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Title: Binaural Bates and the Brain: A Review

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Abstract

The application of binaural beat (BB), as a type of non-invasive auditory beat stimulation, has been considered for its potential applications in cognitive domains. This review presents a detailed summary and aims to deepen our understanding of the soundness of BB technique by looking into its applications, possible mechanisms of action, the effectiveness, limitations, and possible side effects of the technique. BB has been claimed to improve cognitive and psychological functions such as memory, attention, stress, anxiety, motivation, and confidence. We have also looked into preclinical and clinical researches that have been performed using BB and proposed changes in the brain following the application of BB stimulations including EEG changes. The review also presents applications outside cognitive domain and evaluates BB as a possible treatment method.

Keywords: Auditory beat stimulation, Binaural beat, Monaural beat, Cognitive functions, Psychological effects

Introduction

With the expansion of our knowledge about the brain function, new methods are developed to improve cognitive functions and psychological states. Auditory beat stimulation (ABS) is one of these techniques that is claimed to induce brainwave entrainment, a frequency-following response of brainwaves. ABS has been considered for its potential applications for understanding and measurement of auditory system responses, audiometric parameters, and mechanisms of sound localization (Kuwada et al. 1979). ABS can be applied in form of monaural beats (MBs) and binaural beats (BBs). To present MBs to a subject, two sinusoidal waves with near frequencies are instantaneously presented to both ears. When these waves are presented to each ear separately, they are called BBs (Wernick and Starr 1968a; Oster 1973). MBs are also considered as peripheral or objective beats, as they are first distinguished by the cochlear, then are forwarded to the brain stem, and then to the auditory cortex (AC). On the other hand, BBs are considered as central or subjective beats, as the BB percept is formed from the distinctness in phase of the waves that reach the right and left ears. (Kuwada et al. 1979; Draganova et al. 2008). The superior olivary nucleus in the brainstem produces BB auditory responses when the ears are provided with two low-frequency tones (less than 1000 Hz) with steady intensities but different frequencies. Neurons of the inferior colliculus (IC) then recognize the variance in the interaural phase as a beat (Licklider et al. 1950; Perrott and Musicant 1977; Schwarz and Taylor 2005; Ross and Lopez 2020). The beat frequency is halfway between the two carrier tones (Oster 1973; Pantev et al. 1996; Wahbeh et al. 2007; Pratt et al. 2009b; Grose and Mamo 2012).

Experiments in animal models (Wernick and Starr 1968b; Kuwada et al. 1979; Reale and Brugge 1990; McAlpine et al. 1996; McAlpine et al. 1998; Spitzer and Semple 1998) and humans

(Barr et al. 1977; Starr et al. 1991; Lane et al. 1998b) confirmed the involvement of structures in the auditory brainstem and cortex in ABS and BBs.

BB technology has been claimed to have benefits such as reduction in stress and anxiety, improvement in cognitive functions including memory and attention, and improvements in other psychological states such as motivation and confidence (Wahbeh et al. 2007; Chaieb et al. 2015a; Garcia-Argibay et al. 2019d).

Early reports showed that the activity of the neurons in the auditory pathways of the brainstem follows the phase pattern of an incoming sound (Hink et al. 1980). Later research showed that BBs causes brainwave entrainment, which is frequency-dependent EEG responses to an external rhythmic stimulus (Karino et al. 2006; Huang and Charyton 2008; Ozdamar et al. 2011a; Seifi Ala et al. 2018). That is to say, similar EEG patterns during a cognitive function can be induced using synchronized pulsing stimuli (Tang et al. 2015; Lee et al. 2019a).

For example, it is reported that gamma frequencies (40 Hz) entrain brain oscillations and we already know that gamma oscillations play a key role in attention, feature binding, and learning and memory. In addition, BB stimulation has been reported to be beneficial for memory (Tallon-Baudry and Bertrand 1999; Jensen et al. 2007; Tort et al. 2009; Kraus and Porubanov 2015; Beauchene et al. 2017; Jirakittayakorn and Wongsawat 2017a; Garcia-Argibay et al. 2019a), attention (Jensen et al. 2007; Lakatos et al. 2008; Kennel et al. 2010), vigilance (Chaieb et al. 2015a), creativity (Reedijk et al. 2013), anxiety control (Le Scouarnec et al. 2001; Garcia-Argibay et al. 2019d), modulation of mood states (Chaieb et al. 2015a; Jirakittayakorn and Wongsawat 2017a), pain perception (Garcia-Argibay et al. 2019d), induction of meditation (Lavalley et al. 2011), and improvement of sleep quality (Chan et al. 2010; Bellesi et al. 2014; Besedovsky et al.

2017). Recent evidence also suggests that BB provoke cross-frequency connectivity patterns in the brain (Orozco Perez et al. 2020b).

Based on the mentioned findings, it has been proposed that ABS, especially BBs, can be considered as a digital drug and potential therapeutic method either alone or in combination with other ingestible drugs (Barratt et al. 2022). In this review study, we searched the PubMed and Google Scholar databases using keywords including “auditory beat stimulation”, “binaural beats”, “monaural beats”, and “brain” to look further into mechanism of action and preclinical and clinical reports of BBs application and shed lights on BBs effects on the nervous system.

The concept of binaural beats and evoked potentials

BB concept was described by H. W. Dove in 1839. In 1949, it was claimed that rhythmic sensory stimulation, as an alternative to electrical stimulation, can entrain neural oscillations beyond the related brain areas (Walter and Walter 1949). A year later, Licklider et al. explained the assessment of the frequency limits and outlined BBs theory in which they explained how synchronal activity in both auditory nerves results in the BB effect (Licklider et al. 1950). Oster showed that BBs were detectable for carrier frequencies below 1000 Hz (Oster 1973) and further research showed that brain cortex only encodes low carrier frequencies (Schwarz and Taylor 2005).

Steady-state auditory responses (ASSRs) are evoked by acoustic beats. ASSRs originate at the brainstem and the responses to stimulus rates (1-200 Hz) are recordable at the cortical level from the scalp. (Dolphin 1997; Picton et al. 2003). Prominent responses are observed when stimulus rates is near 40 Hz (Galambos et al. 1981; Herdman et al. 2002). Auditory thresholds (Picton et al. 2005) and the depth of anesthesia (Plourde 2006) can also be measured using ASSRs

The carrier frequency is also important in the outcome of BB stimulation. For example, 40 Hz BB potential was observed following a 400 Hz carrier frequency but not when the carrier frequency was above 3 kHz (Schwarz and Taylor 2005). Spectral analyses of the magnetic fields showed that BBs (4.00 or 6.66 Hz; carrier frequency 240 or 480 Hz) evoked small amplitude magnetic fields (Karino et al. 2006). BBs and acoustic beats have similar cortical processing as BBs (3 and 6 Hz) and amplitude-modulated acoustic beats (3&6 Hz; carrier frequency 250&1000 Hz; 2000 ms duration; 1 s intervals) yield comparable cortical activity and perceptions (Pratt et al. 2010). The temporary auditory responses are separable from BB auditory illusion using binaural interaction component analysis (Ozdamar et al. 2011b).

Binaural beat mechanism of action

Action potentials are fired when sound energy passes through the ears and cochlea and reaches the inner hair cells. Auditory nerve fibers carry the auditory information from the cochlea and then join the vestibulocochlear nerve. The information then enters the cochlear nucleus and bifurcate. The branches of the nerve fibers form synapses with stellate, globular-, and spherical-bushy cells, which all have specific temporal and spectral response properties (Wu and Oertel 1984). The sound information then travels to either the superior olivary complex (projections of the bushy cells of the anteroventral cochlear nucleus) or to the IC (outputs of the stellate and dorsal cochlear nucleus cells) (Goldberg and Brownell 1973). The superior olivary complex processes the data related to sound origin from both ears (Moore 2012). The left and right IC make binaural interacts through commissural connections and the ascending pathway subnuclei. The information is then repayed to the medial geniculate nucleus and the AC. The processing of wave specifications

depends on the integration time between the IC and the AC (Fitzpatrick et al. 2009; Bloom 2013; Croom 2014).

Auditory neurons discharge differently at different frequencies. For instance, synchronous discharges happen in response to low frequencies, but not in response to shape synaptic summation. When the frequencies reach higher, neuronal discharges happen in turns. At middle frequencies, neurons respond in many volleys and those involved in each volley fire in synchrony, resulting in the appearance of beats (Licklider et al. 1950).

In an early study, Kuwada et al. studied the interaural phase sensitivity of neurons using BBs and showed that many neurons phase-locked to the beat frequency (Kuwada et al. 1979). Other studies showed that in addition to the primary AC, ASSRs responses to BBs can be recorded from the superior temporal, posterior parietal, and frontal cortices, which primarily originates in the AC especially in response to gamma-frequency stimulation (Pastor et al. 2002). Recording of small amplitude magnetic fields following the application of low frequency BBs (4.00-6.66 Hz) showed that BBs can synchronize the cortex activity (Karino et al. 2006; Pratt et al. 2009b) and reports indicate that the interaural time difference that happens within early rising amplitude (20–25 ms) plays a key role in the prediction of perceived BB lateralization (Haywood and McAlpine 2020). Comparison of the effects of BBs across four levels of subcortical, cortical, scalp-level functional connectivity showed that BBs only weakly entrained the cortex but also generated cross-frequency connectivity patterns (Orozco Perez et al. 2020a). Some other studies recorded ERP N100 to BBs and amplitude modulation stimuli and reported separate processing sites for structure-based spatial processing and envelope-based level processing. The recorded N1 component also showed an age related decline in magnitude (Ungan et al. 2019).

BBs effects have also been studied on the synchronization of the brain hemispheres and it was reported that BBs frequencies (10 Hz, alpha; 4Hz, theta) increased alpha frequencies interhemispheric coherence and was interpreted as binaural integration rather than entrainment (Solcà et al. 2016a).

Nevertheless, the responses to BBs are not always the same and the brain areas respond differently to different beat frequencies. For example, the study by Karino et al. showed that application of four different BBs at 4.00- and 6.66-Hz (240-480 Hz; 10 min) induced ASSRs in the frontal region and also in the temporal and parietal regions, but symmetry did not always occur (Karino et al. 2006). A magnetoencephalography (MEG) study showed right temporal responses to a 40-Hz BB after 1 s of BB application (Draganova et al. 2008). Another study reported that presentation of 7- and 15-Hz BBs (15 min) increased left temporal delta power for the 7-Hz BB and gamma power for 15-Hz BB (Lavalley et al. 2011). In a study using MEG, Chakalov et al. used 26-Hz BBs (250 Hz carrier tone; 500 ms) and reported a 26 Hz ASSR at the right parietal and left middle frontal regions (Chakalov et al. 2014). Also, left hemisphere dominance was observed in 3 Hz BB after 15 minutes and 15 Hz BB after 5 minutes. The right hemisphere dominance occurred in 10 Hz BB after 25 min. The enhancement of all brain areas was observed after a 6 Hz beat within 10 minutes. Differences were also observed in the frontal lobe and responses were enhanced with 40 Hz beats, but 8 Hz and 25 Hz beats did not create any clear responses (Jirakittayakorn and Wongsawat 2015). In a second study, Jirakittayakorn et al. investigated theta activity responses (6-Hz BBs, 250 Hz carrier tone, 30 minutes) and reported that theta waves were observable in all regions of the cortex after 10 min of BB application. They also reported a meditation effect, measured by Brunel Mood Scale (Jirakittayakorn and Wongsawat 2017d).

Distribute processing across hemispheres has also been reported. For instance, BBs amplified the coherence of left and right auditory regions in contrast to MBs and resting state; and it was inferred that independent of BB frequency the increased coherence selectively concerns the alpha band. These changes did not happen along with changes in amplitude (Solcà et al. 2016b).

The effect of carrier tones has also been investigated in EEG studies. At the fronto-central region, BB stimulation (40 Hz) induced higher responses on a lower (400 Hz) carrier tone than a higher (3,200 Hz) one (Schwarz and Taylor 2005). Another study showed the application of BBs (3 & 6 Hz; 250 & 1,000 Hz; 2 s) generated left temporal ERPs that were more prominent for 250 Hz than 1,000 Hz and similarly higher for 3 Hz than for 6 Hz (Pratt et al. 2009a).

A study on the differences in the perception of BBs, which measured BBs for 4, 8, 16, and 32 Hz (500-Hz carrier tone), reported that variability in perceiving BBs is due to the measurement plan (Grose et al. 2012).

EEG activity following BB stimulation

When BB is presented to a subject, two different tones that have close frequencies are presented to the left and right ears and the brain perceives a third sound, the BB that forms from the integration of the presented signals. EEG alterations have been reported differently among the studies. To test if BB affect functional brain connectivity, Mujib et al. measured relative power, phase-locking value, and cross-mutual information in EEG recordings during delta (1 Hz), theta (5 Hz), alpha (10 Hz), and beta (20 Hz) band BB stimulations. The results showed that application of delta and alpha BB increased and decreased relative power in theta and beta bands, respectively. Theta BB stimulation also diminished beta band relative power, No entrainment was reported but the connectivity pattern showed variations (Mujib et al. 2021). In another study, frequency

following responses were reported in delta, theta, and gamma bands but not in alpha and beta bands following exposure to BBs for ten 1-minute epochs (Vernon et al. 2014).

On the other hand, López et al. investigated brainwave entrainment and reported no significant EEG spectral power changes for epochs of 3 min in theta (4.53 Hz), alpha (8.97 Hz), beta (17.93 Hz), gamma (34.49 Hz), or upper gamma (57.3 Hz) bands (López-Caballero and Escera 2017). Goodin et al. also studied brainwave entrainment following BB stimulation at beta and theta frequencies and reported that short presentation of BBs was insufficient to generate entrainment or alter vigilance (Goodin et al. 2012).

Vernon et al. performed a limited recording of EEG (at T3 and T4) during the application of alpha (10 Hz) and beta (20 Hz) BBs and reported greater beta activity in the left temporal region but no alteration in alpha activity (Vernon et al. 2014). ACs showed greater alpha-band synchrony after application of alpha (10 Hz) and theta (4 Hz) BBs, which is a reflection of binaural integration (Solcà et al. 2016b). Kasprzak et al. tested the brain ability to change its main activity frequency in accordance to a dominant applied stimulus. They observed a significant decline in alpha rhythm (8–12 Hz) and simultaneous increment of narrow band share (9.9–10.1 Hz) and proposed that blockade of alpha rhythm was due to the response of CNS to the acoustic stimulus and tuning to enhance the receipt of environmental information (Kasprzak 2011).

Studies have also investigated the effects of MBs and BBs on EEG power, phase patterns, and phase synchronization (Schwarz and Taylor 2005; Becher et al. 2015; Derner et al. 2018). Prominent alterations were observed at theta (5 Hz) range in the temporal regions, rhinal cortex, and hippocampus, the mediotemporal structure important in memory function (Eichenbaum 2000). Fell et al. demonstrated that phase-related mechanisms, including phase synchronization, play a key role in long-term memory processing (Fell and Axmacher 2011). In addition, a study in

presurgical epilepsy patients showed that MB and BB stimulations altered brain activity power and synchronous phase (Becher et al. 2015). A more recent study investigated differential effects of MBs and BBs on phase synchronization and long-term memory performance and showed that theta (5 Hz) range BB increased temporolateral phase synchronization while MB stimulation at the same frequency decreased imediotemporal phase synchronization. In addition, 5-Hz BB increased and 5-Hz MBs diminished both memory for words and association memory. The results indicated that intracranial EEG phases alter threshold of neurons and neural activity, which may result in memory-related activity alterations within the required time window (Derner et al. 2021).

Animal models and our understanding of BBs

The experimental data from animal models help us to better understand the basis of the BB mechanism of action. Early evidence came from the work by Kuwada et al. showed a phase-locked response in most cells in the IC of cats to the BB frequency (Kuwada et al. 1979). The study by McAlpine et al. showed that in guinea pigs single neurons in the IC process BBs at low frequencies similar to other species. They also proposed that interaural-delay sensitivity not only is different for different frequencies but it changes within each frequency band (McAlpine et al. 1996). Two years later studies showed that a different system from spatial processing of position is responsible for interaural phase responses and reported a convergence from simple brainstem coincidence detectors (McAlpine et al. 1998; Spitzer and Semple 1998). Reale et al. studied neurons in the primary AC in cats to evaluate the interaural-phase-difference sensitivity of the neurons using different stimulus frequencies (120 to 2,500 Hz). Data showed a direct association between interaural phase and beat frequency. Many of the studied cells responded equally to BBs and a rise in BB frequency was followed by an increase in action potentials of the neurons. However, after a

certain frequency (35 Hz) the neurons of the AC were unable to follow the rate (Reale and Brugge 1990).

The cognitive effects of binaural beats

Table 1 summarizes the studies regarding auditory beat stimulation, which indicates a rising trend for BBs application since 1947. With the rapid growth in cognitive sciences, the application of BB stimulation is also of interest to many researchers as a non-invasive method that may improve cognitive functions.

Application of 40 Hz gamma BB and MB for the assessment of attention (Flanker task) and working memory (Klingberg task) in high and low emotional participants showed that listening to BB at beta (15 Hz) range during the N-back task altered network connections and resulted in improvement of the accuracy of performance (Beauchene et al. 2017). Another study found that both BB and MB similarly enhanced the speed of performance in the attention task and their effects were also similar in high and low emotional participants (Engelbregt et al. 2019). In a study on the attentional blink (AB) using MEG recordings, it was shown that gamma (40-Hz) BB stimulation during training enhanced the attentional blink task outcomes. However, the improvement was evident only after consolidation during sleep (Ross and Lopez 2020). Using EEG recordings and 5 min-presentation of 40 Hz BB, another study showed that BB stimulation improved attention but no occurrence of neural entrainment was observed (Engelbregt et al. 2021). Application of gamma-frequency (40 Hz) during a global-local task was reported to reduce spotlight of attention (Colzato et al. 2017). A meta-analysis suggested that BBs have positive effects (average effect size 0.58) on attention (Garcia-Argibay et al. 2019c). On the other hand, beta-frequency (16 Hz) BB did not enhance a sustained attention when measured by pupillary

measures (Robison et al. 2021). The application of BB (20 min; 3 times a week; 3 weeks) did not reduce inattention in children and adolescents with attention deficit/hyperactivity disorder (ADHD) (Kennel et al. 2010). However, parents of ADHD children reported improvement in homework problems during the 3 weeks of the study [120].

Application of BBs (beta, 16 and 24 Hz or theta/delta, 1.5 and 4 Hz; 30 min) in visual vigilance task showed that beta-frequency BBs enhanced psychomotor performance and increased the number of correct detections in comparison to theta/delta frequency. Furthermore, the beta-frequency was associated with less negative mood in the subjects under the study (Lane et al. 1998b). Little et al. used the Five Factor Model (FFM) (Little et al. 1992) to assess personality traits and recorded EEG from participants. They did not find any significant effects of theta (7 Hz) or beta (16 Hz) BBs applied during a psychomotor vigilance task, which needs the ability to remain focused and alert to stimuli over prolonged periods. Also, no correlations were observed between the stimulations and personality (Little et al. 1992). The brief duration of exposure to BB stimulation might have had a key role in observed results. However, Lane et al. applied BBs at beta (16 and 24 Hz) throughout a psychomotor vigilance task and reported improved performance in a vigilance task (Lane et al. 1998a).

In a test of verbal memory, Wahbeh et al. reported that application of BBs (7 Hz; 30 min) declined verbal memory recall (Wahbeh et al. 2007). But, the application of 5 Hz BBs (15 min; twice per day; 15 days) raised the number of words recalled (Ortiz et al. 2008). Beta-frequency (20 Hz) BBs in long-term memory test produced better performance for recalled words and a higher sensitivity index in recognition tasks. But theta-frequency (5 Hz) BBs diminished the performance for remembered words and the sensitivity index. Hence, depending on the frequency used BBs have positive or negative effects on long-term memory (Garcia-Argibay et al. 2019b).

Chaieb et al. also mentioned that longer application of BBs affects verbal memory recall (Chaieb et al. 2015b). BB stimulation at theta frequency (5 Hz) over a long time generated a coupling of brain activity and improved the capacity of immediate verbal memory (Ortiz et al. 2008). BBs have also been reported to have positive applications for neurological disorders and the elderly to improve memory. For example, a study showed significant increase for alpha frequency along with a significant decrease in reaction time in alpha (10 Hz; 15 min) and gamma (30 Hz; 15 min) frequencies (Mujib et al. 2021). Listening to beta-frequency (15 Hz) BB stimulation in N-Back test enhanced accuracy and altered cortical network connection strengths (Beauchene et al. 2017). BB at beta (15 Hz) band also improved working memory by inducing beta activity in the brain (Beauchene et al. 2017).

To access the effects of BBs on creativity, Reedijk et al. applied BBs at the alpha (10 Hz) and gamma (40 Hz) bands for 3 min prior to the divergent and convergent thinking tasks. Measurement of dopamine levels in the striatum using spontaneous eye blink rates (EBRs) showed that both applied BBs affected divergent but not convergent thinking. Alpha BBs enhanced divergent thinking mostly in subjects with low EBRs (Reedijk et al. 2013).

The psychological and physiological effects of binaural beats

BB stimulations have also been reported to have positive outcomes in pre-operative state-based anxiety (Padmanabhan et al. 2005; Weiland et al. 2011; Ungan et al. 2019; Ölçücü et al. 2021), anxiety in psychiatric outpatients (Yusim and Grigaitis 2020), patients suffering from traumatic brain injury (Klepp and Summer 2006), and to reduce dental anxiety (Menziletoglu et al. 2021). It has also been reported that BBs reduced pain scores associated with unit status

reporting procedures (Ölçücü et al. 2021), and pain perception (Garcia-Argibay et al. 2019d). In a study on chronic pain patients, Gkolias et al. used theta (5 Hz) band BB to investigate if the resulted brain entrainment will decline pain perception and analgesic medication use and reported the effectiveness of BBs in the reduction of pain intensity, analgesic use, and stress (Gkolias et al. 2020). BB therapy has also been suggested as a therapeutic method that holds promise for the management of chronic pain in conditions like cancer (Zampi 2016), for reducing morphine consumption in patients who underwent knee replacement (Tani et al. 2021), and for reducing pain in cases undergoing colonoscopy without sedation (Tani et al. 2022).

In patients with cataract, BB stimulation reduced state-trait anxiety, heart rate, and systolic blood pressure during surgery and it was suggested that BB embedded musical intervention was beneficial over musical intervention alone (Wiwatwongwana et al. 2016a). Theta BB also diminished subsequent stress responses to an acute, psychological stressor (Kelton et al. 2021). Listening to BB influenced the power of both low-frequency, reflecting sympathetic and parasympathetic activity, and high-frequency, reflecting parasympathetic activity, components of heart rate variability and LF/HF normalized powers, which was accompanied by a subjective report of relaxation (McConnell et al. 2014). Using the mood states questionnaire (McNair and Heuchert 2011), Wahbeh et al. reported a reduction in anxiety (Wahbeh et al. 2007). A study reported that theta-frequency (6 Hz; 250 Hz) BBs enhanced meditative state after 10 min of exposure, which can be used to reduce stress (Jirakittayakorn and Wongsawat 2017c). In dentistry, alpha-frequency (9.3 Hz; 200 Hz) BBs were also found useful in reducing preoperative anxiety (Isik et al. 2017). Music with or without BB decreased anxiety and reduced systolic blood pressure. However, those who received BBs showed an additional decrease in heart rate and operative anxiety (Wiwatwongwana et al. 2016b).

Lane et al. reported a decline in depression following the application of BB in the beta range (16 and 24 Hz) (Lane et al. 1998a), which indicates the association of beta BB with less negative mood (Chaieb et al. 2015b).

Application of BBs in Parkinson's Disease (PD) normalized EEG power and brain functional connectivity and improved working memory with no significant changes in the gait performance or anxiety level (Gálvez et al. 2018). A systematic scoping review also reported that non-invasive brain stimulation methods such as BBs changed quantitative EEG in patients with PD and recommended further research to confirm EEG as a biomarker (Costa et al. 2022).

BBs of theta and delta range during nap increased sleep stability, which can be considered as a non-pharmacologic way of sleep treatment (Shumov et al. 2020). Subsequent reports also showed that BBs enhanced the activity of the parasympathetic part of the autonomic nervous system during naps (Bakaeva et al. 2021). Changing BBs in frequency from 8 to 1 Hz alleviated sleep initiation and maintenance difficulties in patients with chronic insomnia (Tang et al. 2015). Theta range BBs also increased daytime alertness in subclinical insomnia (Bang et al. 2019). In order to discover new nonpharmacological methods for the treatment of sleep disorders, Munoz et al. used a combination of real-time automatic sleep stage classification and a BB generator and showed that BBs improved sleep quality (Munoz and Rivera 2020). BBs at delta (3 Hz) band induced delta activity and increased the duration of non-rapid eye movement (NREM) in the third stage of sleep (Jirakittayakorn and Wongsawat 2018). The BBs at theta (6 Hz) band had meditative effects and induced theta activity in the frontal and parietal-central regions (Jirakittayakorn and Wongsawat 2017b). Subjects who used 6 Hz BB for 30 min before bed time for two 14 days showed reduced hyper-arousal state, which can contribute to sleep induction (Lee et al. 2022).

BB stimulation is used in the treatment of stroke, brain injury, tinnitus, dementia and other cognitive deficits, and studies on the outcomes have provided evidence of the advantage of rehabilitation with music over the one without music (David et al. 2010; Galińska 2015). A summary of the application of BB stimulation has shown that listening to BBs for a suggested period can have the following effects on different behaviors:

1) BBs in the delta (0.5–4 Hz) pattern during sleep caused deeper stages of sleep (Jirakittayakorn and Wongsawat 2018) and reduced mild anxiety (Le Scouarnec et al. 2001) and pre-operative state-based anxiety (Padmanabhan et al. 2005); 2) BBs in the theta pattern (4–7 Hz) improved meditation, creativity, REM sleep (Jirakittayakorn and Wongsawat 2018), and reduced mild anxiety (Le Scouarnec et al. 2001; Wahbeh et al. 2007); 3) BBs in the alpha pattern (7–13 Hz) encouraged relaxation (Jirakittayakorn and Wongsawat 2018) and reduced anxiety (Weiland et al. 2011); 4) BBs in the beta pattern (13–30 Hz) promoted concentration and alertness but also increased anxiety, especially at the higher end of the range (Jirakittayakorn and Wongsawat 2018); 5) BBs in the gamma pattern (30–50 Hz) enhanced the maintenance of arousal (Jirakittayakorn and Wongsawat 2018).

Possible complications of binaural beats

Some reports indicate that the repetitive nature of BBs could make people feel uncomfortable (Lee et al. 2019b). In previous sections, we provided evidence that BBs have beneficial cognitive as well as non-cognitive effects. However, what goes undetected are the side effects. Until now, no study has reported any side effects during or following the listening to BBs. However, it seems sensible to keep the sound level below the maximum safety level of 85 dB, as

they can cause hearing loss over time. (Keith et al. 2008; Tuomi and Jellimann 2009). Also, it is highly recommended that those with epilepsy consult with their doctors before trying BBs (Vernon et al. 2014).

Based on the alterations in behaviors mentioned through this review by some studies, it is warranted to perform more research into the behavior alterations that were observed following intended changes (e.g., improvement of sleep behavior may also cause depression).

Binaural beats and future research directions

In addition to the duration of the stimulation (Chaieb et al. 2015a), the choice of carrier tones for the stimulation should be considered, as reports indicate that lower carrier tones may result in more robust effects (Pratt et al. 2010). Some reports also indicated that the addition of background noise (pink or white) affects the processing of the BBs perception (Reedijk et al. 2013).

It must be considered that cognitive entrainment methods, including BBs, are not universal approaches, and we should consider the individual's state .

The results of a meta-analysis also showed that BBs positively affects cognition more than just reducing anxiety and pain levels (Garcia-Argibay et al. 2019d). Hence, in time of design of a study frequency band, time under exposure, and intervention time must be chosen to maximize the possible magnitude and direction of responses

To sum up, the evidence discussed in this paper shows that auditory beats stimulation may be a useful tool for rehabilitation training in order to enhance both learning and training. However, we need to solve the jigsaw puzzle of involving factors and best configurations for each specific

application. Hence, further research is warranted into the role of personality traits as well as factors such as duration, frequency, and carrier tones of the stimulation.

Abbreviations

Abbreviation	Definitions
AB	Attentional blink
ABS	Auditory beat stimulation
ADHD	Attention deficit/hyperactivity disorder
AI	Primary auditory
ALRs	Auditory late responses
AM	Amplitude modulation
ASSR	Auditory steady state responses
AUT	Alternate uses task
AUT	Divergent thinking task
AVCN	Anteroventral cochlear nucleus
BB	Binaural beats
BBT	Binaural beat technology
BF	Best frequency
BIC	Binaural interaction component
BP	Best phase / blood pressure
BRMUS	Evaluated by Brunel Mood Scale
CAM	Complementary and alternative medicine
CCTT1 and CCTT2	Children's Color Trails Test 1 and 2
CD	Characteristic delays
CMI	Cross mutual information
CN	Cochlear nucleus
CP	Characteristic phase
CVAs	Cerebrovascular accidents
DCN	Dorsal cochlear nucleus
EBR	Eye blink rate
EBRs	Eye blink rates
EEG	Electroencephalographic
EFR	Envelope following response
ERPs	Event-related potentials
FB	Binaural beat frequency
FC	Functional connectivity

FFR	Frequency following response
HF	High-frequency
HRV	Heart rate variability
IC	Inferior colliculus
ICC	Central nucleus
ICH	Imaginary coherence
IPD	Interaural phase differences
IPD	Interaural phase disparity
IPM	Interaural phase modulation
ITDs	Interaural timing differences
LF	Low frequency
MB	Monaural beats
MEG	Magnetoencephalography
MGN	Medial geniculate nucleus
MI	Music intervention
NPL	Non-phase locked
NREM	Non rapid eye movement
PANAS-S	Positive And Negative Affect Scale-mood State questionnaire
PD	Parkinson's disease
PL	Phase locked
PLV	Phase locking value
PN	Pink noise
PPANS	Parasympathetic part of autonomic nervous system
PRISMA	Preferred Reporting Items for Systematic Reviews and metanalyses
QEEG	Quantitative electroencephalography
RAT	Remote associations task
REM	Rapid eye movement
RP	Relative power
RSVP	Rapid serial visual presentation
SAM	Sinusoidal amplitude modulation
SBBs	Speech induced binaural beats
SCR	Skin conductance response
SOC	Superior olivary complex
STA-I	State-trait anxiety inventory
TBB	Theta binaural beat
TBI	Traumatic brain injury
TOVA	Test of Variables of Attention
TSST	Trier social stress test
WN	White noise

Conflict of Interest

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Table 1: A summary of publications and their findings regarding auditory beat stimulation (in form of monaural beats and binaural beats).

ABS method	Band frequency	Carrier type	Applied duration	Sample	Sample size	Impact	Reference
BB	4Hz	256/260 Hz	-	Older adults at the hospital who were undergoing total knee joint replacement with spinal anesthesia participated in the study	40	Reduced morphine consumption in older adults who underwent knee replacement	(Tani et al., 2021)
BB	-	-	-	Male patients undergoing diagnostic cystoscopy and ureteral stent removal under local anesthesia	352	Reduced anxiety levels and pain scores in males	(Ölçücü et al., 2021)
BB	alpha (10 Hz), beta (14 Hz), gamma (30 Hz)	-	15min	Elderly or people with neurological conditions	60	Increased cognitive score and decreased reaction time	(Mujib, Hasan, Qazi, & Vuckovic, 2021)
BB	10Hz	220/210hz	10min	Ninety patients were randomly selected	80	Reduce dental anxiety	(Menziletoglu, Guler, Cayir, & Isik, 2021)
BB	Theta	-	4×5min	Adults recruited from undergraduate classes at the university with a mean age of 19 years and a range from 18 to 30	64	Dampened stress responses to an acute, psychological stressor	(Kelton, Weaver, Willoughby, Kaufman, & Santowski, 2021)
BB	40 Hz	-	5 min	first-year psychology students	25	Improved attention	(Engelbregt, Barmantlo, Keeser, Pogarell, & Deijen, 2021)

BB/MB	BBs (5 Hz), MBs (5 Hz), control tone (220 Hz—no beat)	217.5-222.5Hz	500ms	Neurosurgical patients performing an associative recognition task	5	Is linked to memory performance	(Derner et al., 2021)
BB	-	-	2 weeks to 2 months	Twenty psychiatric outpatients with anxiety disorder and eight individuals (nonpatients) in the healing professions	20+8	Exhibit a positive effect on self-reported measures of anxiety	(Yusim & Grigaitis, 2020)
BB	Theta /delta	-	20 min	-	21	Increased sleep stability	(Shumov et al., 2020)
BB	40Hz/16Hz	Pure tones of 420 Hz and 460 Hz/Pure tones of 431.85 Hz and 448.15 Hz	15 min	Young / healthy volunteers	29	Enhanced training and learning	(Ross & Lopez, 2020)
BB	5Hz-theta	-	30 min	Chronic pain patients	-	Alleviated pain intensity	(Gkolias et al., 2020)
BB	3Hz	250 -253 Hz	256 s	Normal-hearing participants	19	The cortical sites that process temporal information and those that process spatial information are not totally overlapped	(Ungan, Yagcioglu, & Ayik, 2019)
BB	8Hz (Alpha)	-	-	Adults with constant tinnitus and symmetrical hearing	20	No significant benefits	(Munro & Searchfield, 2019)
BB	6 Hz binaural beat corresponding to the center of the theta band (4-8 Hz)	250-256 Hz	Session 1: 3 min Session 2: 10 min	Fifteen healthy right-handed subjects (one female, average age of 24.9 ± 1.81 years)	15	Increased the quality of sleep.	(Lee, Song, Shin, & Lee, 2019)

BB	Beta (20 Hz) or theta (5 Hz)	390-410 Hz 395-400 Hz	17 min	volunteer participants from high schools and universities. Participants' ages ranged from 14 to 51 years	32	Affected long-term memory both positively and negatively, depending on the frequency used.	(Garcia-Argibay, Santed, & Reales, 2019)
BB/MN	40 Hz gamma binaural beat (BB) and 40 Hz gamma monaural beat (MB)	-	-	High and low emotional participants	24	No differences were found between BB and MB conditions.	(Engelbregt, Meijburg, Schulten, Pogarell, & Deijen, 2019)
BB	Theta	-	30 min (2 weeks)	Subjects with subclinical insomnia	43	Increased daytime alertness	(Bang, Choi, & Yoon, 2019)
BB	7 Hz	200-207 Hz	9min	Healthy participants	15	Changed the relative power in the temporal and parietal lobes of the brain	(Seifi Ala, Ahmadi-Pajouh, & Nasrabadi, 2018)
BB	-	-	20 min	Healthy adults	25	Reduced mental fatigue	(Lim, Kim, Jeon, & Cho, 2018)
BB	3Hz	250-253Hz	-	Healthy participants with an average age of 24.12 years and a standard deviation of 2.54 years were included in this study (13 males and 11 females)	24	Enhanced power of delta activity	(Nantawachara Jirakittayakorn & Wongsawat, 2018)
BB	Theta	-	10 min in 7 days	Parkinson's Disease (PD) patients	-	Has an effect as a co-assistant tool in the treatment of PD	(Gálvez, Recuero, Canuet, & Del-Pozo, 2018)
BB/MB	BBs (5 Hz), MBs (5 Hz)	217.5-222.5Hz	-	Presurgical epilepsy patients with depth electrodes implanted in the medial temporal lobe participated in this pilot study (8 females, mean age 36.3 ± 11.4 years)	15	Increased long-term memory performance	(Derner, Chaieb, Surges, Staesina, & Fell, 2018)
BB	4.53 Hz - theta-, 8.97	frequency range:	3min	Participants (five males), ranging in age from 20 to 31 years (mean =	14	No changes in heart rate and skin	(López-Caballero & Escera, 2017)

	Hz -alpha-, 17.93 Hz -beta-, 34.49 Hz -gamma- or 57.3 Hz -upper-gamma	250–4000 Hz		23.3; standard deviation = 3.3) were recruited among University of Barcelona students		conductance were observed	
BB	6Hz	250-256 Hz	-	Participants with an average age of 21.9 years	28	Induced a meditative state	(N. Jirakittayakorn & Wongsawat, 2017)
BB	40Hz	300-340 Hz	-	Students (22 females, 14 males; aged 18–28 years old) from Leiden University participated in this study in exchange for course credit or pay. All had normal or corrected-to-normal sight and hearing	36	Biased the individual attentional processing style towards a reduced spotlight of attention.	(Colzato, Barone, Sellaro, & Hommel, 2017)
BB	Alfa and SMR brain waves/ 0-to-3-minute waves were induced at 8 Hz, the 4-to-6minute waves at 10Hz, the 7-to-9-minute waves at 12Hz, the 10-to-12-minute waves at 14 Hz, and the 13-to-15-minute waves at 15 Hz;	-	15 min	Elderly without dementia diagnosis (EWD), n=15, 76+/-8 years, elderly diagnosed with Parkinson's disease (EDP), n=15, 72+/-7 years, elderly diagnosed with Alzheimer's disease (EDA), n=15, 81+/-6 years. The other groups were named children with Autism (CA), n=10, 11+/-4 years, children with Intellectual Impairment (CII), n=10, 12 +/-5 years and children with normal cognitive development (CND), n=10, 11+/-4 years	75	Indicated gains in memory functions	(Calomeni et al., 2017)

BB	5-10-15Hz	R: 240Hz, L: 245Hz	-	Healthy adults (15 women, 19 men) aged 18 to 46 yr (mean 27.1 yr)	34	In N-Back working memory task increased the accuracy	(Beauchene, Abaid, Moran, Diana, & Leonessa, 2017)
BB	20 Hz in the first 5 min.	109 and 209 Hz	60 min	Patients undergoing cataract surgery under local anesthesia	141	Decreased anxiety level and lowered systolic BP	(Wiwatwongwana et al., 2016)
BB	40 Hz gamma- frequency	300-340 Hz	-	Students (32 female, eight male; aged 18–27 years old)	40	Biased the control style toward more flexibility	(Hommel, Sellaro, Fischer, Borg, & Colzato, 2016)
BB	5-10-15 Hz	R: 240Hz, L: 245Hz	Over 5 minutes	Healthy adults (12 women, 16 men) aged 19 to 46 yr (mean 27.6 yr)	28	Increased the response accuracy	(Beauchene, Abaid, Moran, Diana, & Leonessa, 2016)
BB	Alpha (10Hz) or gamma (40Hz)	300- 340Hz	-	Students (22 females, 2 males; aged 17–25 years old) age between 17 and 30 years; (ii) no history of neurological or psychiatric disorders; (iii) no history of substance abuse or dependence	24	The effect on cognitive performance depends on inter-individual differences	(Reedijk, Bolders, Colzato, & Hommel, 2015)
BB	9.55 Hz - alpha range	230 and 220.45 Hz	12 min	University/college students (M Age = 21.63 years; 29 (72.5%) were women)	40	A temporary positive effect on the capacity of working memory	(Kraus & Porubanova, 2015)

BB	3-15-10-8-40 Hz	250 HZ	30 min	-	-	Brain modulation application to induce the brain activity	(N. Jirakittayakorn & Wongsawat, 2015)
BB	10-20Hz	-	1 min	Healthy participants	22	No effect of BBs on eliciting a frequency following effect in the EEG	(Vernon, Peryer, Louch, & Shaw, 2014)
BB	Theta	-	20 min	Subjects (n = 21; 18-29 years old) college students	21	Exerted an acute influence on both low-frequency and high-frequency components of heart rate variability and increased subjective feelings of relaxation	(McConnell, Froeliger, Garland, Ives, & Sforzo, 2014)
BB	2-8Hz	-	8 weeks	Young elite soccer players	15	Improved perceived sleep quality	(Abeln, Kleinert, Struder, & Schneider, 2014)
BB	Alpha (10 Hz) gamma (40 Hz)	335-345Hz 320-360Hz	3 min	First-year psychology or educational studies students (22 female, 2 male; 17–25 years)	24	Individual cognitive-control systems need to be taken into account when studying cognitive enhancement methods	(Reedijk, Bolders, & Hommel, 2013)
BB	Theta (7 Hz) or Beta (16 Hz)	400 Hz or 416 Hz	2 min	The general public and from a Melbourne university community. (20 females, 11 males) with ages ranging from 18 to 60 (M= 28.90, S.D. = 10.82)	31	Short presentation of steady state BBs are not sufficient to alter vigilance or entrain cortical frequencies	(Goodin et al., 2012)
BB	3 or 6 Hz	250	-	Right-handed subjects, 18–25 years old with normal hearing	18	The perceptions of binaural beats involve a cortical activity that is not different than acoustic beats in distribution	(Pratt et al., 2010)

BB	-	-	20 minutes, three times a week for 3 weeks	Children and adolescents with attention-deficit/hyperactivity disorder	-	Parents and adolescents stated improvements in homework problems	(Kennel, Taylor, Lyon, & Bourguignon, 2010)
BB	3 and 6 Hz	250 Hz	Tones were 2,000 ms in duration and presented with approximately 1 s intervals	16 men and 2 women, 18 to 25 years old right-handed normal hearing subjects	18	Cortical potentials recorded to binaural beats are distinct from onset responses	(Pratt et al., 2009)
BB/MB	1Hz	200 Hz	The duration of the AM tones was 0.5 to 5.1 s	Adult female Dutch-belted rabbits with clean external ear canals were used	37	Intrinsic membrane properties and afferent synapses to the cortical neurons govern the dynamic processing	(Fitzpatrick, Roberts, Kuwada, Kim, & Filipovic, 2009)
ABS	5 Hz-theta, beta-13 Hz frequencies	-	-	-	20	Increased the capacity of immediate verbal memory	(Ortiz et al., 2008)
BB	40Hz	500 and 540 Hz,	1 s	Right-handed subjects (2 females) between 28 and 45 years of age	11	Although the central and peripheral beat interacted at different levels of the auditory system, the initial responses were projected along the afferent auditory pathway and activated common cortical sources.	(Draganova, Ross, Wollbrink, & Pantev, 2008)
BB	Beta (20 Hz), and the theta (7 Hz)	-	7 min	-	12	No effects on blood pressure or pulse	(Carter, 2008)

BB	7Hz	133 Hz L; 140 Hz R	30 min	Healthy adult subjects	4	Increased depression and poorer immediate memory recall	(Wahbeh, Calabrese, Zwickey, & Zajdel, 2007)
BB	delta (0–4 Hz)	-	60 days daily	Healthy adults	8	Positive effect on self-reported psychologic measures, especially anxiety.	("Binaural Beat Technology in Humans: A Pilot Study To Assess Psychologic and Physiologic Effects," 2007)
BB	4.00 and 6.66 Hz	240 Hz	5–10 min	Normal-hearing subjects (6 males, 3 females; age, 23–57)	9	The activity of the human cerebral cortex can be synchronized with slow BBs	(Karino et al., 2006)
BB	-	15000 – 22000 Hz	30 min	Patients scheduled to undergo general anesthesia for elective surgery	108	Decrease acute pre-operative anxiety	(Padmanabhan, Hildreth, & Laws, 2005)
BB	Delta/theta	-	At least 5 times weekly for 4 weeks	Mildly anxious patients	15	Reduced mild anxiety	(Le Scouarnec et al., 2001)
BB	Beta range (16 and 24 Hz) or the theta/delta range (1.5 and 4 Hz)	-	30-min	-	29	Affected psychomotor performance and mood	(Lane, Kasian, Owens, & Marsh, 1998)