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Title: The Efficacy of Theta Binaural Beat on the Absolute Power of Theta Activity in Individuals With Primary Insomnia

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Abstract

Introduction: The pattern of brain waves in primary insomniacs is different from healthy subjects. Studies have shown that binaural beats can alter the pattern of brain waves in healthy individuals, but the efficacy of binaural beats in altering the pattern of brain waves in primary insomniacs has not yet been investigated. The purpose of this study was to evaluate the efficacy of theta binaural beat on the absolute power of theta activity in primary insomniacs.

Methods: This study was a randomized clinical trial with experimental and control groups. Primary insomniacs received theta binaural beats in the experimental group and white noise in the control group. Their brain waves were recorded by EEG for 25 minutes, the first 5 minutes without stimulus (1st block), 15 minutes after receiving stimulus (binaural beat or white noise), and the last 5 minutes without stimulus (5th block). Matlab software (R2019a), EEGLAB toolbox and SPSS-24 were used for data analysis.

Results: The absolute power of theta activity in the experimental group was significantly higher in the last block comparing to the first block in all brain lobes ($P < 0.05$). The largest changes in theta activity were in temporal and parietal lobes, and the last one was in prefrontal lobe. In the control group, none of the brain lobes showed significant difference in the last block compared to the first block.

Conclusion: Theta binaural beat can alter the absolute power of theta activity in primary insomniacs. The implications of the study are discussed.

Keywords: Binaural beat, Electroencephalography (EEG), Primary insomnia, Theta brainwave

Introduction

Sleep is a psycho-physiological and natural phenomenon associated with decreased awareness towards the environment. However, this is not always the case. In fact, people with sleep problems experience this phenomenon differently. Insomnia is one of the most common of these problems. According to the diagnostic and statistical manual of mental disorders (DSM-5), insomnia is a complaint of inadequate or nonrestorative sleep with difficulties in onset, maintenance of early morning sleep and wakefulness (Association, 2013), if not accompanied by significant psychiatric comorbidity and physical illness, it is known as primary insomnia (De Zambotti, Covassin, De Min Tona, Sarlo, & Stegagno, 2011). The incidence of primary insomnia is about 2 to 4 percent, imposing huge costs on the economy of any country (Ohayon, Riemann, Morin, & Reynolds III, 2012). These cases indicate the need for further investigation in primary insomnia.

The EEG activity of sleep and wakefulness can be calculated from power spectral density (PSD) at different frequencies or frequency bands (eg, Delta (0.5 to 4 Hz), Theta (4 to 8 Hz), Alpha (8 to 12 Hz), Sigma (12 to 16 Hz) and Beta I (16 to 20 Hz) and Beta II (20 to 30 Hz)). Several functional electroencephalographic studies have been performed to investigate arousal during sleep and wakefulness in people with insomnia (Appleton et al., 2019; Christensen et al., 2019; Kwan, Baek, Chung, Kim, & Choi, 2018; McCloskey, Jeffries, Koprinska, Miller, & Grunstein, 2019; Perrin et al., 2019; Tang, McCurry, Riegel, Pike, & Vitiello, 2019) and various evidence, including increased beta (Fernandez-Mendoza et al., 2019; Lamarche & Ogilvie, 1997; Wołyńczyk-Gmaj & Szelenberger, 2011) and gamma (Knyazev, 2012; Makeig & Jung, 1996) at different stages of sleep and during wakefulness have been discussed. Other studies have also focused on cortical arousal and its association with insomnia and the fact that gamma, beta, and alpha frequencies in insomnia patients during sleep-wake transition are higher than in healthy people (Cervena et al., 2014; Figueredo-Rodriguez, del Rio-Portilla, Ivan Sanchez-Romero, Perez-Ortiz, & Corsi-Cabrera, 2009; Maes et al., 2014). Likewise, prefrontal cortex and hindbrain connections have been identified as trigger areas in insomnia patients when they attempt to sleep (Corsi-Cabrera, Rojas-Ramos, & del Río-Portilla, 2016). In 2010, Tononi showed higher beta power and its density in the frontal cortex and left-sided areas in insomnia patients than healthy controls (Tononi, 2010). These studies clearly showed that in the EEG

structure of sleep and wakefulness in primary insomniacs, changes have been observed so it can be altered through specific interventions.

A range of interventions have been performed to improve sleep in insomnia patients, including medication and psychological interventions (Morin, Jarvis, & Lynch, 2007; Schroeck et al., 2016). These interventions are usually costly and have a slow and varied impact on sleep structure, but there are a range of noninvasive interventions that can influence the pattern of brain waves at a lower cost. Binaural beats are among these interventions.

Binaural beats are illusions that can be considered as a type of neurological or cognitive coordination (Turow & Lane, 2012; Vernon, 2009). When two tones with slightly different frequencies reach each ear, for example, a 335 Hz tone to the right ear and a 345 Hz tone to the left ear, mentally, a 10 Hz binaural is perceived. Obviously, when listening to two different tones, most people hear only one tone that fluctuates in its frequency or loudness as a beat (Oster, 1973). Some researchers believe that the binaural beat responses occur in the right hemisphere (Draganova, Ross, Wollbrink, & Pantev, 2007; Magezi & Krumbholz, 2010; Schwarz & Taylor, 2005) and some consider the responses dependent on the other hemisphere (Chakalov, Paraskevopoulos, Wollbrink, & Pantev, 2014; Pratt et al., 2010). In addition, areas of the brain that are activated during audio stimulation and cause this illusion, are not fully understood. The binaural beat generates excitatory conditions that ultimately result in specific neural firing patterns in the inferior colliculus that can reflect a binaural beat (Hancock, Chung, McKinney, & Delgutte, 2017). Through this process, the pattern of the brain waves is entrained by the difference in the frequency of characteristic of the two heard tone (binaural beat). Numerous studies have investigated the effects of binaural beats on the entrainment, such as galvanic skin response and hypertension (Kennerly, 2004), mood (Perales, Sanchez, & Ramis, 2019), relaxation (Lee-Harris, Timmers, Humberstone, & Blackburn, 2018; Sharma, Rewadkar, Pawar, Deokar, & Lomte, 2017), attention and memory (Beauchene, Abaid, Moran, Diana, & Leonessa, 2017; Colzato, Barone, Sellaro, & Hommel, 2017; Garcia-Argibay, Santet, & Reales, 2017; Shekar, Suryavanshi, & Nayak, 2018), and other psycho-physical problems. However, their exact effect is still unknown. The beat frequency is important due to neural synchronization. Therefore, beta waves are fast brainwaves which associated with thinking, focusing, and processing information, alpha waves with relaxed attention, theta waves with memory, deep

relaxation and day-dreaming and delta waves with deep sleep (Thatcher, Budzynski, Budzynski, Evans, & Abarbanel, 2009). This pattern of brain waves is important in exploring the state of consciousness (Murat et al., 2011) which, of course, is also seen in the structure of sleep. For example, in a study by Abeln et al. (Abeln, Kleinert, Strüder, & Schneider, 2014) which investigated the effect of binaural beats on subjective sleep quality and improvement of mental health in athletes. They were stimulated with binaural beats of about 2 to 8 Hz every night before bedtime, for 8 weeks. Findings showed that the subjective's quality of wakefulness, sleep and motivational state were significantly improved in the binaural group but it had no effect on their physical state. In another study by Seifiala et al., that examined the cumulative effects of binaural beat of theta on brainpower and functional connectivity in 15 healthy subjects via EEG, the findings showed that the relative power of theta activity was significantly observed in parietal and temporal segments, but such effect was not observed in the prefrontal, frontal and central areas. Beside, no significant change was observed in the absolute power of the different frequency bands on any area of brain (Ala, Ahmadi-Pajouh, & Nasrabadi, 2018). These studies showed that binaural beats can alter the pattern of brain waves in healthy individuals but do not provide enough information in relation to people with certain disorders, such as insomnia.

Besed on the above information, regarding the impact of binaural beats on the EEG structure, cognitive and psychological processes, we hypothesized that binaural beats could influence the brain waves structure of primary insomniacs as well as healthy individuals. Moreover, theta waves are associated with memory, deep relaxation, and day-dreaming, and it has been shown that before bedtime, frequency of brain waves are gradually reduced (Finelli, Baumann, Borbély, & Achermann, 2000; Guerrero & Achermann, 2019). So, to achieve deep sleep (more delta wave activity), one must also experiences theta frequency. As noted earlier, the impact of theta binaural beat is mostly seen on the parietal, temporal, and posterior cortical areas (Ala et al., 2018), which differs from cortical activity in primary insomniacs. These people experience over-stimulation in prefrontal areas (Perrier et al., 2015). Yet, if binaural beats work to change the patterns of primary insomniac's brainwaves, it will provide a scientific breakthrough for implementing a new, low-cost, non-invasive way to improve these people. The purpose of this study was to evaluate the efficacy of theta binaural beat on the absolute power of theta activity in primary insomniacs.

Material and methods

Participants

This study was a randomized controlled trial (IRCT20180205038630N3) with control and experimental groups. The statistical community consisted of people with primary insomnia who live in Kermanshah city. The sample size in this study, based on the average of several recent studies (Abeln et al., 2014; Ham, Lee, Choi, & Choi, 2020; Järnefelt et al., 2014) and considering the cultural and economic constraints for each group was considered to be approximately 15 people. Based on inclusion and exclusion criteria, 31 adults with primary insomnia (15 females) were selected and evaluated (Figure 1). Inclusion criteria included informed consent, diagnosis of insomnia in clinical interview by a psychiatrist, insomnia severity score at clinical level (ISI > 15), severe neurological and psychiatric disorders, healthy physical and hearing status, abstinence from alcohol and medication consumption 12 hours before the intervention, no history of drug abuse, no cardiovascular problems, no pregnancy in female participants. Exclusion criteria included any discomfort as a result of hearing the sounds, unwillingness to continue performing the protocol for any reason.

Intervention protocol

Each participant was evaluated in two sessions. The first session was for diagnosing primary insomnia through the clinical interview of DSM-5, completing the insomnia severity index (ISI), as well as assessing the inclusion and exclusion criteria and their willingness to participate in the study. Subjects were randomly allocated to intervention and control groups. The randomization method was that participants were asked to choose one of two closed envelopes that contained experimental or control words. In the second session (intervention session), as the baseline, participants were at first evaluated by EEG in 5 minutes with closed eyes. Then they were stimulated with theta binaural beat or white noise for 15 minutes [with closed eyes], during that time, the EEG was recorded. Finally, 5 minutes after the intervention, EEG was again recorded without any binaural beat and white noise. All participants were assessed at the same time of day (11:00 AM). Based on research blocks, EEG recording changes were compared. The intervention protocol consisted of 5 blocks as shown in Figure 1. The experimental group received binaural beat in the theta frequency range. Accordingly, binaural beat stimulation for this study was

specifically designed through Audacity Software (<http://www.audacityteam.org>) and provided through headphones recommended by Light et al. (Light et al., 2010). A 250 Hz carrier tone to the right ear and a 256 Hz offset tone to the left ear of the participants in the experimental group were presented and the impact of 6 Hz binaural beat (in the theta domain) was investigated. The control group received white noise. White noises are random signals with the same intensity at different frequencies (Carter & Mancini, 2017). In fact, it is a statistical model for signals and their sources rather than any specific (eg, theta) signal (Stein, 2012). Other studies have also used this type of signal as a placebo intervention (Geers, Close, Caplandies, & Vase, 2019). The method of data recording and research blocks are shown in figure 1.

Figure 1. Research blocks and how to record data

Electroencephalographic (EEG) processing

Recording time for EEG signals was 25 minutes for each participant. In overall, according to specific criteria, the signals were collected in 5 minute intervals. These include: Clear Signals without noise, artifacts, and blinking effect. Components associated with direct current (DC) power fluctuations were eliminated by an one Hertz high-pass at zero-phase butterworth filter.

The Fast Fourier Transform (FFT) was performed to convert the signal from time domain to frequency domain. The absolute power of the theta activity was also used for statistical analysis, which was performed by the Matlab software (R2019a) and the EEGLAB toolbox. The cortical areas and their associated channels are shown in table 1.

Table 1. Cortical areas of the brain and its associated channels

Cortical areas	Channels
Prefrontal	Fp1, Fp2, F7, F8
Frontal	F3, Fz, F4
Central	C3, Cz, C4
Temporal	T3, T4, T5, T6
Parietal	P3, Pz, P4
Occipital	O1, O2

Statistical analysis

Data were analyzed using SPSS-24. Before performing any other statistical tests, the data were assumed to be normal by Kolmogorov-Smirnov test ($P > 0.05$). Chi-square test was used to compare the number (frequency) of the two experimental and control groups. Independent t-test was also used to examine the differences between two groups in terms of mean age. Besides, multivariate analysis of covariance (MANCOVA) and relevant tests with its assumptions was used to determine the effect size and significance of the intervention.

Research tools

Insomnia severity index (ISI): A standard inventory that measures the severity of insomnia in the past two weeks and has five questions. The minimum and maximum scores are also between 0 and 28 (Yazdi, Sadeghniiat-Haghighi, Zohal, & Elmizadeh, 2012). A score of 0 to 7 indicates to no significant insomnia, 8 to 14 below the clinical threshold, 15 to 21 moderate clinical insomnia, and a score of 22 to 28 indicates on severe clinical insomnia. This test was first presented and used by Morin et al. Its construct validity was 0.72 and its reliability with

Cronbach's alpha method was 0.74 and 0.78 (Bastien, Vallières, & Morin, 2001; Yazdi et al., 2012).

Electroencephalography (EEG): A physiological way of recording electrical activity which produced by brain . It was done by placing electrodes on the surface of the scalp. EEG signals which were used in this study produced from 19 active electrodes based on the 10-20 system overhead with a sampling frequency of 512 Hz (Ala et al., 2018).

Results

Out of 31 participants, 15 were female. As shown in Table 2, there was not a significant difference between the mean age of men and women who participated in this study. There was also no significant difference between two groups regarding mean age (based on independent t-test) and frequency of male and female's participants (based on Chi-square test) ($P > 0.05$). Also, there was no significant difference between the two groups in terms of severity of insomnia (based on independent t-test) ($P > 0.05$).

Table 2. Demographic characteristics of the participants

Parameteres	Experimental Group	Control Group	P-value
Age (Year)	26.88 $\pm$ 3.01	27.01 $\pm$ 2.97	0.24
Male	26.24 $\pm$ 3.44	26.58 $\pm$ 3.37	0.44
Female	27.87 $\pm$ 2.04	28.03 $\pm$ 2.15	0.10
Gender			0.09
Male	8 (% 50)	8 (%53.33)	
Female	8 (%50)	7 (%46.67)	
Insomnia severity	17.24 $\pm$ 1.44	17.19 $\pm$ 1.19	0.14

Multivariate analysis of covariance is one of the types of inferential statistical methods that can show the effect of the intervention performed simultaneously with the control of the covariate variable (s) (Zimmermann, Pauly, & Bathke, 2019). This statistical test has several hypotheses that need to be confirmed to perform multivariate analysis of covariance. The first assumption is the normality of research data that was verified using the Kolmogorov-Smirnov test ($P > 0.05$). The second assumption is the homogeneity of variances, which Levin test showed that the difference in the variance of target variables is not significant ($P > 0.05$). So this assumption was also confirmed. The third assumption is the

study of the homogeneity of the regression slope of the variables, which shows the significance of the relationship between the dependent and independent variables. The data of this study also confirmed the third hypothesis ($P < 0.05$). Table 3 shows the results of multivariate analysis of covariance.

Table 3. Multivariate analysis of covariance results

Dependent variable	F	P	Effect size	Statistical power
Prefrontal	21.73	< 0.001	0.29	0.84
Frontal	29.15	< 0.001	0.42	0.92
Central	32.91	< 0.001	0.47	0.91
Temporal	41.12	< 0.001	0.55	0.89
Parietal	38.99	< 0.001	0.51	0.94
Occipital	23.88	< 0.001	0.35	0.88

Table 3 presents the multivariate analysis of covariance results of the absolute power of theta activity with the control of the covariate variables. According to this table, the absolute power of theta activity in the experimental group who receiving theta binaural beat was significantly higher in the last block comparing to the first block in all brain lobes ($P < 0.05$). The largest changes in theta activity were in temporal (Effect size= 0.55, $P < 0.001$) and parietal (Effect size= 0.51, $P < 0.001$) lobes, and the least one was in prefrontal (Effect size= 0.29, $P < 0.001$) lobe based on effect size. The changes were significant in all brain lobes.

Table 4 shows the exact position of the electrodes that showed a significant difference in the experimental group compared to the first block (pre-test) based on the mean of absolute power of theta activity. In fact, this table clearly shows specific areas of the brain that have undergone significant changes in the absolute power of theta activity in each brain lobe and block of research. Accordingly, the third block of the study showed the most changes in the levels of the electrodes, while in the second block, none of the electrodes showed significant difference.

Table 4. Cortical positions that showed a significant difference ($P < 0.05$) in the absolute power of theta activity in the experimental group in each block compared to the pretest based on dependent t-test (block 1)

Research blocks	Electrod positions
2	-
3	Fp1, Fp2, F3, F4, F7, Fz, C3, Cz, P3, P4, Pz, O1, O2
4	Fp1, Fp2, F3, F4, F7, Fz, Cz, P3, P4, Pz, O1, O2
5	Fp2, F7, F3, F4, Fz, Cz, P4, O2

Discussion

The purpose of this study was to investigate the efficacy of theta binaural beat in altering the pattern of the absolute power of theta activity in primary insomniacs. The findings of this study indicated on the theta binaural beat's effect on all brain lobes compared to the pretest (block 1) along with altering the absolute power of theta activity. But, white noise did not affected any of the brain lobes. Seifi ala et al. (2018) investigated the cumulative effects of binaural beats of theta on brain power and functional connectivity in healthy subjects through an EEG (Ala et al., 2018). Their findings showed that although the relative power of theta activity changes in parietal, temporal and occipital lobes were significant, however it was not in anterior, frontal and central areas. No significant changes were also observed in the absolute power of different frequency bands in any parts of the brain in healthy subjects. Obviously, these results are not in line with the present study. Some of the most important factors that explain this conflict of findings are the differences in the design of intervention protocol, statistical community and binaural beat music which used in two studies. On one hand, the seven hertz binaural beat which were used in Seifi ala et al. research was combined with 10 percent pink noise and presented to participants at different times. On the other hand, the statistical population of the two studies was also different, which should have important influences.

As mentioned before, the pattern of brain waves in primary insomniacs was different from healthy subjects. Corsi-Cabrera et al. in 2016 showed that primary insomniacs experience more arousal in the anterior and posterior brain regions, which was distinctly different from healthy subjects (Corsi-Cabrera et al., 2016). The present study strongly showed although the degree of

changes in the absolute power of theta activity was not same in different regions, but primary insomniacs were significantly influenced by theta binaural beats in all areas of the brain. This inequality of effect is a confirmation of the hypothesis that different areas of the brain are affected by different frequencies (Laufs et al., 2003) and besides, the efficacy of theta binaural beats on primary insomniacs is differentiated from healthy subjects (Ala et al., 2018).

The effect of theta binaural beat on temporal and parietal areas was higher than other brain segments, whereas the prefrontal and occipital regions had the least significant changes in the absolute power of theta activity. Also the electrode's significant changes in the absolute power of theta activity compared to the first block of research (pre-test) also confirm this result. On the other hand, a study by Wołyńczyk-Gmaj and Szelenberger investigated wake electroencephalography in insomnia patients and found that the density of beta waves in different brain areas was higher than in good sleepers (Wołyńczyk-Gmaj & Szelenberger, 2011). In fact, beta waves are at a frequency of at least 16 Hz and are responsible for thinking, concentration and processing of information, and are in high exact density when insomniacs want to go to sleep [sleep-onset] (Fernandez-Mendoza et al., 2019; Lamarche & Ogilvie, 1997). Good sleepers, while falling asleep, the frequencies of the brain waves gradually decrease, so passing through the surface of theta waves to delta (Guerrero & Achermann, 2019). Theoretically, primary insomniacs tend to process and concentration on everyday information when trying to calm their attention, achieve deep relaxation and day-dreaming (Carciofo, Song, Du, Wang, & Zhang, 2017; Nie et al., 2015). In the present study, it has been shown that theta binaural beat can alter the pattern of brain waves in these areas in line with the major activity of beta waves.

Limitations of the study were included the followings. Since the study participants were primary insomniacs and were taking medication at the time of diagnosis, the type and dose of the medication were not controlled. In future studies, it is recommended that primary insomniacs be screened for the same type and dose of the medication. Small sample size was another limitation so, to generalize the findings of this study, it is recommended to use a larger sample size in future studies. Due to the high cost of data recording, the analysis of the least valid and reliable sample size was used. Yet, it was not possible to investigate changes in subcortical tissue and function through sophisticated brain imaging modalities such as positron emission tomography (PET), polysomnography (PSG) or functional magnetic resonance imaging (fMRI).

Based on data obtained from electroencephalography in primary insomniacs and considering the limitations, the present study has two major implications: 1) Theta binaural beat through entrainment can alter the absolute power of theta activity in primary insomniacs, 2) The theta binaural beat can probably affect information processing and relaxation when people try to sleep.

Ethical considerations

Compliance with ethical guidelines

Participants were informed about the research process and conditions and completed the informed consent form. All research data were kept confidential and the results were debriefed for the subjects at the end. Finally, after completing the intervention process in two groups, the binaural beat music at different frequencies was made available to all participants. This study was approved by the Ethics Committee of Kermanshah University of Medical Sciences (IR.KUMS.REC.1397.771).

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Authors' contributions

All authors contributed in preparing this article.

Conflict of Interests

The authors have declared no conflict of interests.

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