuli. MMN occurs as a negative peak about 100–250 ms after the presentation of deviant stimuli. The repetition of standard stimuli leads to a reduction in prediction error and the deviant stimuli violate the existing pattern, resulting in a prediction error. This prediction error is widely accepted as a marker of MMN (Garrido et al. 2009). Studies have shown abnormalities in MMN responses in tinnitus patients, possibly, stemming from impairment in the predictive coding mechanism (Mahmoudian et al. 2013; Sedley et al. 2019; Sendesen, Erbil, and Türkyılmaz 2022). Frequency deviants in MMN have been commonly studied in tinnitus research, and studies have consistently reported smaller amplitudes in tinnitus subjects (Mahmoudian et al. 2013; Sendesen, Erbil, and Türkyılmaz 2022; Yang et al. 2013). However, it appears that MMN findings on intensity deviants depend on the frequency of the stimulus, whether it is close to the tinnitus frequency or lower than the tinnitus frequency, as most subjects experience tinnitus at high frequencies. Studies that have used intensity deviants lower than the tinnitus frequency tend to find smaller MMN amplitudes in individuals with tinnitus compared to the control group (Sendesen, Erbil, and Türkyılmaz 2022). On the other hand, larger MMN responses have been found in tinnitus subjects when the frequency of the intensity deviant is around the tinnitus frequency,

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which has been linked to a stronger representation of auditory predictions at the tinnitus frequency (Sedley et al. 2019; Yukhnovich, Alter, and Sedley 2024a, 2024b). Other types of deviants, such as location, duration and silent gap, have been used in multi-featured oddball paradigms in MMN testing in individuals with tinnitus. Most of these studies have reported smaller MMN amplitudes in tinnitus subjects compared to individuals without tinnitus (Mahmoudian et al. 2013; Sendesen, Erbil, and Türkyılmaz 2022). Previous MMN work on tinnitus reveals a potential association between abnormal auditory predictions and tinnitus perception. Impaired MMN mechanism in tinnitus might indicate that MMN could be a potential objective tool for monitoring neural changes following clinical intervention.

Tinnitus retraining therapy (TRT) is a therapeutic approach that combines counselling and sound therapy to alleviate tinnitus symptoms based on the neurophysiological model (Jastreboff 2007). The primary objective of TRT is to mitigate tinnitus perception by regulating connections within the autonomic, limbic and auditory systems in the central nervous system. Studies have reported that approximately 80% of individuals undergoing TRT show improvements in tinnitus perception (Bartnik, Fabijańska, and Rogowski 2001; Herraiz et al. 2005; Jastreboff 2015). The exact neural mechanism of this improvement remains unknown; however, Kim et al. (2016) found a positive relationship between improvement in tinnitus perception with TRT and activity in the rostral and pregenual anterior cingulate cortex, which is responsible for a well-functioning noise-cancelling mechanism (Song, Vanneste, and De Ridder 2015).

TRT is one of the most widely used therapies in tinnitus management. However, the limited evidence on the efficacy of TRT so far is subjective rather than objective. In this study, we aimed to investigate the neural changes potentially associated with TRT in individuals with tinnitus using MMN. We hypothesised that effective TRT would result in higher post-TRT MMN amplitudes compared to the pre-TRT condition in tinnitus patients. This hypothesis is grounded in the expectation that successful TRT might regulate the noise-cancelling mechanism and, thus, possibly the predictive coding mechanism.

Material and methods

Participants

Twenty-six patients (14 females, 12 males) aged between 20 and 56 suffering from chronic tonal tinnitus (lasting more than six months), participated in the study. All the participants reported persistent, bothersome tinnitus. Individuals with potential organic problems related to the tinnitus aetiology, such as objective tinnitus, somatic tinnitus, benign tumours and diagnosed psychiatric disorders, were excluded based on medical history, radiological images and audiological evaluation. All the participants underwent tympanometric and otoscopic examinations to rule out abnormal external and middle ear functions, minimising potential interference from conductive hearing loss. Pure tone audiometry was conducted using an Interacoustics AC-40 audiometer with calibrated TDH-39P headphones (for frequencies of 0.125–8 kHz), a Sennheiser HDA200 (for frequencies 9–20 kHz) and a Radioear B-71 bone vibrator. Participants received TRT before the study. Psychoacoustic characteristics of tinnitus, the tinnitus handicap inventory (THI) and MMN were retrospectively collected one week before the start of TRT and one week after its completion of TRT previously applied in clinical routine.

Psychoacoustic measures of tinnitus

We used TDH-39P headphones to assess tinnitus frequencies up to 8 kHz, while frequencies higher than 8 kHz were assessed using Sennheiser HDA200 headphones. To match the tinnitus pitch, stimuli were presented to the contralateral ear at 30 dB SL to prevent confusion between the auditory stimulus and the tinnitus. In the case of bilateral tinnitus, stimuli were presented to the ear with the less severe or less bothersome tinnitus. If both ears were equally affected, the right ear was chosen for presenting the stimuli. A two-alternative forced choice procedure with a frequency range of 0.125 kHz to 20 kHz was carried out. The tinnitus loudness level (TLL) was matched in 5 dB HL increments based on the participants' ipsilateral hearing threshold at the tinnitus frequency.

The minimum masking level (MML) was determined as the level at which the tinnitus centre frequency was masked by narrowband noise in 5 dB SPL increments. Participants with bilateral or central tinnitus were presented with narrowband noise bilaterally. Narrowband noise was presented monaurally to the ear with tinnitus in cases of unilateral tinnitus.

Residual inhibition (RI) was assessed using narrowband noise presented at 10 dB above the MML, with a centre frequency matching the perceived tinnitus frequency, for 60 s. The noise was presented unilaterally to the ear with tinnitus in cases of unilateral tinnitus and to both ears in cases of bilateral tinnitus. A decrease in tinnitus perception indicated positive RI, while an increase or unchanged tinnitus perception indicated negative RI.

Tinnitus handicap inventory (THI)

The THI was gathered from the participants to assess the impact of tinnitus on their daily lives (Aksoy et al., 2007). The THI comprises 25 questions aimed at measuring the psychological effects of tinnitus. It is composed of three subscales focusing on the functional, emotional and catastrophic aspects of tinnitus. The participants responded on a scale of "Yes", "Sometimes" or "No", each corresponding to 4 points, 2 points and 0 points, respectively.

Mismatch negativity

A multi-featured paradigm proposed by Näätänen et al. (2004) has been widely used in MMN studies. In this study, we also employed a multi-feature paradigm to elicit MMN responses. One advantage of using this paradigm is that it enables the evaluation of different sound discrimination abilities within a short recording period. The paradigm comprises a standard stimulus and five different deviant stimuli, all generated using the Praat program. The stimuli were presented through calibrated ER-3A insert earphones. The standard stimulus consisted of three sinusoidal tones with a 75-ms duration at 0.5, 1 and 1.5 kHz, each with a rise and fall time of 5 ms. The frequency of the tones was lower than our participants' tinnitus frequencies, which ranged from 4 to 12 kHz. Sounds were presented binaurally at an intensity level of 65 dB SPL, with equal phases in both ears.

In this paradigm, there are five different deviant conditions: frequency, intensity, duration, location and a silent gap. Half of the frequency deviant tones were 10% higher (0.55, 1.1 and 1.65 kHz) than the standard, while the other half were 10% lower (450, 900 and 1350 Hz). The intensity of half of the deviant stimuli was 10 dB lower than the standard stimuli, while the other half was 10 dB higher. Interaural time difference, which provides important localisation cues in daily life, was used to generate location deviant tones. An interaural time difference of 800 ms was created to be distributed equally to the right ear and the left ear. Thus, a difference of approximately 90 degrees was detected between the standard stimulus and the position deviation. The duration of deviant tones was shorter (15 ms flat time, 5 ms rise and 5 ms fall times) than the standard stimulus. The silent gap deviant tones included a 7 ms silent gap in the middle of the standard stimulus, with the standard stimulus having 1 ms rise and fall times. The first 15 tones in each sequence correspond to the standard stimulus. Deviants from each category were presented once in a series of five deviants, ensuring that no two deviants from the same category were presented consecutively. Stimuli were presented at a stimulus-onset-asynchrony of 500 ms in three 5-min trains (1845 stimuli in total). The total recording time for the five types of deviants was, thus, 15 min.

EEG recording

Our participants watched a silent movie with subtitles to prevent them from paying attention to deviant sounds while seated in a relaxed chair in a Faraday Cage room. They were instructed to minimise motor movements and blinking to reduce artefacts. Stimuli were presented using Neurobehavioral Systems, Inc. Presentation Software 15.0. An EEG was continuously recorded at 0.5 kHz with a NuAmps II Amplifier and Scan 4.2 acquisition software (Neuroscan Inc., Herndon, VA), with filters set to 0.5–70 Hz. In addition to a 20-channel EEG cap with silver electrodes based on the classical 10–20 system (EasyCap GMBH, Germany), external electrodes were placed on both left and right ear lobes. Electrode impedances were kept below 10 kΩ. The data were collected in four sessions, each consisting of 50 deviant stimuli. All the sessions included each type of deviant.

The processing of EEG data

The data were analysed using MATLAB2015a and the EEGLAB toolbox. Epochs were adjusted from 100 ms pre-stimulus to 400 ms post-stimulus for both the standard and each deviant stimulus. Epochs with amplitudes over 80 µV were rejected as they were considered noisy. Baseline correction was performed based on the amplitude from 100 ms before the sound onset (0 ms).

EEG data analysis

To reveal the MMN response, we subtracted the auditory evoked potentials of the deviant stimulus from those of the standard stimulus for each individual and deviant condition. The amplitude was identified as the most negative point in the MMN waveform. We calculated the MMN response area (under the x-axis) to determine latencies, with latency determined as the mid-point of the line dividing this area into two equal parts. Data were recorded using external earlobe electrodes and referenced to combined A1/A2. We focused on the largest MMN peaks recorded at the Fz electrode for both amplitude and latency calculations. Data were analysed in a window ranging from −100 to 400 ms, with a 30 Hz low pass filter applied. In baseline correction, we extracted the averages from all the MMN curves.

Tinnitus retraining therapy (TRT)

Counselling was provided to participants during their initial appointment, which took place the day after the tinnitus psychoacoustic assessments and lasted for 1 h. The counselling content was based on Jastreboff's neurophysiological model and included information on hearing mechanisms and theories, along with examples illustrating how hearing loss and emotional responses contribute to disturbing tinnitus. Subsequently, on the same day, participants were briefed on the specific aspects of sound therapy to which they should pay special attention. This briefing session lasted approximately 30 min.

Wideband noise for sound therapy was generated using Praat, with a frequency spectrum ranging from 0.125 to 20 kHz. The noise was then converted into a "wav" file format, allowing participants to easily listen to it on their smartphones. The noise level was adjusted to just below the level required to suppress the participant's tinnitus (i.e. the mixing point) using the volume controls on their smartphones. The participants were instructed to wear headphones and listen to the noise for 6 h per day, either continuously or intermittently, adjusting the volume settings on their phones accordingly.

Participants were scheduled for a follow-up appointment one week later to check that they had followed the instructions. This follow-up relied on self-reported adherence to the program. Tinnitus intensity levels were evaluated during follow-up appointments at one, three and six months after their initial counselling session. If any changes in tinnitus intensity were noted, the volume of the noise played through their smartphones was adjusted accordingly.

Statistical analysis

The G*Power program was used to determine the sample size required for the study. Based on the mean and standard deviation values obtained from the pilot study, this study aimed to include 24 participants with a 5% type I error level and 95% power to detect a minimal, clinically significant difference. All statistical analyses were conducted using SPSS version 25.0 (IBM Inc., Armonk, NY, USA). The variables showed a normal distribution. The paired sample t-test was employed to compare the amplitude, latency values, THI, TLL and MML scores of MMN deviant stimuli before and after TRT. The correlation between subjective tinnitus perception and neural changes in MMN was analysed using the Pearson correlation. A p value <0.05 was considered statistically significant.

Results

Descriptive statistics

The mean age of the participants was 34.23 ± 5.81 years. Table 1 shows the general tinnitus characteristics of the participants, and Figure 1 shows their hearing thresholds.

THI and tinnitus psychoacoustic assessment

Table 2 shows the THI, MLL and TLL scores before and after TRT. A statistically significant decrease was found in all three

Table 1. Tinnitus characteristics of the participants.

Tinnitus location	
Right ear	8
Left ear	6
In the head/bilateral	12
9 **Tinnitus frequency** (kHz)	7.2 ± 1.1 (4–12)
9 **Tinnitus duration** (months)	18.21 ± 6.2 (8–31)
Hearing threshold at the tinnitus frequency (dB HL)	44.26 ± 9.15

The tinnitus characteristics of the participants are shown in bold.

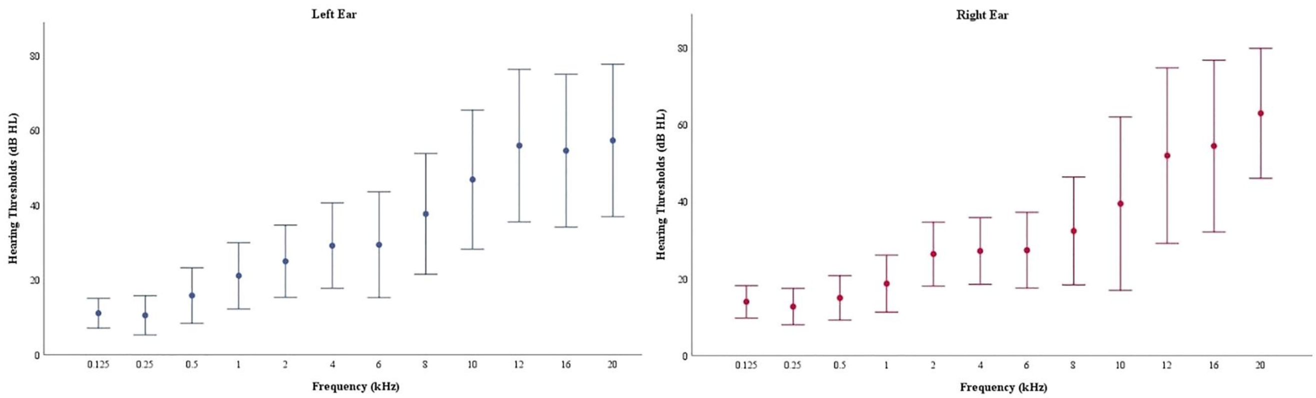

Figure 1. Participants' hearing thresholds.

Table 2. THI, MML and TLL scores pre-and post-TRT.

		Pre-TRT		Post-TRT		
N	Time	Mean	Std.	Mean	Std.	*p* value**
9	THI	59.38	20.93	40.23	23.31	**< 0.001***
9	MML	45.96	15.23	31.34	21.75	**0.001***
9	TLL	57.11	20.10	39.61	26.22	**0.001***

Notes: This table presents the Tinnitus Handicap Inventory (THI), Minimum Masking Level (MML) and Tinnitus Loudness Level (TLL) scores for participants before and after Tinnitus Retraining Therapy (TRT). The mean and standard deviation (Std.) are shown for both pre-TRT and post-TRT scores. The p-value indicates the statistical significance of the changes observed, with statistically significant differences shown in bold.
**Paired samples t-test

Table 3. MMN amplitude and latency values for each deviant stimulus before and after TRT.

Variable	Feature	Pre-TRT		Post-TRT		
		Mean	Std.	Mean	Std.	*p* value
Frequency	Amplitude	−3.16	0.88	−3.75	0.96	**0.02***
	Latency	198.01	19.45	190.72	21.60	0.21
Intensity	Amplitude	−2.64	0.51	−3.11	0.74	**0.01***
	Latency	187.91	29.13	196.74	17.79	0.19
Location	Amplitude	−2.94	0.78	−3.27	0.41	**0.03***
	Latency	182.16	8.61	183.91	11.74	0.52
Duration	Amplitude	−2.61	0.28	−3.89	0.44	**<0.001***
	Latency	192.22	20.65	186.01	16.78	0.21
Silent gap	Amplitude	−1.51	0.37	−1.81	0.27	**<0.01***
	Latency	202.71	14.32	197.95	13.24	0.13

Notes: This table presents the mean and standard deviation (Std.) of MMN amplitude and latency values for each type of deviant stimulus before and after TRT. The *p* value indicates the statistical significance of the changes observed. Significant differences ($p < 0.05$) are marked with an asterisk (*). The deviant stimuli include frequency, intensity, location, duration and silent gap.
The tinnitus characteristics of the participants are shown in bold.

measures in the post-TRT condition compared to the pre-TRT condition (for THI: $t(19)=4.91$, $p < 0.001$; for MLL: $t(14)=3.69$, $p = 0.001$; for TLL: $t(17) = 3.67$, $p = 0.001$).

Mismatch negativity

Table 3 presents the MMN amplitude and latency values for each deviant stimulus before and after TRT. We found significantly higher post-TRT MMN amplitudes for all deviant conditions compared to pre-TRT MMN responses (for D1: $t(0.5) = 2.34$, $p = 0.02$; for D2: $t(0.4) = 2.65$, $p = 0.01$; for D3: $t(0.3) = 2.26$, $p = 0.03$; for D4: $t(1.2) = 11.78$, $p < 0.001$; for D5: $t(0.2) = 3.44$, $p = 0.002$). Figure 2 illustrates the MMN waveforms for each deviant stimulus before and after TRT. We ran a correlation analysis between the differences in pre- and post-TRT subjective tinnitus perception (THI and psychoacoustic measures of tinnitus) and MMN amplitudes. We did not find a significant correlation between the changes in subjective tinnitus perception and MMN amplitudes following TRT ($p > 0.05$; see Supplemental Material for the correlations for each variable).

Discussion

Previous studies on MMN in tinnitus patients have suggested abnormal MMN responses, indicating that tinnitus patients encode sensory violations poorly. Here, our primary objective was to use MMN as a potential objective indicator to monitor tinnitus management and possible TRT-related alterations. We found greater MMN amplitudes in all deviant conditions following the TRT program. The THI scores of the tinnitus patients also improved following therapy. Our findings may suggest a potential improvement in tinnitus handicap following a six-month TRT program, and MMN might be a useful tool to show its possible association with changes in tinnitus perception.

Studies have shown that TRT improves subjective tinnitus perception (Jastreboff 2015). However, neural projections of this improvement have been mostly overlooked. In this study, we investigated these neural mechanisms using a multi-featured MMN paradigm and found greater amplitudes after the TRT program. The THI scores of the patients also significantly improved following the therapy. These findings may indicate that improved subjective tinnitus perception is associated with neural changes in MMN. The mechanism of neural changes may be linked to the sources of MMN. It is known that the amplitude values in electrophysiological evaluation methods such as MMN are related to the number of neural sources that produce synchronised responses (Näätänen et al. 2007). Koshiyama et al. (2021) found the orbitofrontal and anterior cingulate cortex to be major contributors to the MMN recorded at the Fz electrode. Studies have indicated that the anterior cingulate cortex is the core of the noise cancelling mechanism (Kim et al. 2016; Song, Vanneste, and De Ridder 2015). The perception of tinnitus after TRT may be reduced by a more active role of the noise cancelling mechanism. Therefore, the increase in MMN amplitude may be attributed to the enhanced utilisation of neural sources involved in the noise-cancelling mechanism, which are also implicated in the generation of MMN.

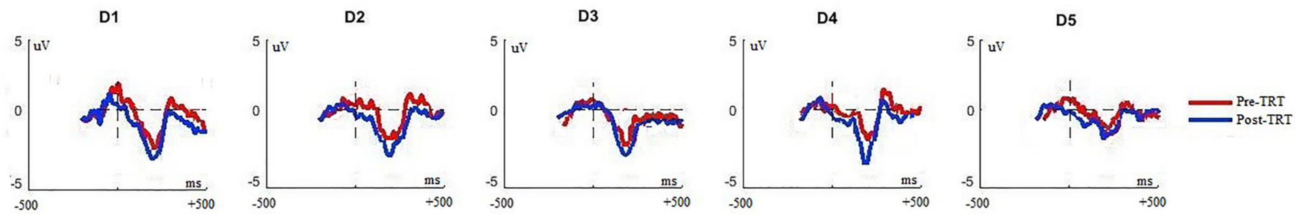

Figure 2. MMN waveforms for each deviant stimulus before and after TRT. D1: frequency deviant stimulus, D2: intensity deviant stimulus, D3: location deviant stimulus, D4: duration deviant stimulus, D5: silent gap deviant stimulus.

Previous studies on tinnitus patients have demonstrated abnormal findings regarding MMN (Mahmoudian et al. 2013; Sedley et al. 2019; Sendesen, Erbil, and Türkyılmaz 2022). Recently, studies have proposed explanations for tinnitus perception and its possible generation mechanism within the predictive coding framework (De Ridder, Vanneste, and Freeman 2014; Sedley et al. 2016). A review by Garrido et al. (2009) argued that the MMN response represents prediction errors in the sensory brain. Predictive coding models often involve feedback loops in which higher-order brain regions send predictions to lower-order sensory regions and lower-order regions send prediction errors back to higher-order regions. In the case of tinnitus, this feedback loop causes a phantom sound perception that can result in a daily life handicap for some people. It has been suggested that attention can modulate the strength of these feedback signals (Talsma 2015), influencing the refinement of predictive models. One of the main purposes of sound therapy in TRT is the shift in attentional focus away from tinnitus (Scherer et al. 2020). Here, the white noise used in sound therapy may act as an attentional distractor, thus reducing the strength of the feedback loop that causes tinnitus over time. The weakening of the maladaptive feedback loop may contribute to larger amplitudes in MMN following TRT.

In this study, we used a multi-featured paradigm that includes several deviant conditions such as frequency, intensity, location, duration and silent gap to record the MMN. Across all conditions, we observed significantly larger MMN amplitudes following the TRT. In particular, the most substantial amplitude increase was observed in the duration and silent gap conditions. Previous studies using the multi-featured paradigm in MMN have suggested that duration and silent gap conditions are particularly impaired in tinnitus patients compared to individuals without tinnitus (Mahmoudian et al. 2013; Sendesen, Erbil, and Türkyılmaz 2022). It is possible that this finding is associated with the inhibitory transmission mechanism, which is affected in tinnitus (Caspary et al. 2008; Felix, Gourévitch, and Portfors 2018). It should also be noted that the encoding of sound offset may be driven by inhibitory mechanisms. A possible impairment in inhibitory mechanisms may impact sound offset encoding and the temporal domains of auditory processing (Colak, Sendesen, and Turkyilmaz 2024). This could, potentially, explain the temporal abnormalities observed in the silent gap and duration conditions in MMN among tinnitus patients. In this study, we speculate that TRT may facilitate the restoration of the noise cancelling mechanism and, thus, the function of the inhibitory mechanism.

An association between pre- and post-TRT changes in subjective tinnitus perception and MMN amplitudes can be expected. However, we did not find any significant correlation between the pre- and post-TRT difference scores for subjective tinnitus perception and MMN amplitudes. Several factors may underlie this lack of relationship between subjective measures of tinnitus and electrophysiological changes. Emotional and psychological factors significantly influence how individuals perceive their tinnitus (Durai and Searchfield 2016; Patil et al. 2023). Stress, anxiety and depression can impact subjective reports of tinnitus severity, and such complexity in tinnitus may hinder a direct correlation with neural responses in this study. Another factor could be that our sample size might not be large enough to demonstrate the correlation between subjective tinnitus measures and MMN amplitudes, as MMN might reflect more physiological alterations and be a different dimension from subjective tinnitus perception.

One important limitation of the current study is the lack of a control group, which limits the generalisability of our findings due to the possible placebo effect. However, it should be noted that improved results in three different domains (subjective, psychoacoustic and electrophysiological) post-TRT measures may reduce the likelihood of placebo-related effects in our findings. Additionally, MMN is a pre-attentive evoked potential primarily affected by physiological alterations in the auditory system (Näätänen 2008). This aspect of MMN may also mitigate the involvement of potential placebo effects. A possible learning effect for the stimuli and paradigm or test-retest related amplitude increase in MMN responses may also interfere with our findings. However, a recent study by Atalık et al. (2022) investigated the test-retest reliability of multi-featured paradigm MMN responses and did not find a significant amplitude increase in the latter MMN testing. In addition, by distracting the test subjects from attending to the stimuli, such as watching a silent movie in this study, we might improve the stability of MMN amplitudes and reduce the potential learning effect. Also, the six-month period during the TRT program was considered a limitation based on the possibility that tinnitus patients may develop habituation to tinnitus irrespective of TRT. Finally, the participants were asked to listen to the noise for 6 h per day. Although they reported completing these periods at the specified intensity and duration, no actual monitoring of the duration and intensity of its use was conducted.

Conclusion

Overall, the present study has revealed greater MMN amplitudes following the TRT program. Additionally, our participants reported improvements in the subjective (THI) and psychoacoustic (TLL and MML) domains of tinnitus perception. These findings underscore the improved tinnitus perception following a TRT program and may indicate that TRT is a viable option in tinnitus management. Current evidence suggests a possible relationship between improved tinnitus perception and greater amplitudes in MMN, raising the possibility that MMN can be a potential biomarker in tinnitus research and follow-up of tinnitus patients. Future studies should aim to investigate the association between other tinnitus management alternatives and MMN.

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Ethical approval

Ethical approval for this study was obtained from Clinical Research Ethics Committee (SBA 23/257) and completed in conformity with the standards set by the Declaration of Helsinki.

Consent form

Informed consent was obtained from all individual participants included in the study.

Author contributions

Eser Sendesen: Designing, performing experiment, analysing data, writing paper, providing statistical analysis. Hasan Colak: Designing, analysing data, writing paper.

Disclosure statement

No potential conflict of interest was reported by the author(s).

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Data availability statement

The data that support the findings of this study are available from the corresponding author (H.C), upon request.

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