

The Efficacy of Binaural Beat Stimulation Mixed with Acoustic Music in Chronic Low Back Pain Management: A Randomized Controlled Trial

Kwanchanok Thanyawinichkul MD¹, Nuj Tontisirin MD¹, Rungwipa Mahawan RN¹, Sirima Kumdang RN¹, Traisak Yamsa-ard MEng², Moncharin Maneepairoj MD³, Daochompu Nakawiro MD⁴

¹ Department of Anesthesiology, Faculty of Medicine Ramathibodi Hospital, Mahidol University, Bangkok, Thailand

² Brain-Computer Interface Laboratory (BCI LAB), Department of Biomedical Engineering, Mahidol University, Nakhon Pathom, Thailand

³ Chulabhorn Hospital, Bangkok, Thailand

⁴ Department of Psychiatry, Faculty of Medicine Ramathibodi Hospital, Mahidol University, Bangkok, Thailand

Background: By using an external stimulus with different beat frequencies to generate an optimal brain wave pattern, binaural beat stimulation provides a similar effect to mindfulness meditation. While it has been found to have a beneficial effect in chronic pain conditions, its effect in patients suffering from low back pain has not been examined.

Objective: To investigate the efficacy of binaural beat stimulation mixed with acoustic music compared to acoustic music alone in individuals with chronic low back pain.

Materials and Methods: Adults with chronic low back pain were randomly allocated into two groups, where Group A listened to 20 minutes of acoustic piano music per day for 14 days, and patients in group B listened to 20 minutes of piano music mixed with 6 Hz-theta binaural beats per day for 14 days. The primary outcome was the pain score at 14 days as measured by the Thai Brief Pain Inventory (BPI). The secondary outcomes included quantitative electroencephalogram (QEEG) changes, pain interference, and changes in the Thai Hospital Anxiety Depression Scale (HADS). All participants, outcome assessors and QEEG evaluator were blinded.

Results: Twelves participants were enrolled in each group. No intergroup differences were found in pain, pain interference, or QEEG measures. In addition, a significant improvement in the HADS-D (depression subscale) was found in both groups.

Conclusion: The authors were unable to find a benefit to the addition of binaural beats stimulation to acoustic music in patients suffering from chronic low back pain. More studies are warranted.

Keywords: Binaural beat stimulation; Chronic low back pain; Theta brain wave

Received 4 April 2022 | Revised 28 July 2022 | Accepted 9 August 2022

J Med Assoc Thai 2022;105(9):806-14

Website: <http://www.jmatonline.com>

In Thailand, up to 20% of the population will be elderly, above 65 years of age, in 2022⁽¹⁾. The prevalence of chronic back pain increases with age, and it has a major effect on the socioeconomic status and quality of life in older people⁽²⁾. Chronic low back pain encompasses physical, psychological,

and emotional components⁽³⁾, and its' treatment is challenging. Because pharmacological treatments can have significant side effects with long term use, non-pharmacological techniques are becoming increasingly important.

Neuro-modulatory approaches, such as mindfulness meditation, relaxation therapy, and music therapy can provide psychological benefits in addition to relieving pain and improving health. Mechanisms of action include a reduction in pain-related primary somatosensory cortex activation, as well as activation of higher-order brain regions that control the emotional response to pain, such as the anterior cingulate cortex, prefrontal cortex, and anterior insula^(4,5). Mindfulness meditation can generate theta and slow-alpha electroencephalogram (EEG) power, predominantly in frontal brain areas^(6,7). Previous studies showed mindfulness

Correspondence to:

Tontisirin N.

Department of Anesthesiology, Faculty of Medicine Ramathibodi Hospital, 270 Rama VI Road, Ratchathewi, Bangkok 10400, Thailand.

Phone: +66-2-2011513, **Fax:** +66-2-2011569

Email: doctornuj@gmail.com, nuj.ton@mahidol.ac.th

How to cite this article:

Thanyawinichkul K, Tontisirin N, Mahawan R, Kumdang S, Yamsa-ard T, Maneepairoj M, et al. The Efficacy of Binaural Beat Stimulation Mixed with Acoustic Music in Chronic Low Back Pain Management: A Randomized Controlled Trial. *J Med Assoc Thai* 2022;105:806-14.

DOI: 10.35755/jmedassocthai.2022.09.13598

meditation can reduce pain interference but not pain intensity by changing in pain control beliefs and pain catastrophizing⁽⁸⁾. However, mindfulness meditation training is time consuming and difficult to practice. In contrast, binaural beat stimulation can be easier to implement and produces similar brain wave changes.

Binaural beat stimulation uses an external stimulus with different beat frequencies in each ear to generate the desired brain waves in the frontal-midline region that influences the neural firing pattern, resulting in changes in cognitive function and mood⁽⁶⁾. Frequency of 4 to 8 Hz can generate theta waves similar to those observed in deep meditation or deep relaxation at the frontal midline. These changes can be demonstrated by quantitative electroencephalogram (QEEG)⁽⁶⁾. The evidence of efficacy of binaural beat in management of chronic pain is limited. Zampi demonstrated that theta-binaural beat stimulation decreased chronic pain of various causes by 77%⁽⁴⁾. However, the present study did not measure changes in the theta or low-alpha-EEG power at the midline frontal region. The authors' previous study found an enhancement of theta waves in the brain in volunteers after listening to binaural beat mixed with acoustic piano music daily for seven days⁽⁹⁾. Since the binaural beat sound alone is disturbing, adding acoustic piano music makes it more pleasant.

The aim of the present study was to investigate the efficacy of theta-binaural beat stimulation combined with acoustic music compared to acoustic music alone in the management of chronic low back pain. Outcomes included changes in pain intensity, change in pain interference, and change in theta and alpha EEG power in frontal brain areas.

Materials and Methods

Ethics approval for the present study was obtained from the Ethics Review Board of Mahidol University (approval number 11-60-56) and the trial registered with the Thai Clinical Trials Registry (TCTR20190819003).

Participants

After obtaining written and informed consent, participants aged 27 to 70 years with moderate to severe chronic back pain for more than three months and that were treated and followed at the Ramathibodi pain clinic were enrolled in the present study between August 2019 and January 2020. Exclusion criteria were patients with a history of brain disease, psychiatric disorder, marked anxiety or depression with the Thai Hospital Anxiety Depression Scale

(HADS) greater than 11, hearing impairment from a negative whispered voice test, inability to read or write, as well as those that underwent surgery or other invasive pain treatments.

Sample size calculation

The power calculation was based on a previous study in patients with chronic non-cancer pain that demonstrated the effectiveness of the theta-binaural beat in reducing perceived pain severity using the West Haven-Yale Multidimensional Pain Inventory (MPI) from 4.60 to 2.74 (Partial $\eta^2=0.74$). Using an alpha error of 0.05 and power of test 95%, eight participants were needed per group (G*Power for Windows, Version 3.1). With allowance for 20% loss to follow-up, the required sample size was 12 participants per group.

Randomization and masking

The participants were randomized and allocated into two groups using a computer-generated randomization list with random block size of four (Sealed Envelope™; Sealed Envelope Ltd. 2017). Group A participants listened to 20-minutes of acoustic piano music per day for 14 days using a head set or ear buds in a quiet room in their residences, comfortably sitting or lying down. The sound pressure level depended on participants' preference. Group B participants listened to 20-minutes of combined acoustic piano music and theta-binaural beat daily for 14 days. All participants, outcome assessors and the QEEG evaluator were blinded to the intervention allocation. All participants were suggested to not change pain medication or having new therapy during the 14-day of music therapy.

Data collection

Demographic data including age, gender, education, current occupation, and underlying medical diseases were recorded. Dominant hand and meditation history such as frequency of meditation and past meditation practice, and pain history including causes, duration of chronic back pain and current pain medications were also collected. The history of depression or anxiety disorder, which was diagnosed by psychiatrists, was also recorded. The outcomes were assessed by pain nurses (RM, SK) blinded to the assigned group.

Questionnaires/instruments

The Thai Brief Pain Inventory (BPI), Thai HADS, and QEEG were assessed two times, at the

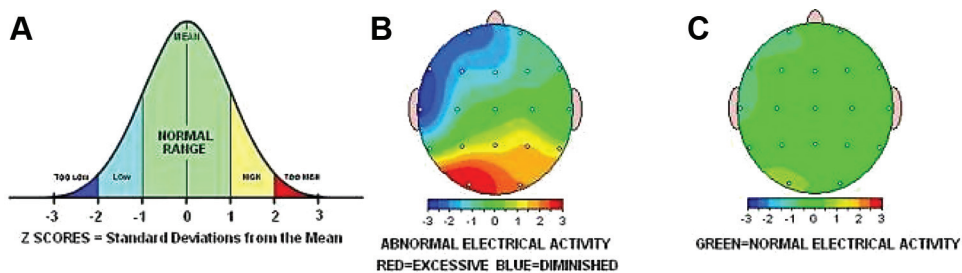


Figure 1. Graphically displayed z-score.

first visit before the intervention and 14 days later. Additionally, the Patient Global Impression Scale of Improvement (PGI-I) was collected at 14 days after the intervention.

1. Thai BPI⁽¹⁰⁾ was used to measure two aspects of pain including pain severity and pain interference and comprised of:

- Body pain mapping
- Pain intensity consisted of 1) worst pain, 2) least pain, and 3) average pain intensity during last 24 hours, and 4) pain right now (0 to 10 scale; 0 indicating none and 10 indicating worst possible pain)
- Pain interference in 1) normal work, 2) walking ability, 3) general activity, 4) life enjoyment, 5) mood, 6) relationship, and 7) sleep (0 indicating no interfere and 10 indicating most disturbing)
- One question about current pain medications with name, indication, dose, route, and started date
- One question about how the participant rated their improvement in past 24 hours

2. Thai HADS⁽¹¹⁾ was used for the screening for anxiety and depression. The HADS consists of two subscales, anxiety (HADS-A) and depression (HADS-D). Each subscale is composed of seven items with scores ranging from 0 (least) to 3 (worst). The total scores for HADS-A and HADS-D range from 0 to 21, with scores 11 or greater suggestive of a diagnosis of anxiety or depression.

3. QEEG was used to evaluate brain activity. Nineteen-channel EEGs based on the 10 to 20 international system were acquired by the Brain Master Discovery 24ETM device, which has 24-bit resolution with 0.001 to 100 Hz bandwidth and sampling rate of 1,024 samples per second. After checking the reliability of raw EEG data by using split-half test and test-retest reliability, the authors analyzed data based on frequency domain to observe the power of each EEG rhythm which were:

- Delta (<4 Hz), associated with deep dreamless sleep and loss of body awareness.

- Theta (4 to 8 Hz), associated with deep meditation or deep relaxation or both.

- Alpha (8 to 13 Hz), associated with relaxation when awake, pre-sleep, and pre-wake drowsiness.

- Beta (13 to 30 Hz), associated with being mentally active, busy, or anxious, and active concentration, arousal, and cognition.

- Gamma (30 to 100 Hz), associated with increased mental activity, including learning, perception, problem solving, fear, and consciousness.

QEEG analysis:

- The Fast Fourier Transform (FFT) technique was used to convert a signal from the time domain to frequency domain (amplitude, μV^2).

- The mean of amplitudes of each EEG rhythm was presented as “an absolute power”.

- Absolute power was compared to a normative data base collected from QEEG studies in 625 screened and evaluated Thai normal individuals (age 2 months to 82 years) using NeuroguideTM(12,13) software.

- The difference from normal values was presented as “z-score” (+ value=more amplitudes, – value=less amplitudes).

QEEG comparison:

- Z-scores before and after the intervention were compared between groups and within each group.

- The trend of normalization of z-score using color coding as following (Figure 1);

- Green: EEG in normal range
- Yellow: excessive activities (>1 SD)
- Red: excessive activities (>2 SD)
- Blue: diminished activities (<1 SD)
- Navy blue: diminished activities (<2 SD)

There was no standardized statistical comparison of normalization of brain activity. The normalization of brain activity was determined by using the picture of the z-score of each individual as shown example in Figure 1B and C⁽¹⁴⁾ before and after the intervention. If there were green color in the frontal areas of the brain after, compared to before the intervention, the

intervention was interpreted as normalizing the brain activity, especially theta and alpha activities, in the pain perception area (including channel FP1, F3, F7, Fz, FP2, F4 and F8).

4. The Thai PGI-I was used to rate the response to the intervention. PGI-I is a transition scale that is a single question asking the patient to rate their pain condition now, as compared with how it was prior to beginning the intervention on a scale from 1 indicated very much better to 7 indicated very much worse.

5. Acoustic beat music and binaural beat music

The authors used Gnaural⁽¹⁵⁾, a freely licensed software, which is a programmable audio generator for binaural beats. Audacity software was used to mix the beat frequency into the piano music.

- The acoustic beat music consisted of piano music with a steady-state base frequency of 300 Hz.

- The theta-binaural beat music consisted of the piano music described above with the following additions:

- Began with a beta frequency at 20 Hz (300 Hz and 320 Hz) for 30 seconds,

- Then decremented to a 12-Hz and 9-Hz alpha frequency (300 Hz and 312 Hz, 300 Hz and 309 Hz) and 7-Hz theta frequency (300 Hz and 307 Hz) over the first 2 minutes and finally 6 Hz (300 Hz and 306 Hz) until minute 19.

- Then, the frequency increased over the last minute to 7 Hz, 9 Hz, and 12 Hz, finally returning the brain a beta frequency at 20 Hz. One 12 Hz (300 Hz and 312 Hz) frequency spike was included at minute 10 to keep the participant from falling asleep.

Hearing test

Hearing was assessed using the standardized whispered voice test⁽¹⁶⁾.

Outcomes

The primary outcome was change in pain severity. Secondary outcomes were the change in pain interference, anxiety, and depression, global change, and change in brain activities using z-score comparison and trend of normalization of brain activities after the intervention

Statistical analysis

Data were analyzed using PASW Statistics for Windows, version 18.0 (SPSS Inc., Chicago, IL, USA). Descriptive statistics were presented as frequency and percentage, mean \pm standard deviation (SD), median and interquartile range (IQR). For continuous data, Shapiro-Wilk's test was used to test

the distribution. The Mann-Whitney U test or Student t-test was used as appropriate. Chi-square test was used for comparison of categorical data. The paired t-test was used for within group and between groups comparisons. The p-values lower than 0.05 were considered to be statistically significant.

Results

Demographic data

Twenty-four participants were enrolled in the present study, two participants in group B (8%) withdrawn from the study (Figure 2). Therefore, 22 participants (92%) underwent the intervention.

There was no difference between groups in the demographic data, which included age, gender, education, occupation, dominant hand, underlying medical diseases, duration of back pain, meditation history, depression and anxiety disorder, current pain medication, and antidepressant usage (Table 1). The most common causes of back pain were spondylosis and post-spinal surgery (Table 1).

No intergroup differences were found in any of the outcomes. In contrast, almost all BPI-measurements were lower after the intervention in both groups (Table 2). While none of these changes were significant in group A, group B had a significant reduction in maximum pain in the past 24 hours, average pain, and disturbance in relationship with other people (Table 2). Both groups had significantly lower HADS-D scales after the intervention. Group B also showed a trend toward significant reduction in HADS-A score ($p=0.06$).

QEEG analysis

Z-score analysis: Three participants in group A and two participants in group B had outlying z-scores ($\pm 2SD$ values). The z-score analysis excluded these individuals.

- Theta wave comparison after the intervention:
 - There was no difference in z-score between groups after the intervention. There was a trend toward an increase in z-score of the theta wave frequency in group A compared to group B in the FP1 channel ($p=0.054$).

- In Intra-group comparison, group A showed a significant increase in z-score in the FP1 channel (Table 3). There were no significant differences in theta z-scores in any channel in group B.

- Alpha wave comparison after the intervention:
 - There was no significant difference in alpha wave z-score frequencies between groups as well as within groups.

Table 1. Participant characteristics (n=22)

| Characteristics | Group A (n=12): Acoustic beat | Group B (n=10): Binaural beat | p-value |
|--|-------------------------------|-------------------------------|---------|
| Age (years); mean±SD | 53.50±12.99 | 51.30±16.34 | 0.738 |
| Sex; n (%) | | | 0.348 |
| Male | 2 (16.7) | 4 (40 (0.0)) | |
| Female | 10 (83.3) | 6 (60.0) | |
| Education; n (%) | | | 0.790 |
| Primary school | 0 (0.0) | 0 (0.0) | |
| Secondary school | 2 (16.7) | 0 (0.0) | |
| Diploma | 3 (25) | 3 (30.0) | |
| Bachelor's degree | 5 (41.7) | 4 (40.0) | |
| Master's degree | 2 (16.7) | 2 (20.0) | |
| Doctor's degree | 0 (0.0) | 1 (10.0) | |
| Occupation; n (%) | | | 0.974 |
| Government official | 2 (16.7) | 2 (20.0) | |
| Self-employed | 2 (16.6) | 1 (10.0) | |
| Employee | 4 (33.3) | 5 (50.0) | |
| House wife | 4 (33.3) | 2 (20.0) | |
| Dominant hand; n (%) | | | 0.481 |
| Right | 10 (83.3) | 10 (100) | |
| Left | 2 (16.7) | 0 (0.0) | |
| Underlying medical diseases; n (%) | | | 0.384 |
| Diabetes mellitus | 1 (8.3) | 2 (20.0) | 0.571 |
| Hypertension | 5 (41.7) | 4 (40.0) | >0.999 |
| Hyperlipidemia | 5 (41.7) | 2 (20.0) | 0.381 |
| Chronic kidney disease | 1 (8.3) | 0 (0.0) | >0.999 |
| Musculoskeletal | 4 (33.3) | 4 (40.0) | >0.999 |
| Heart disease | 1 (8.3) | 0 (0.0) | >0.999 |
| Respiratory tract | 0 (0.0) | 1 (10.0) | 0.455 |
| Cerebrovascular disease | 0 (0.0) | 0 (0.0) | - |
| Gastrointestinal tract | 0 (0.0) | 2 (20.0) | 0.195 |
| Hematologic disease | 1 (8.3) | 0 (0.0) | >0.999 |
| Major depressive disorder | 2 (16.7) | 0 (0.0) | 0.481 |
| Anxiety disorder | 0 (0.0) | 0 (0.0) | - |
| Adjustment disorder | 1 (8.3) | 1 (10.0) | >0.999 |
| Duration of chronic back pain (months); median (IQR) | 60 (30.0, 81.75) | 72 (51.75, 150) | 0.381 |
| Cause of low back pain; n (%) | | | 0.790 |
| HNP | 1 (8.3) | 0 (0.0) | |
| Spondylosis (spinal stenosis) | 3 (25.0) | 4 (40.0) | |
| Spondylolisthesis | 1 (8.3) | 1 (10.0) | |
| Facet arthropathy | 0 (0.0) | 1 (10.0) | |
| Post-spinal surgery with chronic low back pain | 4 (33.3) | 1 (10.0) | |
| Myofascial pain | 1 (8.3) | 2 (20.0) | |
| Other: infection, tumor | 2 (16.7) | 1 (10.0) | |
| Current pain medication; n (%) | | | |
| Antidepressant (venlafaxine or duloxetine) | 5 (41.7) | 2 (20.0) | 0.381 |
| Anticonvulsant (gabapentin or pregabalin) | 9 (75.0) | 6 (60.0) | 0.652 |
| Opioids (tramadol or codeine or methadone) | 10 (83.3) | 8 (80.0) | >0.999 |
| Muscle relaxant (clonazepam or baclofen or tizanidine) | 6 (50.0) | 4 (40.0) | 0.691 |
| Combined antidepressant, anticonvulsant | 0 (0.0) | 0 (0.0) | - |
| Combined antidepressant, anticonvulsant, opioid | 2 (16.7) | 0 (0.0) | 0.495 |
| Combined antidepressant, anticonvulsant, opioid, muscle relaxant | 3 (25.0) | 1 (12.5) | 0.619 |
| Other combination | 7 (58.3) | 7 (87.5) | 0.325 |
| Meditation history; n (%) | 2 (16.7) | 5 (50.0) | 0.172 |

SD=standard deviation; IQR=interquartile range; HNP=herniated nucleus pulposus

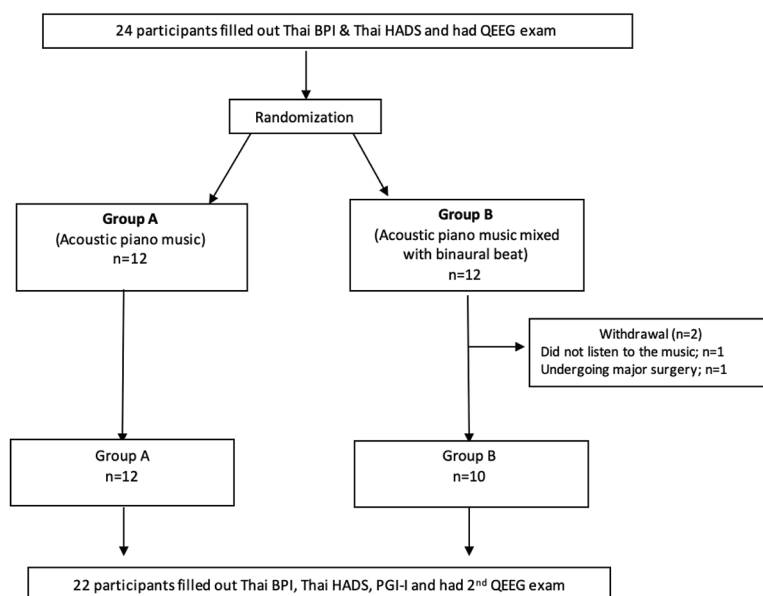


Figure 2. Patient selection flow chart.

Thai-BPI=Thai Brief Pain Inventory; Thai HADS=Thai Hospital Anxiety and Depression Scale; QEEG=quantitative electroencephalogram; PGI-I=Patient Global Impression Scale of Improvement

Table 2. Thai BPI and Thai HADS

| Thai BPI items | Intra-group comparison: Group A (n=12); mean±SD | | p-value | Effect size | Intra-group comparison: Group B (n=10); mean±SD | | p-value | Effect size | Intergroup comparison | | | |
|--------------------------------|---|----------|---------|-------------|---|----------|---------|-------------|-----------------------|--------------------------|----------------|--------------------------|
| | Day 1 | Day 14 | | | Day 1 | Day 14 | | | Day 1; p-value | Mean difference (95% CI) | Day 2; p-value | Mean difference (95% CI) |
| Maximum pain score in 24 hours | 6.42±2.6 | 5.67±2.6 | 0.445 | 0.29 | 6.60±1.7 | 5.30±2.1 | 0.004* | 0.68 | 0.842 | -0.183 (-2.083 to 1.717) | 0.724 | 0.367 (-1.733 to 2.506) |
| Minimum pain score in 24 hours | 2.83±1.9 | 3.33±2.6 | 0.324 | -0.22 | 3.60±1.7 | 3.30±2.5 | 0.496 | 0.14 | 0.329 | -0.767 (-2.365 to 0.832) | 0.976 | 0.033 (-2.233 to 2.30) |
| Average pain score | 5.58±1.8 | 5.25±2.2 | 0.586 | 0.16 | 5.40±1.1 | 4.70±1.7 | 0.045* | 0.49 | 0.779 | 0.183 (-1.161 to 1.528) | 0.529 | 0.550 (-1.240 to 2.340) |
| Pain score now | 4.58±2.4 | 4.50±2.7 | 0.898 | 0.03 | 5.40±2.0 | 4.60±2.3 | 0.087 | 0.37 | 0.407 | -0.817 (-2.827 to 1.194) | 0.926 | -0.100 (-2.319 to 2.119) |
| Degree of pain relief | 5.33±3.0 | 5.08±2.3 | 0.768 | 0.09 | 5.10±3.0 | 4.20±2.8 | 0.337 | 0.31 | 0.858 | 0.233 (-2.443 to 2.910) | 0.425 | 0.883 (-1.381 to 3.147) |
| General activity | 5.33±2.7 | 4.50±2.5 | 0.376 | 0.32 | 5.30±1.8 | 5.30±1.8 | >0.999 | 0.00 | 0.973 | 0.033 (-2.030 to 2.097) | 0.411 | -0.800 (-2.788 to 1.188) |
| Mood | 4.42±2.9 | 3.50±3.4 | 0.288 | 0.29 | 4.90±2.5 | 4.70±2.5 | 0.591 | 0.08 | 0.680 | -0.483 (-2.895 to 1.928) | 0.363 | -1.200 (-3.888 to 1.488) |
| Walking ability | 5.00±2.8 | 4.17±3.0 | 0.349 | 0.29 | 4.90±3.3 | 4.30±3.1 | 0.343 | 0.19 | 0.939 | 0.100 (-2.601 to 2.801) | 0.918 | -0.133 (-2.811 to 2.544) |
| Normal work | 5.83±2.6 | 5.08±3.2 | 0.326 | 0.26 | 5.60±2.5 | 4.60±2.5 | 0.138 | 0.40 | 0.830 | 0.233 (-2.009 to 2.476) | 0.700 | 0.483 (-2.100 to 3.067) |
| Relationship | 3.25±2.3 | 3.58±2.8 | 0.730 | -0.13 | 4.30±2.7 | 2.10±2.2 | 0.008* | 0.89 | 0.329 | -1.050 (-3.241 to 1.141) | 0.189 | 1.483 (-0.792 to 3.759) |
| Sleep | 5.50±3.9 | 4.75±4.1 | 0.212 | 0.19 | 5.30±3.0 | 4.40±3.0 | 0.159 | 0.30 | 0.896 | 0.200 (-2.952 to 3.352) | 0.825 | 0.350 (-2.911 to 3.611) |
| Life enjoyment | 5.33±3.1 | 4.33±3.4 | 0.255 | 0.31 | 5.10±2.1 | 4.70±2.2 | 0.534 | 0.19 | 0.844 | 0.233 (-2.209 to 2.676) | 0.772 | -0.367 (-2.977 to 2.243) |
| Anxiety (HADS-A) | 8.75±3.7 | 7.58±4.4 | 0.260 | 0.29 | 6.90±4.2 | 5.60±2.7 | 0.064 | 0.37 | 0.280 | 1.850 (-1.627 to 5.327) | 0.226 | 1.983 (-1.330 to 5.297) |
| Depression (HADS-D) | 6.25±2.3 | 4.92±2.6 | 0.039* | 0.54 | 6.50±3.2 | 4.50±3.4 | 0.010* | 0.61 | 0.833 | -0.250 (-2.686 to 2.186) | 0.749 | 0.417 (-2.258 to 3.092) |

SD=standard deviation; CI=confidence interval

* p<0.05, statistical significance

Trend of normalization of alpha and theta waves in frontal brain after the intervention

- Theta wave comparison after the intervention:

• Group A had less normal brain activities or less green color, but more excessive theta wave activities or yellow, orange, red color, which is consistent with the significant increase in z-score seen

in channel FP1 (Table 3).

• Group B had more normalization of theta wave activities with more green color.

- Alpha wave comparison after the intervention:

• Group A had less change in alpha wave activities. Whereas, group B had more normalization of alpha wave activities (Figure 3).

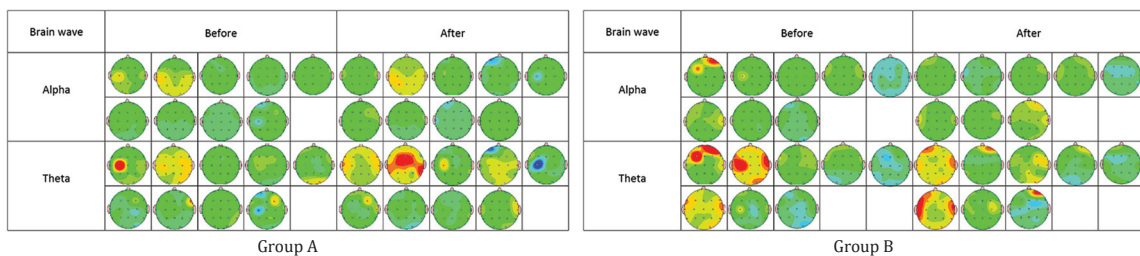


Figure 3. Normalization in mean z-score in frontal brain of each subject.

Green color=z-score close to 0; Yellow, orange, red=z-score >0; Light blue, blue, navy blue=z score <0

Table 3. Intra-group comparison of z-score in theta-wave in frontal brain

| EEG channel | Group A (n=9); mean±SD | | | Effect size | Group B (n=8); mean±SD | | | Effect size |
|-------------|------------------------|-----------|---------|-------------|------------------------|-----------|---------|-------------|
| | Day 1 | Day 14 | p-value | | Day 1 | Day 14 | p-value | |
| FP1 | -0.77±0.9 | 0.20±0.6 | 0.019* | -1.27 | 0.23±0.9 | -0.39±0.9 | 0.088 | 0.69 |
| F3 | -0.18±0.4 | 0.03±0.6 | 0.538 | -0.41 | 0.28±1.1 | -0.15±0.5 | 0.297 | 0.50 |
| F7 | -0.16±0.4 | 0.13±0.8 | 0.359 | -0.46 | 0.45±0.9 | 0.04±0.6 | 0.208 | 0.54 |
| Fz | -0.29±0.4 | -0.12±0.5 | 0.480 | -0.38 | -0.01±0.8 | -0.28±0.5 | 0.424 | 0.40 |
| FP2 | -0.19±0.3 | 0.16±0.6 | 0.111 | -0.74 | 0.42±1.1 | -0.04±0.5 | 0.202 | 0.54 |
| F4 | -0.08±0.5 | 0.06±0.6 | 0.618 | -0.25 | 0.13±0.7 | -0.07±0.6 | 0.555 | 0.31 |
| F8 | -0.01±0.4 | 0.24±0.6 | 0.360 | -0.49 | 0.32±0.8 | 0.05±0.6 | 0.450 | 0.38 |

SD=standard deviation; FP1=left pre-frontal; F3&F7=left frontal; Fz=frontal mid-sagittal; FP2=right pre-frontal; F4&F8=right frontal

* p<0.05, statistical significance

Discussion

The present study found no differences in pain scores and pain interference after 14 daily sessions of binaural beat music therapy compared to music therapy alone in individuals with chronic low back pain. Both interventions significantly reduced depression as measured by the HADS. In addition, the authors did not observe significant changes in theta and alpha frequencies as measured by QEEG.

Previous studies had shown that binaural beat interventions could be an effective treatment for chronic pain, reducing pain perception, and influencing cognition, as well as mental states^(4,17). Zampi conducted a crossover study to investigate the effect of a theta-binaural beat intervention in 32 patients with chronic pain and demonstrated a 77% decline in perceived pain severity⁽⁴⁾. Gkolias et al also conducted a crossover study in 21 patients from various chronic pain condition. They showed on-demand 30-minute binaural beat stimulation of 5 Hz can alleviate pain intensity and analgesic consumption one week after the intervention⁽¹⁸⁾. A meta-analysis including 22 studies also concluded that binaural beat exposure can affect cognition and reduce anxiety and the perception of pain without prior training or blinding⁽¹⁹⁾. In contrast, binaural

beat interventions may not be effective for treatment of depression. Indeed, da Silva Junior et al applied a 20-minute binaural beat of 5-Hz for ten sessions to six different individuals and echoing the present study findings, found only a trend of decreasing scores for the State-Trait Anxiety Inventory and Beck Depression Inventory⁽²⁰⁾.

Binaural beat stimulation may enhance theta waves as demonstrated by EEG, especially in frontal brain areas that are similar to that induced by a meditative state^(8,21-23). However, existing studies used a variety of binaural beat protocols with 5 to 6 Hz, duration of stimulation from 5 to 30 minutes, duration of treatment from 1 session to 14 days, and timing of EEG. The present study used the protocol of 6 Hz in combination of 300 and 306 Hz, which was the center of the theta range of 4 to 8Hz, as found in meditation⁽²⁴⁾. Licklider et al noted that the frequency range from 300 to 600 Hz was within the optimal binaural beat detection⁽²⁵⁾. Nonetheless, the authors failed to show enhancement of theta EEG activity. Similar negative results were reported by others⁽²⁶⁻²⁸⁾. For example, Stevens et al failed to support the efficacy of 4-hour theta binaural beat training in either increasing frontal theta EEG activity or in increasing hypnotic susceptibility⁽²⁴⁾. Additionally,

Gao et al showed no clear brainwave entrainment after 5-minute binaural beats with four different frequencies of 1-Hz delta band, 5-Hz theta band, 10-Hz alpha band and 20-Hz beta band⁽²⁷⁾. López-Caballero et al studied five different frequencies, including 4.53-Hz theta, 8.97-Hz alpha, 17.93-Hz beta, 34.49-Hz gamma, and 57.3-Hz upper gamma, and demonstrated no enhancement in EEG power in the corresponding frequencies. This lack of effect on theta waves might be explained by inter-individual differences, a need for individualized frequency⁽²⁷⁾, or the influence of other study parameters^(29,30).

The effect of binaural beats on the normalization of EEG power had been examined in only one study in which 14 individuals with Parkinson disease were exposed to 14 Hz binaural beats over 10 minutes daily for seven days. The authors found a normalization of EEG power and brain connectivity, as well as working memory improvement. However, there was no significant changes in gait performance, heart rate, or anxiety levels⁽³¹⁾. The present study showed a trend toward more normalization of theta and alpha EEG power in combined binaural beat and acoustic music than acoustic music alone group.

The present study had limitations. Firstly, the control group was subjected to acoustic music, which might have a pain reducing effect⁽³²⁻³⁴⁾. However, the effect on the present study findings should have been minimal as acoustic music was used in both groups as some individuals find isolated binaural beat stimulation unpleasant. Secondly, patient compliance might have influenced the treatments effects, as some patients reported falling asleep during the interventions. Lastly, because of the individual variability in EEG patterns, detecting treatment related changes can be challenging. Indeed, multiple factors can influence EEG patterns including the time of day, mood, and sleep. The use of real-time EEG monitoring could be considered in the future studies to further detect intervention-related changes.

Conclusion

When compared to acoustic music alone, the addition of binaural beat stimulation did not provide a reduction in pain or related interference in individuals with chronic low back pain. In addition, both modalities improved depression-related symptoms.

What is already known on this topic?

Binaural beat stimulation with a frequency of 4 to 8 Hz can generate theta waves similar to those observed in deep meditation or deep relaxation at the

frontal midline, which influences the neural firing pattern, resulting in cognitive function, and mood changes. It also decreased chronic pain of various causes by 77%. However, there was no information about the efficacy of binaural beat stimulation in chronic low back pain management.

What this study adds?

This study showed no benefit of additional binaural beat to acoustic music in reducing chronic low back pain. Both types of music, acoustic music alone or combined with binaural beat stimulation can reduce depressive mood significantly.

Acknowledgement

The authors gratefully acknowledge the assistance of Professors Roderick Finlayson (Department of Anesthesia, University of British Columbia, Canada) and Christina Marra, (Department of Neurology, University of Washington, USA) for English proofreading as well as generosity in manuscript editing.

Conflicts of interest

The authors declare no conflict of interest.

References

1. Foundation of Thai Gerontology Research and Development Institute (TGRI). Situation of the Thai elderly 2018. Nakorn Pathom: Printery; 2018.
2. Hoy D, Bain C, Williams G, March L, Brooks P, Blyth F, et al. A systematic review of the global prevalence of low back pain. *Arthritis Rheum* 2012;64:2028-37.
3. Nicholas M, Molloy A, Tonkin L, Beeston L. Manage your pain: practical and positive ways of adapting to chronic pain. 2nd ed. Sydney: Souvenir Press; 2012.
4. Zampi DD. Efficacy of theta-binaural beats for the treatment of chronic pain [dissertation]. Arizona: North Central University; 2014.
5. Zeidan F, Vago DR. Mindfulness meditation-based pain relief: a mechanistic account. *Ann N Y Acad Sci* 2016;1373:114-27.
6. Yamsa-ard, T, Wongsawat, Y. The relationship between EEG and binaural beat stimulation in meditation. In: The 7th 2014 Biomedical Engineering International Conference (BMEiCON). Fukuoka: IEEE; 2014. p. 1-4. doi: 10.1109/BMEiCON.2014.7017405.
7. Takahashi T, Murata T, Hamada T, Omori M, Kosaka H, Kikuchi M, et al. Changes in EEG and autonomic nervous activity during meditation and their association with personality traits. *Int J Psychophysiol* 2005;55:199-207.
8. Day MA, Ward LC, Thorn BE, Burns J, Ehde DM, Barnier AJ, et al. Mechanisms of mindfulness meditation, cognitive therapy, and mindfulness-based

- cognitive therapy for chronic low back pain. *Clin J Pain* 2020;36:740-9.
9. Yamsa-Ard T, Wongsawat Y. The observation of theta wave modulation on brain training by 5 Hz-binaural beat stimulation in seven days. *Annu Int Conf IEEE Eng Med Biol Soc* 2015;2015:6667-70.
 10. Chaudakshetrin P. Validation of the Thai Version of Brief Pain Inventory (BPI-T) in cancer patients. *J Med Assoc Thai* 2009;92:34-40.
 11. Nilchaikovit T, Lortrakul M, Phisansuthidet U. Development of Thai version of Hospital Anxiety and Depression Scale in cancer patients. *J Psychiatr Assoc Thai* 1996;41:18-30.
 12. Applied Neuroscience. NeuroGuide™ conventional and quantitative EEG at the same time [Internet]. 2018 [cited 2019 Jun 1]. Available from: <https://appliedneuroscience.com/neuroguide/>.
 13. Thatcher RW, Walker RA, Biver CJ, North DN, Curtin R. Quantitative EEG Normative Databases: Validation and Clinical Correlation. *J Neurother* 2003;7:87-121
 14. Zelek V. Quantitative EEG and LORETA [Internet]. New York: Homestead; 2019 [cited 2019 Jun 1]. Available from: <http://www.victorzelek.com/testimonials.html>.
 15. Gnaural. SBaGen Binaural Wave generator [Internet]. 2013 [cited 2019 Jun 1]. Available from: <https://sourceforge.net/projects/sbagen/>.
 16. Pirozzo S, Papinczak T, Glasziou P. Whispered voice test for screening for hearing impairment in adults and children: systematic review. *BMJ* 2003;327:967.
 17. Aalbers S, Fusar-Poli L, Freeman RE, Spreen M, Ket JC, Vink AC, et al. Music therapy for depression. *Cochrane Database Syst Rev* 2017;11:CD004517.
 18. Gkolias V, Amaniti A, Triantafyllou A, Papakonstantinou P, Kartsidis P, Paraskevopoulos E, et al. Reduced pain and analgesic use after acoustic binaural beats therapy in chronic pain - A double-blind randomized control cross-over trial. *Eur J Pain* 2020;24:1716-29.
 19. Garcia-Argibay M, Santed MA, Reales JM. Efficacy of binaural auditory beats in cognition, anxiety, and pain perception: a meta-analysis. *Psychol Res* 2019;83:357-72.
 20. da Silva Junior M, de Freitas RC, dos Santos WP, da Silva WWA, Rodrigues MCA, Conde EFQ. Exploratory study of the effect of binaural beat stimulation on the EEG activity pattern in resting state using artificial neural networks. *Cogn Syst Res* 2019;54:1-20.
 21. Brady B, Stevens L. Binaural-beat induced theta EEG activity and hypnotic susceptibility. *Am J Clin Hypn* 2000;43:53-69.
 22. Jirakittayakorn N, Wongsawat Y. Brain responses to a 6-Hz binaural beat: effects on general theta rhythm and frontal midline theta activity. *Front Neurosci* 2017;11:365.
 23. Sharma V, Singh DK, editors. Effect of binaural beats on brain EEG signals - A study. Proceeding of the National Conference on Soft Computing and Intelligent Techniques in Science and Engineering National Institute of Technology; 2017 Nov 25; Raipur, India. Raipur: National Institute of Technology; 2017.
 24. Carter C. Healthcare performance and the effects of the binaural beats on human blood pressure and heart rate. *J Hosp Mark Public Relations* 2008;18:213-9.
 25. Licklider J, Webster JC, Hedlun JM. On the frequency limits of binaural beats. *J Acoust Soc Am.* 1950;22:468-73.
 26. Stevens L, Haga Z, Queen B, Brady B, Adams D, Gilbert J, et al. Binaural beat induced theta EEG activity and hypnotic susceptibility: contradictory results and technical considerations. *Am J Clin Hypn* 2003;45:295-309.
 27. Gao X, Cao H, Ming D, Qi H, Wang X, Wang X, et al. Analysis of EEG activity in response to binaural beats with different frequencies. *Int J Psychophysiol* 2014;94:399-406.
 28. López-Caballero F, Escera C. Binaural beat: A failure to enhance EEG power and emotional arousal. *Front Hum Neurosci* 2017;11:557.
 29. Reedijk SA, Bolders A, Colzato LS, Hommel B. Eliminating the attentional blink through binaural beats: A case for tailored cognitive enhancement. *Front Psychiatry* 2015;6:82.
 30. Schwarz DW, Taylor P. Human auditory steady state responses to binaural and monaural beats. *Clin Neurophysiol* 2005;116:658-68.
 31. Gálvez G, Recuero M, Canuet L, Del-Pozo F. Short-term effects of binaural beats on EEG power, functional connectivity, cognition, gait and anxiety in Parkinson's disease. *Int J Neural Syst* 2018;28:1750055.
 32. Mitchell LA, MacDonald RAR, Knussen C, Serpell MG. A survey investigation of the effects of music listening on chronic pain. *Psychol Music* 2007;35:37-57.
 33. Guétin S, Giniès P, Siou DK, Picot MC, Pommié C, Guldner E, et al. The effects of music intervention in the management of chronic pain: a single-blind, randomized, controlled trial. *Clin J Pain* 2012;28:329-37.
 34. Schorr JA. Music and pattern change in chronic pain. *ANS Adv Nurs Sci* 1993;15:27-36.