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EFFECT OF TONE-BASED SOUND STIMULATION ON BALANCE PERFORMANCE OF NORMAL SUBJECTS: PRELIMINARY INVESTIGATION

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ABSTRACT

Sound is known to affect the human brain, hence sound or music therapy is sometimes used to improve a subject's physical and mental health. In this study, the effects sound stimulation has on balance were investigated by means of computerized dynamic posturography tests performed with eyes closed on an unstable surface using a CAPS® system, exceeding the International Society for Posture and Gait Research (ISPGR) recommended metrological performance standards. Subjects were tested without listening to any music (baseline), listening to "pure music", and listening to the same music with different tones embedded into it (one for each key). We found that different subjects react differently to different tones. Music alone did not have a statistically significant effect on balance compared to the baseline, but the "best" tone significantly improved balance compared to the baseline or the "pure music" conditions. Furthermore, the "worst" tone reduced the balance compared to "pure music", but the reduction was not statistically significant relative to the baseline. The results therefore indicate that, at least relative to balance performance, the tone-based sound stimulation we investigated is effective and inherently safe, but that tone selection depends on the individual subject.

Keywords: Music Therapy, Sound Therapy, Posturography, Balance, Safety, Effectiveness

INTRODUCTION

The auditory system and its projections affect numerous areas of the brain and brainstem structures associated with postural control [1]. In essence, the brain projections of the auditory system consist of five basic relay nuclei with bilateral projections up to the ventral and dorsal nuclei of the lateral lemniscus and primarily contralateral projections to the inferior colliculus, tectum, thalamus and auditory cortex [2]. Furthermore, neuroimaging studies have shown that music may activate areas of the brain associated with emotional processing and higher cognitive process such as the limbic system and frontal lobes respectively [3], [4]. Menon and Levitin showed that there is an enhanced functional connectivity between the auditory system and brain regions that mediate reward, autonomic, and cognitive processing [3]. They postulated that this may be the reason why listening to music can be one of the most pleasurable human experiences. Platel and colleagues used PET to determine the areas of brain activated while listening to music and found that different areas of the brain were activated in relationship to pitch, rhythm and timbre [5]. However, the effects of sound stimulation are not limited to the auditory system. Alessandrini and colleagues showed that sound specifically activates the vestibular system, and that the use of posturography during sound stimulation may represent an alternative approach in assessing vestibular function [1]. The relationship of sound stimulation and vestibular activation is supported by the notion that the saccule and the cochlea have a common embryologic origin, and since they are anatomically located next to each other, the proximity of the saccule to the stapes may explain its mechanical stimulation during sound stimulation [1]. Moreover, in lower species the saccule functions as an acoustic receptor and in some vertebrates it serves as the only acoustic organ [6], [7]. Furthering this idea of an integrated auditory-vestibular system is the fact that the two systems share common target projections within the cortical temporo-parietal areas [8]. Other studies have shown that there exists a network of cortical and subcortical regions in the parietal and temporal lobes that respond not only to auditory inputs but also to vestibular, somatosensory and visual inputs [9]. Jones and colleagues showed that the vestibular system mediates the sensation of low frequency sounds in mice, thus having the potential to extend the hearing range of mammals and their ability to detect low frequency sounds [10]. This shows that not only there is an auditory-vestibular influence but there exists a vestibular-auditory relationship as well; both systems influence one another and work in concert.

There is gaining support for the idea that sensory modalities in and of themselves are not separate modalities and that cross-modal integration occurs across vast levels of the brain [11]. For example, the perceived duration and rate of visual stimulation has been shown to be influenced by auditory input [11]. The peripheral linkage between auditory stimulation and vestibular activation appears to occur at the saccule as it has the highest acoustical sensitivity of the vestibular apparatus [10]. With regards to postural control, it is important to note that the saccular afferents project to both the medial and inferior vestibular nuclei. In humans, this pathway mediates the vestibular-evoked myogenic potentials in which acoustic excitation of the vestibular system results in contraction of various muscles in the neck [12]. Lewis and colleagues showed that tone burst-evoked myogenic potentials in extra-ocular muscles are frequency tuned, thus suggesting that there is a relationship to the frequency of auditory stimulation and the final integrative motor response [13].

Posturography has been used for many years to assess the functionality of the vestibular system and has been investigated with regards to numerous disease states including but not limited to asthma, cerebellar disease, central and peripheral vestibular disease, Parkinson's disease and stroke. The effect of music on posturographic changes has also been investigated [1], [7], [14]. It appears that music not only affects the activation of the vestibular system but also activates the lateral pre-motor and supplementary motor areas [15]. Other studies have shown that the type of music one listens to activates different parts of the brain and cerebellum [16]. Many studies have shown that each cerebral hemisphere is specialized as to the characteristic of the sound that each one processes [17] - [19].

However, to date there appears to be no protocol describing the application of music/sound/tone therapy. Therefore, in this work we evaluated the efficacy and safety of a sound stimulation protocol specifically tailored for improving a subject's physical and mental health. Due to the wide variability of the response of the human central nervous system to environmental stimuli, it is important for the clinician to choose an appropriate biomarker to judge the effectiveness of any given treatment paradigm. In our clinical experience, we found that in this respect the measurement of balance is a good biomarker: using dynamic computerized posturography is an accurate, fast and cost effective way to quickly ascertain the response of the human brain to environmental stimuli. Therefore, we decided to use the subject's ability to maintain balance as an outcome measure of the music/sound/tone therapy.

METHODS

The protocol we investigated used sinusoidal tones, consisting of key notes for the 4^{th} octave version of the seven major musical keys. The specific frequencies of these tones are provided in Table 1.

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Table 1 – Tones and their frequencies used in this study.

Tone	Frequency (Hz)	Note
C	261.63	Often called "middle C"
D	293.66	
E	329.63	
F	349.23	
G	392.00	
A	440.00	Used as a tuning reference
B	493.88	

While no digitally generated artificial tone is an absolutely pure sinusoid (i.e., containing only a single frequency value with no harmonics), the tones we used were sufficiently pure that the second harmonic was over 36 dB lower in average power than the fundamental frequency, the third harmonic was over 30 dB below the second harmonic, and so forth (as measured from a Welch periodogram using a Hamming window, via the default settings of the `pwelch` command in MATLAB). This level of tonal purity is very high, and a typical listener should only be aware of the fundamental frequency. Spectrograph analysis confirmed the frequency stability of the tone was also not an issue: no variation in the fundamental frequency could be measured over the duration of the tone.

These tones were individually embedded into a short musical piece by adding the two digitized audio files (and ensuring the summed amplitude levels did not result in any clipping). Only one tone was added in each case; simultaneous multiple tones were not investigated. The amplitude of the tones began at zero and smoothly increased to a constant value, then toward the end the tone amplitude smoothly decreased back to zero; this eliminated any jarring effect on the listener. The musical piece used was specially scored so it could be played in each of the major musical keys while still sounding pleasing to the listener. For a given tone, the music was adjusted to be in the same key as the tone so that in each case the tone that was added would seem to be "part" of the music as far as the listener was concerned. The amplitude of the tones to be added was decreased relative to the amplitude of the music as the pitch (frequency) increased to maintain the same perceived relative volume level, based on empirical feedback from the listeners. The audio files were originally created at "CD quality" (2 channels, 16 bits per sample, 44.1 kHz sampling frequency) or better (2 channels, 24 bits per sample, 48 kHz sampling frequency) as uncompressed WAV files, but were then converted to MP3 format digital audio files (MPEG-1 Audio Layer III), with relatively low compression (14.4:1 or less), such that the effective bit rate for the audio files was 160 kbps at a sample frequency of 44.1 kHz. While the compression used by the MP3 format is lossy, a 160 kbps MP3 file is higher quality than the typical 128 kbps used for most portable music players. The compression we selected significantly reduced the file size yet maintained sufficient audio quality, and the MP3 format was compatible with the equipment used in this study to deliver the sound stimulation. There was no measurable aliasing, as the frequency content of the musical piece dropped almost exponentially to over 66 dB down by 15 kHz and to essentially zero average power by 20 kHz. The sound stimulation was administered to the subjects using high-fidelity headphones at a volume deemed comfortable by the subjects.

Thirty nine subjects (18 males and 21 females, age 46.4±16.3 years, height 1.71±0.09 m, weight 72.15±14.48 kg, BMI 24.58±4.02 kg/m^2) participated in this study, approved by the Carrick Institute for Graduate Study IRB #1 – Neurology (IRB #20150216001).

A commercially available, FDA registered medical device proven [20] to exceed the International Society for Posture and Gait Research (ISPGR) metrological performance standards [21] (CAPS® Lite –

Vestibular Technologies, LLC, Cheyenne WY, U.S.A.) was used to collect and analyze computerized dynamic posturography tests performed with eyes closed on an unstable surface (PSEC). Each subject performed nine PSEC tests in the following order of conditions: no sound (Baseline), pure music (Music Only, played in the F key), and music-tone combinations (in order in the F, G, E, A, D, B and C keys). For the baseline, the subject was wearing the same headphones but no sound/music was playing through them. All PSEC tests were performed using the CAPS® default settings (pre-test duration of 5 s, test acquisition duration of 20 s, sampling frequency of 64.011 Hz, sampling resolution of 20 bits). The subjects listened to the appropriate sound for 10 seconds before each test started and kept listening to the same sound throughout the test. The different tests were performed in sequence without the subject stepping off the instrument. All other test conditions were kept equal during the testing session.

Of all the possible posturographic parameters calculated by the CAPS® software, the stability score (SS, an overall measure of balance), the average sway velocity (V_{ave}), the sway velocity moment (VM_{ave}) and the sway area (SA) were considered [22]. The V_{ave} was normalized by the subject's height, and the VM_{ave} and the SA by the square of the subject's height, to remove any gender/subject dependency and allowing inter-subject comparisons [23]. The SS did not require any normalization as it is already independent of the subject's anthropometric characteristics.

For each subject, the SS results obtained in the PSEC tests during which the subject was listening to the music-tone combinations were independently ranked from the highest to the lowest thus allowing to identify the "best" (corresponding to the highest stability score) and the "worst" (corresponding to the lowest stability score) tones.

Since the reaction of each subject to the sound stimulation was found to be unique, each subject was used as their own control. Normality of the distribution of the data was verified using the Kolmogorov-Smirnov (with the Lilliefors Significance Correction) and the Shapiro-Wilk Tests of Normality. The efficacy of the sound stimulation to improve balance was assessed by comparing the posturographic measures obtained when the subject was listening to the "best" tone with those from the Baseline and Music Only tests. The safety was assessed by comparing the posturographic measures obtained when the subject was listening to the "worst" tone with those from the Baseline and Music Only tests. To make sure the effect was indeed due to the tone and not the music into which it was embedded, an additional comparison between the Baseline and Music Only test results was conducted. All comparisons were performed by repeated measures General Linear Model (GLM) analysis using IBM® SPSS® Statistics release 20.0.0 (IBM Corporation, Armonk, NY, U.S.A.). Because of the multiple comparisons involved, the Holm-Bonferroni method was used to maintain the desired 95% significance ($p<0.05$).

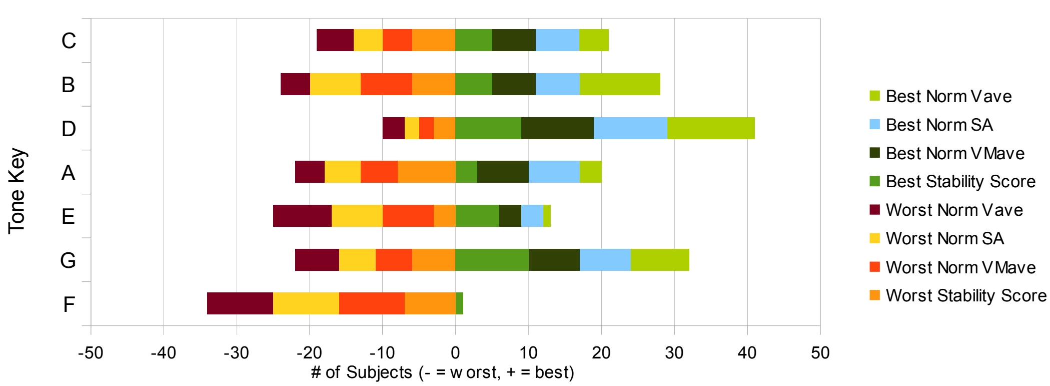

Figure 1 – Number of subjects for whom a specific tone produced the best and worst results for each variable of interest.

RESULTS

For each variable of interest, Figure 1 shows, in a population pyramid format, the number of subjects for whom specific tones produced the best and worst results respectively. Table 2 shows mean and standard deviation of the balance measures across all subjects for different PSEC test conditions. Table 3 shows the *p*-values and observed power for the repeated measures General Linear Model analyses verifying the effect of music alone (comparison between Baseline, and Music Only) as well as the efficacy (comparison between Best Tone, Baseline, and Music Only) and the safety (comparison between Worst Tone, Baseline, and Music Only) of the sound stimulation.

Table 2 – Mean (Standard Deviation) of the balance measures considered in this work for the different testing conditions.

	Stability Score	**Normalized V_{ave} [(mm/s)/m]**	**Normalized VM_{ave} [(mm/s)*mm/m²]**	**Normalized SA [mm²/m²]**
Baseline (No Sound)	62.9 (12.7)	48.6 (18.6)	210.7 (140.3)	4213.1 (2804.7)
Music Only	65.0 (13.6)	44.2 (16.8)	191.3 (168.1)	3689.7 (2741.3)
Best Tone	75.8 (6.2)	33.9 (11.0)	98.7 (55.0)	1974.6 (1099.7)
Worst Tone	60.3 (14.0)	44.1 (16.8)	191.5 (137.6)	3829.1 (2751.3)

Table 3– *p*-values (observed power at α = 0.05) for the repeated measures GLM analyses.

	Stability Score	**Normalized V_{ave}**	**Normalized VM_{ave}**	**Normalized SA**
Baseline – Music Only	0.255 (0.203)	0.052 (0.497)	0.435 (0.120)	0.196 (0.250)
Best Tone – Music Only	**0.000 (1.000)**	**0.000 (1.000)**	**0.000 (1.000)**	**0.000 (1.000)**
Best Tone – Baseline	**0.000 (1.000)**	**0.000 (1.000)**	**0.000 (1.000)**	**0.000 (1.000)**
Worst Tone – Music Only	0.013 (0.723)	0.969 (0.050)	0.994 (0.050)	0.715 (0.065)
Worst Tone – Baseline	0.138 (0.315)	0.023 (0.634)	0.271 (0.193)	0.271 (0.193)

DISCUSSION

The results of this preliminary study confirm that sound stimulation has an effect on a subject's ability to maintain balance: music alone, best and worst tone all produce a change in the average value of the variables of interest as depicted in Table 2. As it can be expected, these changes differ in amount, direction and significance.

Just listening to the music alone does not have any statistically significant effect when compared to the baseline: although Table 2 indicates an improvement in all variables (higher values for the SS, smaller for the other variables), the results of the repeated measures GLM (Table 3) show that these improvements are not statistically significant (p >0.05, power <0.50).

Listening to the best tone produces an improvement in the SS compared to the Baseline that is large (Table 2: 13 points, from 62.9 to 75.8) and statistically significant (Table 3: p = 0.000, power = 1.000), as is the improvement in the SS compared to the Music Only (a change of almost 11 points (Table 2), with (Table 3) p = 0.000, power = 1.000). Furthermore, the tone producing the best results for the SS, produces statistically significant improvements in all considered variables, as indicated by the significance of the GLMs reported in Table 3. Considering for instance the V_{ave}, although in only 43.6% of the cases the best tone for the SS was also the best tone for the V_{ave}, the average improvement across all subjects using this tone compared to the baseline is 14.7 (mm/s)/m (Table 2) or 30%, which is highly statistically significant (Table 3: $p = 0.000$, power = 1.00). Similarly, by using the best tone for the SS, the Normalized VM_{ave} and Normalized SA are reduced to less than half their Baseline values. Given these results, the use of the stability score as the parameter of choice when deciding which tones is the "best" for a particular subject seems appropriate, and the music/sound/tone stimulation protocol we investigated is an effective way to change a subject's ability to maintain balance, at least short term.

When considering the Worst Tone, the average value of the SS (Table 2: 60.3) is smaller than the Baseline (Table 2: 62.9), but this difference is not statistically significant (Table 3: $p = 0.138$, power = 0.315). Only when comparing the SS results obtained with the Worst Tone with those obtained with the Music Only the change (Table 2: 60.3 vs. 65.0) seems to become statistically significant (Table 3: $p = 0.0126$, power = 0.723), but in fact it is not when using the Holm-Bonferroni method (for 95% significance, $p > 0.0042$). For all the other variables, the Worst Tone actually causes a small improvement compared to the Baseline, i.e. the values are smaller (Table 2) and very similar to the one produced by Music Only. However, these changes are not statistically significant when using the Holm-Bonferroni method (Table 3). Therefore, the use of the subject-specific music/sound/tone stimulation protocol we investigated does not appear to have any negative effect on a subject's balance, i.e, it is safe.

Given the fact that Music Only does not have any statistically significant difference when compared with the Baseline (whereas the best tone does) and the fact that there is not one tone that is consistently the best or worst tone for all subjects (Figure 1), we can conclude that the response to the sound stimulation is subjective and cannot be assumed *a priori*. Hence, an objective quantification is required to determine which tone to choose for each individual as the same tone can be the best for one subject and the worst for another.

It is also evident that the tones have different effect on the different posturographic measures: for some subjects, the same tone produces better/worse results on all measures; for others the different tones have different effects on each of the posturographic measures. For instance, the tone producing the best (largest) SS was the same tone producing the best (smallest) V_{ave} in 17 subjects (43.6% of the cases) and the best (smallest) VM_{ave} and SA in 21 subjects (53.9% of the cases). The tone producing the worst (smallest) SS was the same tone producing the worst (largest) V_{ave} in 17 subjects (43.6% of the cases) and the worst (largest) VM_{ave} and SA in 25 subjects (64.1% of the cases). It is therefore necessary to decide which measure to optimize using the sound stimulation therapy. However, the "best" tone for the SS and the V_{ave} produced results that across all measures were better than the Baseline in all subjects and were better than Music Only in 36 subjects (92.3% of the cases). The "best" tone for the VM_{ave} and the SA produced results that across all measures were, better than the Baseline in 38 subjects (97.4% of the cases) and better than the Music Only in 37 subjects (94.9% of the cases). These results indicate that of all the measures considered, the stability score (SA) or the normalized average sway velocity V_{ave} are the optimizing variables of choice when deciding which tones is the "best" for a particular subject.

Form a neurologic point of view, these results suggest that the total summative and integrative effects of auditory stimulation on the central nervous system are tone specific and dependent upon the interplay between the type of tonal stimulation and the individual's own central integrative state governing backward masking mechanisms. Therefore, it appears that subject-specific sound/tone/music stimulation has a more powerful effect than generalized standard music therapy. The neurophysiological mechanisms of why different tones affect balance differently still needs to be determined and further studied. Some answers may lie in the hemispheric specialization for tonal analysis and the vestibular processing of different sound frequencies. Busahara and colleagues have shown using PET that sound localization includes increased activity of the superior parietal lobule, middle temporal and lateral prefrontal cortices [24]. Kaiser and colleagues showed that with regards to sound shifts from the midline the right parietotemporal areas respond to both ipsilateral shifts and contralateral shifts while the left parietotemporal region responded only to contralateral shifts [25]. Okamoto and Kakagi showed using the N1m auditory evoked potential that decrement patterns elicited by repetitive sound stimulation depended on the sound types [26]. They postulated that both refractoriness and habituation mechanisms were involved in the decrement and that it was different based upon the type of sound used [26]. Mitsudo and colleagues studied the effects within frequency and between frequency of cortical processing of gap detection and found different activation patterns within the brain in both spatial and temporal dimensions [27]. Lewald and Karnath in 2000 showed that the ability to localize sound in space is dependent upon vestibular stimulation in that vestibular information is used by the central nervous system to generate a world-centered representation of auditory space [28]. All these studies suggest that the brain processes auditory stimulation differently based upon the specific features of the stimulus itself. This difference in processing is not confined to the cortical areas of one hemisphere to the other, but also involves the brainstem auditory relays and vestibular centers. Our study goes further, suggesting that tone frequency is processed differently dependent on the tone used and this processing can be observed as changes in the motor responses governing postural control as measured using the PSEC test.

CONCLUSIONS

The current line of thinking has been that any form of auditory therapeutic stimulation will have a positive impact on the central nervous system from the shear point of its own stimulatory process. However, by comparing the effect that music/sound/tone stimulation containing specific frequencies has on subject's ability to maintain balance (as measured with the PSEC test) with standard music therapy and with no sound at all, this preliminary study showed that the individualized music/sound/tone stimulation investigated is effective at producing positive changes in all variables considered, something not seen with standard music therapy. Furthermore, it proved to be safe in that it does not produce negative effects compared with baseline (no sound) results.

Since of all the variables considered the stability score was the only one that showed a worsening, albeit non-significant, in the worst condition relative to the baseline (no sound) results, these results justify the use of such a variable as the parameter of choice to decide which tone is the best/worst for a subject. However, independent of the specific parameter chosen as the biomarker, our findings suggest that in clinical practice the use of posturography equipment meeting or exceeding the ISPGR recommended metrological characteristics can help the clinician determine the effectiveness of auditory stimulation.

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