Monitoring of Auditory Discrimination Therapy for Tinnitus Treatment Based on Event-Related (De-) Synchronization Maps

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Abstract— Tinnitus is an auditory condition that causes humans to hear a sound at any time anywhere. Chronic and refractory tinnitus is caused by the synchronization of neurons, and a treatment alternative has been created on the basis of the re-synchronization of neural activity by means of sound. To date, several acoustic therapies have been proposed to treat tinnitus. However, the effect is not well understood yet. Therefore, the aim of this study is to evaluate the effect of auditory discrimination therapy (ADT) by monitoring the level of neural synchronization before and after the ADT-based treatment. To this end, we mapped and analyzed the neural (de-) synchronization response of 11 tinnitus patients in two experimental conditions: (1) auditory material encoding and (2) auditory material retrieval. The results suggest that event-related (de-) synchronization (ERD/ERS) maps could indicate ADT reduces attention towards tinnitus if we consider incremental alpha-ERS responses elicited after the acoustic therapy during auditory encoding tasks. Furthermore, there were statistical changes in at least one of the brain frequency bands in each subject, which could indicate a decrease in attention headed for tinnitus or towards everyday acoustic environments.

I. INTRODUCTION

Tinnitus is the perception of sound in the absence of an external source [1]. It affects between 5-15% of the world population [2]. Chronic and refractory tinnitus is caused by the over synchronization of neurons, which affects cognitive, attentional, emotional, and even motor processes [1]. In particular, cognitive impairment is frequently reported in patients with tinnitus [3]. Working memory and attentional processes such as deficits in (1) executive control of attention [4], (2) attentional changes [3], and (3) selective and divided attention [5] have been particularly studied over the last years.

The neurophysiological mechanisms occurring at a cortical neural level can be recorded over the human scalp using the Electroencephalography (EEG) technique [6]. EEG allows monitoring brain rhythmic and ongoing electrical activity. It is made up of several simultaneous oscillations at different frequencies [7][8][9]. The event-related brain electric oscillatory responses at different frequency bands reflect different stages of neural information processing [7][8][10]. Event-related oscillations are typically studied as: (1) event-related desynchronization (ERD), which refers to the phasic relative power decrease of a certain frequency band, and (2) event-related synchronization (ERS), which implies a relative power increase. As the term indicates, both ERD and ERS are neural patterns occurring in relation to emotional, cognitive, motor, sensory and/or perceptual events [11][12][13][14]. In tinnitus patients, power changes in various frequency bands reflect changes in neural synchrony. Some of the findings in spontaneous EEG and MEG include decreased auditory alpha and increased slow-wave delta activity [15][1].

ERD/ERS maps have been extensively used to study auditory information processing at a cortical level. For instance, Klimesch and colleagues have reported theta and alpha oscillatory responses during cognitive processing in different studies [16][17][18][19]. On the functional level, attention and semantic memory (cognitive processes responsible for accessing and / or bringing back information from long-term memory) are strongly related to brain oscillatory responses within alpha frequencies [20] whereas working memory functions (memory needed to retain auditory stimulus for some time) are associated with the brain activity in the theta frequency range [21][22][23]. Krause and colleagues have extensively studied auditorily elicited ERD/ERS responses using a wide variety of cognitive tasks. One consistent finding from these studies is that the encoding of acoustic information typically elicits widespread alpha-ERS responses whereas recognition of the same acoustic material elicits widespread alpha-ERD responses [24].

A wide variety of treatments for tinnitus have been proposed to date, including hearing aids, counselling, acupuncture, herbal treatments, bio- and neurofeedback, transcranial magnetic stimulation, and acoustic therapies [25]. However, none of them are fully reliable or effective [26][27]. It is well established that sound brings about physiological, cognitive and psychological changes, which is why sound-based therapies have become seven of the twenty-five most widely used treatments for tinnitus according to [26]. One of these acoustic therapies is auditory discrimination therapy (ADT), based on the oddball paradigm principle, which is designed to reduce attention towards tinnitus, thereby reducing its perception [28]. The Oddball paradigm consists of a pair of stimuli: standard and deviant pulses which are randomly presented. The patient must identify deviant (40%) from standard (60%) pulses.

ERD/ERS monitoring has become a widely applied EEG monitoring tool. ERD/ERS maps are currently employed as quantitative measures derived from the EEG (EEG biomarkers) to assess cognitive engagement in stroke patients during motor rehabilitation [29][30][31], to monitor deterioration of the attention network of people with Alzheimer's and Parkinson's disease [32], and to estimate the effect of sporadic seizures on cognitive abilities in very young people with non-symptomatic focal epilepsy receiving antiepileptic medication [33]. Although this method has been used to monitor cognitive engagement during certain therapies, with applications in stroke patients or patients with epilepsy, this method has not yet been applied to assess acoustic therapies in tinnitus patients, as far as we know. Based on this evidence, we propose to evaluate the effect of ADT for tinnitus treatment by mapping ERD and ERS responses before and after the therapy, and decide whether this EEG technique could be feasible to monitor sound effects. In particular, the effects of ADT on attentional and memory processes are of special interest since ADT looks to reduce attention towards tinnitus in order to increase attention on everyday acoustic environments.

II. Methodology

Figure 1 depicts the methodology applied in this study, divided into sections, which are vertically stacked, and the steps to be taken depicted horizontally. Each section is described as follows.

A. EEG Database

An EEG database acquired by Ibarra et. al (2021) [34] was used for this research study. (The database is available at https://data.mendeley.com/datasets/kj443jc4yc/1). Of the initial cohort reported, 11 patients were selected. They were the group treated with ADT for 8 weeks. All the patients were instructed to use the ADT for one hour every day, at any time of the day. The therapy was monitored before and after the 8-week treatment. At each monitoring session, an adapted version of the Tinnitus Handicap Inventory (THI) created by the National Institute of Rehabilitation was applied and an EEG recording was produced. THI was applied to report the perception of tinnitus during the sound-based treatment. The questionnaire responses were categorized in (1) normal, (2) borderline normal and (3) abnormal condition before and after treatment. For the EEG recording, two everyday acoustic environments were played, while five associated auditory stimuli were randomly played. In order to identify auditory stimuli, patients pressed a keyboard button. The acoustic environments along with their related auditory stimuli in each monitoring session comprised: (1) sounds of construction in progress: human sound

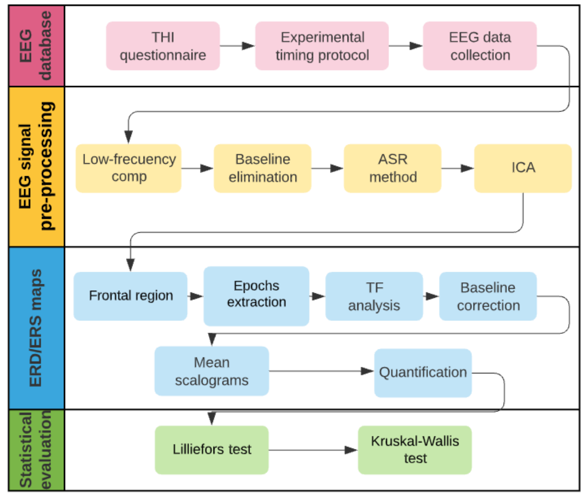

Figure 1. Methodology applied in the current study

(yelling), police siren, mobile dialing, bang and hit; and (2) restaurant sounds: human sound (tasting food), microwave sound, glass breaking, door closing, and soda can being opened. All the stimuli lasted 1s and were repeated 50 times at a random rate. Participants kept their eyes closed during the stimulation. Every monitoring session was around 60 minutes long [35]. The experimental timing protocol is included in Figure 2. To record EEG data, a g.USBamp amplifier was used, which was configured as stated in Table 1.

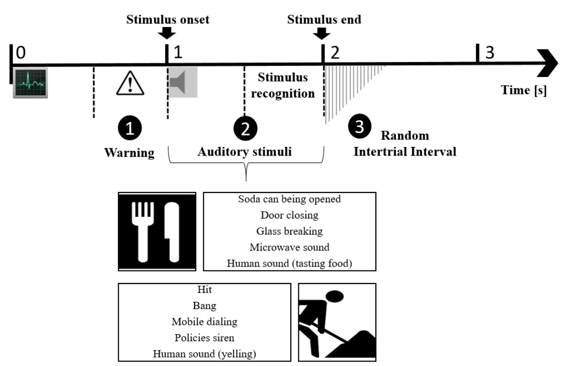

Figure 2. Timing protocol for EEG data collection

Table 1. EEG recording system configuration

Sampling rate	256 Hz
Number of channels	16
Channels used by region	Prefrontal (FP1, FP2), Frontal (F7, F3, Fz, F4, F8), Temporal (T3, T4, T5, T6), Central (C3, C4), Parietal (Pz), Occipital (O1, O2)
Reference method	Monopolar Cz
Electrode placement system	International 10-20 system

B. EEG Signal Pre-Processing

The EEG signals were pre-processed as follows in order to increase the signal-to-noise ratio. Firstly, the low-frequency components were eliminated by applying a Butterworth type Band Pass digital filter with order 6 of zero phase, and with cutoff frequencies at 0.1 and 30 Hz. Secondly, the baseline was removed. Thirdly, Artifact Subspace Reconstruction (ASR) methodology was used to eliminate transient or large amplitude artifacts. Finally, Independent Component Analysis (ICA) decomposition was applied with the RunICA function, which was implemented via the Infomax algorithm, for the elimination of physiological and non-physiological artifacts, including ocular and cardiac activity, and pop-up electrode artifacts.

C. ERD/ERS Maps

Most of the changes in neural activity due to tinnitus have been observed over the frontal lobe. In [1], delta and theta band oscillations were enhanced because of tinnitus loudness and tinnitus-related distress. Patients in greater distress from tinnitus showed larger theta oscillations. According to [36], most tinnitus patients showed a decrease in alpha power since their attention had been redirected to their tinnitus as their minds wandered off, resulting in low alpha synchronization. Based on this evidence, the EEG signals over the frontal lobe (Fp1, Fp2, F7, F3, Fz, F4, F8) were averaged to monitor the ADT effect on tinnitus sufferers.

The epochs were extracted 500 ms before and 1 s after the stimulus onset in line with the timing protocol presented in Figure 2. There were two types of events: (1) auditory material encoding and (2) auditory material retrieval. Regarding auditory memory mechanisms, the first event induces long-lasting alpha ERS responses, while the second event is associated with long-lasting alpha ERD responses [24].

The Continuous Wavelet Transform (CWT), was the time-frequency analysis applied to each epoch. Wavelet of the Complex Gaussian family (Eq. 1) was selected since they are based on complex-valued sinusoids constituting an analytic signal, possessing the shift invariance property. The sampling frequency was 256 Hz and the frequency range oscillated between 0.1 and 30 Hz.

$$f(x) = C_p e^{-ix} e^{-x^2} \tag{1}$$

The integer p is the parameter of this family built from the complex Gaussian function. C_p is such that $\|f^p\|^2 = 1$ where f^p is the p^{th} derivative of f.

The baseline correction was carried out using the subtraction method based on

$$Subtraction = P(t,f) - \bar{R}(f) \tag{2}$$

where P (t, f) is the power value given a time-frequency point subtracted by the average value of the baseline values from -400ms to -100ms at each frequency range prior to the appearance of an auditory encoding or recognition event [37].

The coefficient matrices resulting from the CWT per epoch were averaged and the absolute value was carried out to obtain only real estimations. CWT scalograms were plotted as a function of time windows from -500ms to 1s and a frequency ranging from 0.1 to 30 Hz, for the purpose of representing the auditory Synchronization and Desynchronization Activity over the Frontal lobe before and after the ADT-based procedure.

Based on the reference and the two experimental conditions (encoding and recognition of acoustic material), the ERD/ERS values were determined for each of the subjects using the following mathematical expression:

100% (power during reference - power during experiment)/ (power during reference) in the different frequency bands from 4-8 Hz, 8-13 Hz and 13-30 Hz [33].

D. Statistical Evaluation

The statistical analyses were conducted separately for each frequency band under two conditions: (1) ERD/ERS response before and after the treatment, and (2) considering two auditory processes: encoding and recognition of auditory material. The Lilliefors test was used to assess data distribution. After getting a non-normal distribution, the statistical significance of any differences between ERD/ERS values of the two groups was evaluated with the Kruskal-Wallis test. P-values were stated at 5% for both statistical processes.

III. Results

A. ERD/ERS Maps

ERD/ERS maps of 11 subjects, delimited by brain frequency bands (delta (1–4 Hz), theta (4–8 Hz), alpha (8–13 Hz) and beta (13–30 Hz)), were obtained for encoding and recognition of auditory material events before and after the ADT-based treatment, resulting in a total of 22 ERD/ERS maps linked with the encoding task, and 19 ERD/ERS maps linked with the recognition task. The three missing maps were due to the lack of auditory material recognition responses obtained from three subjects in the initial monitoring session during the acoustic therapy.

On a first analysis, shown in Figure 3, event-related (de) synchronizations maps extracted during the auditory encoding task before and after the ADT-based treatment were grouped based on the perception of tinnitus reported by the patients at the end of the therapy (THI questionnaire).

Figure 3a and Figure 3b show the median of ERD / ERS responses obtained before and after the ADT-based treatment, of six subjects who reported no therapeutic benefits. Figure 3c and Figure 3d show the ERD / ERS responses elicited in both monitoring sessions of one subject who perceived a worsening on tinnitus perception. Figure 3e and Figure 3f show the ERD / ERS responses of one subject who perceived a decrease in the perception of his tinnitus. Regarding the three missing subjects, their THI outcomes were not obtained, so they could not be associated with ERD / ERS maps.

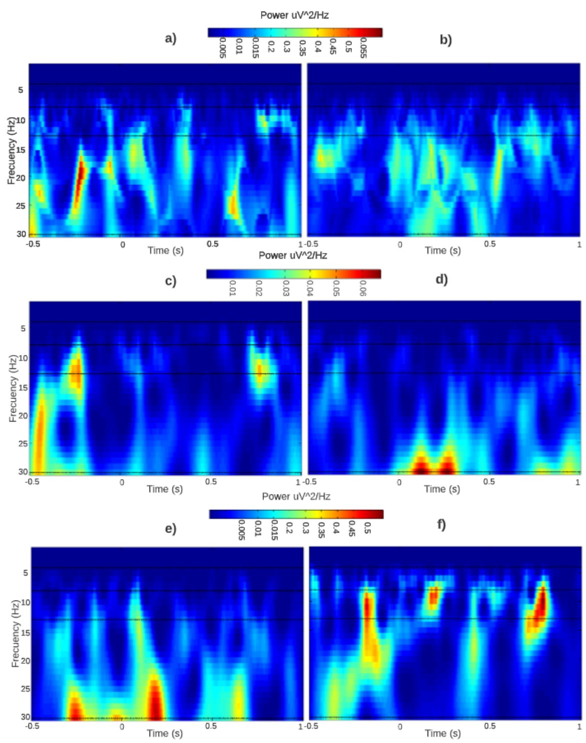

Figure 3. (ERD/ERS) responses over the frontal lobe before and after the ADT-based treatment during the auditory material encoding event. (a-b) Median of 6 patients who exhibited normal condition in the THI. (c-d) A patient who exhibited abnormal condition in the THI. (e-f) A patient who exhibited borderline condition in the THI.

B. Quantification Of ERD/ERS Responses

On the other hand, in Table 2, we can see p-values as a result of the Kruskal-Wallis test to statistically verify the existence of significant differences by frequency bands in 11 patients with tinnitus before and after the ADT-based treatment under two experimental conditions: encoding and recognition of acoustic material.

Estimations in bold fonts refer to those p-values under .05. These represent significant differences in the responses of the ERD / ERS maps between the sessions undertaken before and after the ADT-based treatment during both tasks by each brain frequency band.

Table 2. P-values as a result of the Kruskal-Wallis test to obtain the statistical significance differences between patients with tinnitus before and after the ADT-based treatment

Subjects	**EEG rhythms**	**Encoding of Acoustic Material**	**Recognition of Acoustic Material**
Subject 1	**Theta rhythm**	P>.05	*
	Alpha rhythm	P>.05	*
	Beta rhythm	**P<.05**	*
Subject 2	**Theta rhythm**	**P<.05**	**P<.05**
	Alpha rhythm	**P<.05**	**P<.05**
	Beta rhythm	**P<.05**	**P<.05**
Subject 3	**Theta rhythm**	**P<.05**	**P<.05**
	Alpha rhythm	P>.05	**P<.05**
	Beta rhythm	**P<.05**	**P<.05**
Subject 4	**Theta rhythm**	**P<.05**	**P<.05**
	Alpha rhythm	**P<.05**	**P<.05**
	Beta rhythm	**P<.05**	**P<.05**
Subject 5	**Theta rhythm**	**P<.05**	**P<.05**
	Alpha rhythm	**P<.05**	P>.05
	Beta rhythm	**P<.05**	P>.05
Subject 6	**Theta rhythm**	**P<.05**	*
	Alpha rhythm	**P<.05**	*
	Beta rhythm	**P<.05**	*
Subject 7	**Theta rhythm**	**P<.05**	**P<.05**
	Alpha rhythm	**P<.05**	**P<.05**
	Beta rhythm	**P<.05**	**P<.05**
Subject 8	**Theta rhythm**	**P<.05**	**P<.05**
	Alpha rhythm	**P<.05**	**P<.05**
	Beta rhythm	**P<.05**	P>.05
Subject 9	**Theta rhythm**	**P<.05**	*
	Alpha rhythm	**P<.05**	*
	Beta rhythm	**P<.05**	*
Subject 10	**Theta rhythm**	**P<.05**	**P<.05**
	Alpha rhythm	**P<.05**	**P<.05**
	Beta rhythm	**P<.05**	**P<.05**
Subject 11	**Theta rhythm**	**P<.05**	**P<.05**
	Alpha rhythm	**P<.05**	**P<.05**
	Beta rhythm	**P<.05**	**P<.05**

*Missing values

IV. Discussion

The aim of this study was to evaluate the effects of ADT for tinnitus treatment by mapping ERD and ERS responses before and after the therapy, and to decide whether this EEG technique could be feasible to monitor attentional and memory processes. According to Klimesch and colleagues, alpha frequency responses reflect processes related to semantic memory and attention. On the other hand, 4-8 Hz EEG frequencies responses are associated with working memory modulated by memory load and task demands [20]. Although beta rhythm responses were first associated with the activity of the motor cortices, some studies have reported that beta desynchronization is also associated with cognitive processing [24].

According to [15][1], electrophysiological studies in tinnitus patients have revealed that brain oscillatory activity decreases in the alpha band and increases in delta bands when high volume and affliction is perceived due to tinnitus-related distress variables, which affect emotional and attentional processes.

Regarding the ERD/ERS responses of the patients reporting negative effects at the end of the therapy, the increase in the initial 4-13 Hz ERS during the first monitoring session and the decrease in the ERD response during the second monitoring session are consistent with Klimesch and colleagues, as this may indicate a decrease in cognitive demands related to attention processes, semantic and working memory at the end of the therapy. Moreover, beta power presence in this scenario is more attenuated before than after the ADT-based treatment, which could suggest difficulties in the cognitive processing according to Krause and colleagues. Regarding [15][1], attenuated delta power is related to positive effects, as it reflects a decreased tinnitus loudness and a reduction in tinnitus-related affliction. However, this contrasts with the condition reported in the THI test. Furthermore, alpha power decrease in the second monitoring session may indicate that ADT-based treatment has reduced attention towards tinnitus; nonetheless, the perceptions of tinnitus patients have worsened at the end of the therapy.

Regarding the ERD/ ERS responses of the patients reporting borderline condition at the end of the therapy, the decrease in the ERD response during the first monitoring session and the increase in the final 4-13 Hz ERS during the second monitoring session is consistent with Klimesch and colleagues as this could indicate increased cognitive demands during the performance of the experimental task. Furthermore, according to Krause and colleagues, beta power presence in this scenario is more attenuated after the ADT-based treatment than before, which could suggest improvements in the auditory cognitive processing at the end of the therapy. Moreover, regarding [15][1], alpha power increase in the second session may indicate that the ADT-based treatment has increased attention to everyday acoustic environments, which is consistent with the positive effective reported in the THI test at the end of the therapy.

For patients who did not report effects after the ADT-based treatment in the THI questionnaire, ERD/ERS responses did not change either. Hence, auditory cognitive demands may not be altered.

In the statistical analysis of Table 2, the ERD/ERS responses of at least one of the frequency ranges (delta, theta, alpha and beta) differ significantly before and after the ADT-based treatment, suggesting that although the median of the ERD/ERS responses of patients suggested no changes concerning tinnitus perception, it was indeed statistically significant. This result points out either to an increase or decrease in auditory cognitive demands related to semantic memory and working memory after the end of the acoustic therapy. As a further matter, it is worth mentioning that THI responses show a different pattern compared with the neural trend. This is partly due to the fact that self-reported tinnitus measures have an associated risk of variability, along with the significant placebo effect of tinnitus, which may mask the effect of the treatment [27]. In this study, we observed that regardless of the reported perception of tinnitus patients at the end of therapy, the neural patterns differed notably in the frontal lobe during two conditions: (1) ERD/ERS response before and after the treatment, and (2) during two auditory processes: encoding and recognition of auditory material.

V. Conclusions

In conclusion, the ERD/ERS technique seems to be feasible to detect alterations in cognitive functioning in terms of attentional and memory processes, hence it could function as a method to assess event-related (de-) synchronization of neural activity in tinnitus patients treated with an auditory discrimination therapy. Regarding the effectiveness of ADT, ERD/ERS maps, along with THI results may suggest that ADT reduces attention towards tinnitus if incremental alpha-ERS responses elicited after the ADT-based treatment during an auditory encoding task are found.

Furthermore, there were statistical changes in at least one of the brain frequency bands in each subject which could indicate a decrease in attention headed for tinnitus or towards everyday acoustic environments.

Future work will entail measuring sensitivity by performing either a longitudinal or cross-sectional study, comparing the patient with her own evolution or with regard to a control subject at the end of the ADT-based treatment.

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