Controlled Audio-Visual Stimulation for Anxiety Reduction

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Controlled audio-visual stimulation for anxiety reduction

<Authors hidden for blind review>

Abstract

Background and Objective: Recent clinical data suggest that 75% of patients undergoing surgery are anxious, despite pharmacological measures to relieve anxiety. As an alternative to the administration of drugs, the scientific literature reports the relevant psychophysiological effects of auditory and visual stimulation in reducing preoperative anxiety. The main objective of this study is the development of a portable computer-controlled device for the simultaneous combined administration of audio-visual stimuli and the evaluation of this device through the collection and the statistical analysis of psychophysiological parameters strictly related to the state of anxiety.
Methods: A new algorithmic approach for the real-time association of sounds and colors is proposed and implemented in a low-cost architectural platform. The combined administration of auditory and visual stimuli is tested on 220 subjects undergoing dental surgery; in particular, psychophysiological parameters are collected and evaluated in four experimental conditions, in order to demonstrate the efficacy of cross-modal stimulation (auditory and visual) compared to non-pharmacological treatments based on monomodal stimuli (auditory or visual).
Results: Non-parametric statistical techniques applied to the recorded experimental data show that the experimental conditions considered significantly differ. Pairwise comparisons between experimental groups show that the combined administration of sounds and colors significantly reduces the level of anxiety, systolic blood pressure and heart rate to a greater extent than monomodal stimulation.
Conclusion: The study demonstrates the potential benefits of a device for the combined administration of auditory and visual stimuli. The developed device has proven effective in reducing preoperative anxiety levels, becoming a serious candidate for non-pharmacological therapies. The study also encourages a deeper investigation of models capable of better capturing the potential of cross-modal stimulation, maximizing the desired effects (relaxation, arousal) on patients awaiting specific medical treatments.

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1. Introduction

According to the World Health Organization, 266 to 360 million surgeries are yearly performed in the world [1]. Surgical patients often suffer from preoperative anxiety, despite anxiety-decreasing measures [1] usually based on pharmacological treatment (midazolam) with frequent side-effects [2] [3]. These patients commonly show a slower and more painful surgical course [4].

This context comprehensively explains the interest that has recently been reported in non-pharmacological solutions, such as Clown doctors' interventions for managing children's and parents' anxiety [5]. The diffusion of new technologies has made it possible to introduce further distraction tools for the management of preoperative anxiety, such as virtual reality tours through a mirroring display [6], video glasses [7] and video games [8]. Although they are proven effective in pediatric patients and parents, they are difficult to be applied to adult surgical patients.

Among all non-pharmacological interventions, music therapy and music medicine [9] are suitable for both pediatric and adult patients and are supported by a considerable number of case-studies in clinical practice. The use of sound stimuli as a non-pharmacological measure, both in preoperative anxiety and postoperative pain management, has shown relevant psychological, physiological, and physical effects [2] [3] [10] [11]. In a randomized controlled trial [2], relaxing music (characterized by the slow tempo of 60 to 80 bpm, mimicking the heart rate at rest) has been used as pre-medication before surgery. Music treatment had a better anxiolytic effect than pharmacological treatment. According to data analysis, heart rate and blood pressure decreased in both the drug-treated and non-drug-treated groups.

Humans are also very sensitive to visual stimuli through light. Light profoundly influences the regulation of several aspects of physiology and behaviour; on the basis of spectral components [12], light treatment can also regulate cognitive functions and influence emotional brain responses [13] [14]. The majority of studies [15] [16] [17] have explored the antidepressant effect of bright light but did not investigate its potential anxiolytic effects [18], which are mainly related to low sensory, color-based stimulation. Low-intensity colored lights (and specific colors in particular, like green or red) seem to induce physiological reactions (arousal-based theory) [19] or to influence cognition and behavior, promoting a relaxing state, through learned association (context-based theory) [20].

In the current state of the art audio-visual stimulation (AVS) is a well known technique used to elicit a cerebral response that can be recorded by EEG [21]. AVS has been reported as a promising method of non-drug correction of functional disorders and in the normalization of the human functional state [22] [23]; effects of AVS have been also reported to relieve tension and in the therapy of insomnia [24].

Most of the works in AVS share the way the stimuli are administered: synthesized or pre-recorded songs (often popular classical themes) are presented to the subjects without feedback. Listening to music is accompanied by light flashes at a frequency that is somehow correlated to audio stimulation or gradually covering a given frequency range. Only sporadic contributions in the literature experiment with more complex administration of auditory and visual stimuli. For instance, Barsasella and colleagues [25] report on virtual reality tools, showing how VR sessions can influence the well-being and functional fitness of older adults and support the process of healthy and active ageing. Bergomi et al. [26] focus on audio-visual distraction tools, showing that animated cartoons can help children to reduce pain and anxiety during venipuncture. Further results [27] suggest that AVS, under the form of an audiovisual slide presentation, can alleviate anxiety after maxillofacial surgical intervention. Pan and colleagues [28] recently investigate the audio-visual integration effect on emotions elicited by positive (congruent) or negative (non-congruent) music; they proved in particular that the intensity of the emotional experience elicited by the music is influenced by visual stimulation.

Moving from the above described theoretical framework, the focus of this paper is two-fold. The first objective is to propose a novel algorithm for the cross-modal real-time association of audio and visual stimuli; the algorithm is implemented by exploiting a low-cost embedded architecture featuring environmental microphones and integrated controllers for external LED units and surround speakers. The second objective is testing the efficacy of such a system in decreasing anxiety; in particular, preoperative anxiety and physiologic stress levels of subjects waiting for dental surgery are considered.

2. Methods

The functional diagram of the system for the controlled administration of audio-visual stimuli is depicted in Fig. 1. The generic audio data (pre-recorded or live, that is acquired in real-time from built-in or environmental microphones) is first analyzed and converted into pure (spectral) color information; this step must take place in real-time to avoid time delays and asynchronous piloting of the lights. Once defined the reference spectral wavelength, the perceptual effect of the color must be fully determined and specified through a three-component system such as HSL or HSV; this step is critical in order to provide the user with congruent visual stimulation. The final module of the diagram is devoted to the synchronous piloting of LED lights and/or speakers, depending on the operating mode of the system. In pre-recorded audio mode, as in the experimental framework detailed below, both outputs are activated. The system, however, can also limit the output to the lighting subsystem only; in this case, the ambient sounds will directly drive the lights.

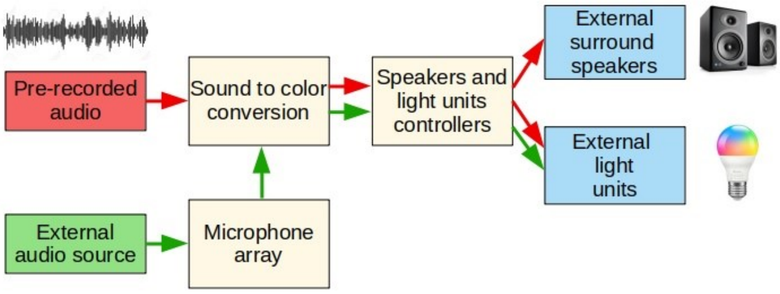


Fig. 1. Functional diagram of the system with two operating modes: “Pre-recorded Sound Processing Mode” (red flow) and “Live Mode” (green flow).

2.1 *Sound-to-color conversion*

The Sound-to-color conversion topic has a very poor bibliography. The most important scientific contributions essentially refer to the synesthesia phenomenon, a rare condition in which stimulation of one sensory system causes involuntary experiences in a second, unstimulated pathway [29]. The concept of the octave has great relevance in this context [30]; in fact, it is demonstrated that human perception is characterized by a well known effect, referred to as "tone circularity", which is based on tones standing in the octave relation (the frequency of the second is twice the frequency of the first). Stimulation through octaves shows a sort of perceptive equivalence and this peculiarity allows the creation of scales that ascend (or descend) endlessly in pitch. A second important concept concerning sound perception is the timbre; timbre is what makes different the perception of the same note when played by different musical instruments. This effect is mainly due to the harmonic content of the frequency spectrum which is characterized by the sum of a fundamental frequency and many additional harmonics (frequencies that are integer multiples of the fundamental but with different amplitudes).

A third and final concept that plays a part in human perception is rhythm, which, differently from tone and timber, has slow dynamics and refers to the audible recurrence of sounds and silence in time.

The following sections examine the relationship between auditory and visual stimuli from both a qualitative and quantitative perspective; parameters necessary to completely characterize the audio signal are explored, and the proposed approach is motivated in light of previous experimental findings.

2.1.1 Preliminary evaluation of audio-visual mapping

A preliminary activity considered two essential elements of the audio track: the energy of the signal (well representing the static spectral content, as clarified later) and the rhythm (well representing the dynamic content and expressed in beats per minute). Most of the work in AVS uses these two elements to associate visual stimulation with synthesized or pre-recorded pieces, with controversial results. For example, a very common procedure is to use the beat to drive flashing lights, in order to provide some sort of coherent stimulation for both the auditory and visual systems [21]. The intensity and color of the light are usually fixed but the researchers also proposed the use of spectral energy to drive color or intensity, resulting in different types of perceptual effects [31].

To preliminarily evaluate these elements, in particular with the aim of a calming function of the system and a reduction of anxiety levels, a limited number of subjects (40 students, 21 males, and 19 females, three sessions each) was recruited for a preliminary experiment. Subjects were required to stay in a dark room and asked to listen to a classic theme for 10 minutes, accompanied by flashing or fixed light stimulation. At the end of the experiment, they were asked to express their feelings using a 5-point Likert scale (very-low to very-high comfort). As better detailed in Fig. 2, the subjects were randomly involved in 12 different experimental configurations which can be categorized to three main groups in relation to the color (red, green, or blue) of the light used in the experiment. For each group, the intensity and flashing of the light were controlled in two different ways, for a total of 4 experimental subgroups.

Fig. 2. A preliminary evaluation of the audio-visual mapping was made by expressing a level of comfort while listening a classic theme accompanied by flashing or fixed light stimulation. Flashing is driven by the beat of the song; when flashing is off the lamp remains constantly on. The result of the evaluation is denoted by colors: red indicates very-low comfort, orange low comfort, light green indicates high comfort, green very-high comfort, yellow   stands for a neutral evaluation.

The results of this preliminary experiment, even though purely qualitative, are important to properly design the audio-visual mapping proposed in the next sections. In particular, with reference to Fig. 2, three points clearly emerge:

- independently from the intensity and flashing control of the light, the green color seems to be the most promising candidate to the aim of a relaxing and calming effect; this result substantially agrees with the literature findings and suggests a careful (not random) determination of hue for the experimental purposes.
- A proportional relationship between intensity of the light and energy of the signal seems to always bring a comfortable effect; this result suggests to avoid fixed lights and pushes towards an algorithmic determination of the intensity based (or partly based) on the spectral energy.

- Flashing always seems to reduce comfort; this result is once again in line with the literature, where the exciting function of the beat is often used to improve functional activities such as fitness or physical exercises, and suggests avoiding the beat as a driving element of the light.

In the proposed approach, the sound to color conversion algorithm thus proceeds by two well distinguished steps: at first, the audio signal is characterized by its spectral content (including but not limited to spectral energy), then characterizing parameters are used to fully identify the corresponding visual output, but paying particular attention to the possibility of limiting the wavelengths of color within regions potentially useful for a calming effect.

2.1.2 Proposed audio signal charaterization

Digitally sampled audio data, in the time domain, is processed by Fast Fourier Transform (FFT) in order to derive the signal spectrogram. More in detail, the input data stream is broken up into blocks or data packets of programmable size (we used 1024 samples as the best block size), which usually overlap in time, and Fourier transformed to calculate the squared magnitude of the frequency spectrum. Spectral transforms generated at different time instants by the sliding window method are commonly referred as Short-Time Fourier Transforms (STFT) [32]; they are extremely helpful in order to better determine the spectral content of local sections of a signal as it changes over time. The mathematical discrete representation of STFT is:

$$STFT\{s[n]\}(\tau,\omega) \equiv X(\tau,\omega) = \sum_{n=-\infty}^{\infty} s[n]w[n-\tau]e^{-j\omega n} \qquad (1)$$

where the signal is denoted by $s[n]$ and the block window by $w[n]$. Note that the STFT outcome is a set of complex numbers that represent the amplitude (magnitude) and phase of the signal harmonics. Phase information is neglected in the spectrogram (SG) representation; more precisely, at a given time instant SG corresponds to the Power Spectral Density (PSD or Power Spectrum) of the original signal:

$$SG\{s[n]\}(\tau,\omega) \equiv |X(\tau,\omega)|^2 \qquad (2)$$

As spectrograms commonly refers to multiple time instants, they are often placed side by side to create a 2D color image or a sliding three-dimensional surface (see Fig. 3).

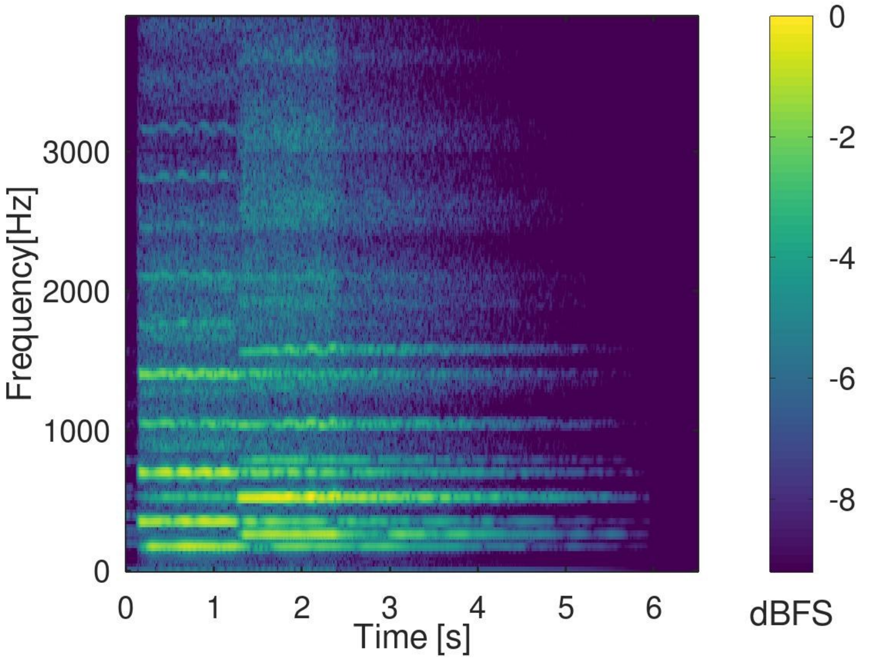


Fig. 3. Simple spectrogram of a short audio track showing the sound of a flute (two notes, F4 and C5). The magnitude of the frequency spectrum (colors from black to yellow) is given in decibels relative to full scale (dbFS).

Once the spectrogram has been created from a time-domain signal, the sound signal characterization, based on spectral analysis, can take place. In more detail, with reference to Fig. 3 and Fig. 4, the power spectrum corresponding to each time instant is processed in order to derive the following parameters:

- total energy (TE) of the signal;
- the frequency corresponding to the absolute maximum of the spectrum (FM), after interpolation by inverse distance weighting;
- sparsity index (SI).

The total energy TE of the signal is directly obtained by integration of the spectrogram with respect to ω and for each instant of time:

$$TE \equiv \sum_{\omega=-\infty}^{\infty} |X(\tau, \omega)|^2 \quad (3)$$

In other words, this corresponds to the processing of each vertical slice of the spectrogram, deriving a single value capable of representing the intensity of the sound.

The computation of the maximum of the spectrum FM is slightly more elaborate. In particular, interpolation by inverse distance weighting is essential in order to consider the sparse nature of the audio signal. In practice the power spectrum is processed by a sliding window whose amplitude respects the notion of octave:

$$ISG(\tau, \omega) = \frac{\sum_{\omega_i=\omega/2}^{2\omega} SG(\tau,\omega) \cdot w_{\omega_i}(\omega)}{\sum_{\omega_i=\omega/2}^{2\omega} w_{\omega_i}(\omega)} \text{ where } \begin{cases} w_{\omega_i}(\omega) = 1 if d(\omega_i, \omega) = 0 \\ w_{\omega_i}(\omega) = \frac{1}{d(\omega_i,\omega)^p} if d(\omega_i, \omega) \neq 0 \end{cases} \quad (4)$$

Note that the weights are inversely proportional to the distance d between the current frequency processed $(\omega)$and the frequencies $\omega_i$falling in the sliding window; the parameter p is a real integer useful to shape the weights in the window.

For the computation of the sparsity index SI different criteria can be adopted [33]; in our case both the Hoyer and the Gini indexes proved to be effective in order to detect very sparse spectra. The Hoyer index finally adopted is defined as:

$$SI = \left(\sqrt{N} - \frac{l^1}{l^2}\right) \cdot \left(\sqrt{N} - 1\right)^{-1} \quad (5)$$

where the notation l^p indicates the norm-like measure of order p for a generic vector: $x = \{x_1 .. x_n\}$:

$$l^p = \|x\|_p = \left(\sum_i x_1^p\right)^{1/p} \quad (6)$$

The application of the above formulas to the spectrogram $SG(\tau, \omega)$ at a given time instant τ is better clarified by Fig. 4.

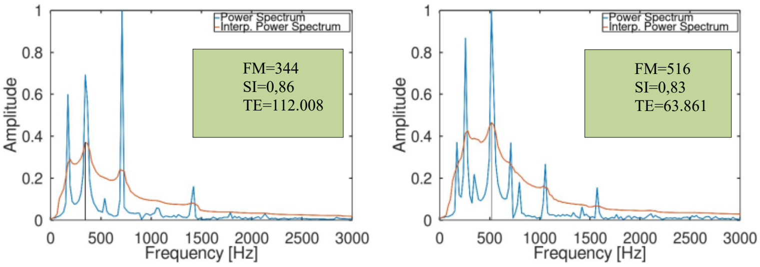


Fig. 4. Simple spectrograms of the soundtrack of figure 2 for two different time instants: ($t = 1sec$,and $t = 2sec$. The amplitude of the power spectrum is normalized to the full scale. Note the effect of the octave-based interpolation that in the left plot weakens the main peak. The maxima of the interpolated spectra for both plots (black vertical bars, left 344 Hz, right 516 Hz) are very close to the correct frequencies of F4 (349 Hz) and C5 (523 Hz).

2.1.3 Color identification

To the aim of a full identification of the color corresponding to a specific time instant, the HSV representation is adopted (Fig. 5).

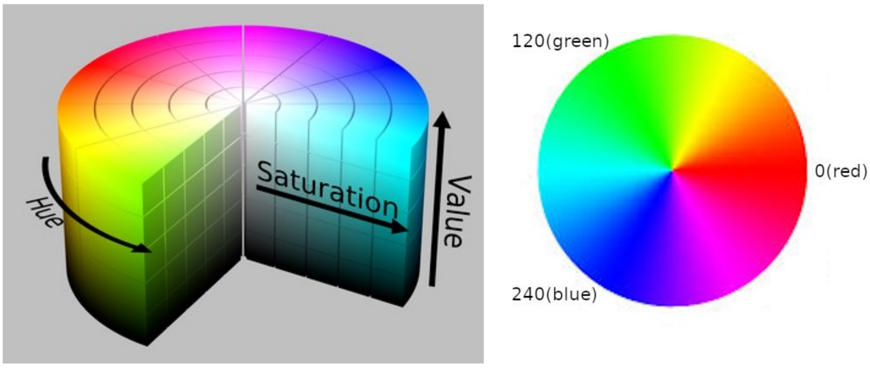


Fig. 5. (left) The hue-saturation-value colormap used to identify the color corresponding to a given power spectrum. Value and Saturation are represented in the range [0-1], Hue in the range [0-359]. (right) Top view of the same colormap showing more precisely the correspondence between colors and hue.

The association of V (value of the colormap) to TE (total energy of the signal) is quite straightforward, as this parameter represents the global “intensity” or “brightness” of the color. Similarly, S (saturation of the colormap) can be directly associated with SI (sparsity index of the signal). In fact, S represents the purity of a color, that is the amount of distribution across the spectrum of different wavelengths: S is maximum for a color characterized by a single wavelength, such as the color generated by a laser source. Similarly, SI is maximum for a non-sparse power spectrum, that is a sound characterized by a few harmonics or a digitally synthesized sound based on a single frequency. Both V and S are represented in the range [0-1]; as a consequence, SI (which is yet a normalized index in the range [0-1]) can be directly assigned to S while TE requires a further normalization with respect to a full-scale value. In the proposed implementation this value is set to a fairly low level (100.000), which often makes it necessary to truncate the value of V to 1:

$$V = min\left(1, \frac{TE}{100000}\right) \tag{7}$$

The last parameter required in order to determine the resulting HSV color is H (hue of the colormap). To this purpose, FM is first mapped to a pre-defined part of the visible spectrum, called scenario by the piecewise linear function given in Fig. 6.

This step is inspired by the observation that in most cases FM is contained in a very limited band, between 50 and 4000 Hz, which roughly coincides with the band of maximum sensitivity of the human ear, with the peak around it at 3000 Hz (although the sensitivity of the human ear is between 20 and 20000 Hz.). Note that the conversion is purely linear in the range [128-2048 Hz] and that an increase in sound frequency (low to high pitch) corresponds to a decrease of the wavelength color (violet to red). Frequencies below 32Hz are set to the minimum wavelength color (violet); frequencies above 8192Hz are set to the maximum color (red). The shape of the function in the intervals [32-128 Hz] and [2048-8192 Hz] has proved experimentally effective in managing low and high peaks without generating unpleasant perceptual effects.

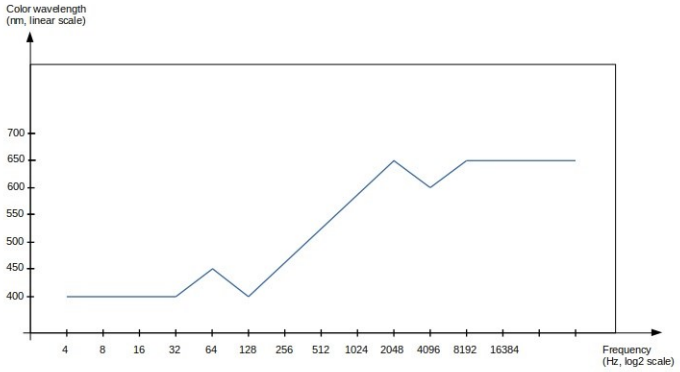


Fig. 6. The piecewise function adopted to map the sound frequency [0-20.000 Hz] to the wavelength color; in the plot all of the visible spectrum [400-650 nm] is considered for mapping.

Concerning this point, note that the mapping of FM to the full visible spectrum or a part of the spectrum denoted as "scenario" does not change the general approach. Simply, following the scientific theory behind our experimental analysis, this option allows to select an optimal wavelength range for the specific application foreseen.

The selected wavelength color is finally converted to H taking into account the peculiarity of the HSV colormap; in particular, considering that values of hue over 270 are not part of the visible spectrum, H is computed as:

$$H = \frac{270}{(650 - 400)} \cdot (650 - \lambda) \tag{8}$$

where λ is the selected wavelength color.

Table 1 summarizes by pseudocode the algorithm implemented.

```
INPUT: buffered audio signal 44100 Hz
WHILE (input is available)
  WAIT for a ready buffer (1024 samples)
  LOCK the buffer
  compute STFT
  UNLOCK the buffer
  compute power spectrum
  compute TE and SI of the power spectrum
  interpolate power spectrum by inverse distance weighting
  compute FM
  compute HSV from TE, SI and FM
```

```
  drive external light units
ENDWHILE
```

Tab. 1. Pseudocode of the implemented algorithm. Note that the conversion proceeds in parallel with respect to the sampling of the audio signal; the synchronization between sampling and conversion is guaranteed by a protected buffer area.

2.2 *Experimental validation*

The hardware architecture used for the implementation of the system is depicted in Fig. 7. The device, based on a low-cost power-optimized multi-core platform, combines computational, control and communication modules; as previously mentioned, it can operate in two alternative ways: in “Live Mode” with continuous environmental interaction, and “Pre-recorded Sound Processing Mode” to process recorded soundtracks.

For the purpose of this study, an external LED unit (18 RGBW x 1W high-power LEDs, 2700-3500K Color Temperature for warm white and 6000-7000K for pure white) has been used

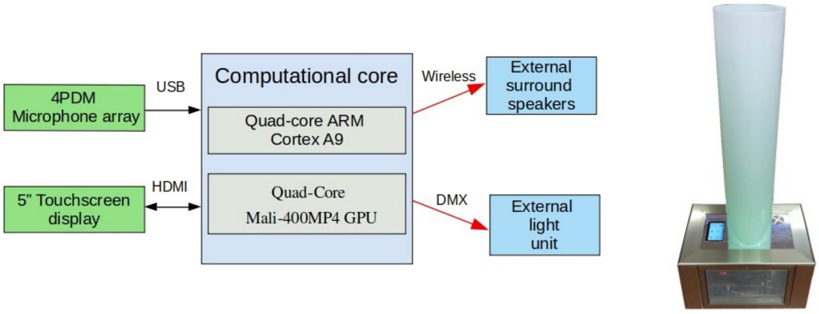


Fig. 6. (left) Main hardware components of the system. (right) photo of the system showing the box containing the electronics and the external LED unit within a cylindrical polycarbonate diffuser.

The proposed validation is based on a simple evaluation protocol involving four groups of participants; each group is subjected to a different type of stimulation: audiovisual for group 1, auditory for group 2 and visual for group 3. Absence of stimulation characterizes group 4, hereinafter denoted as control group. The following hypothesis system is tested:

H1: The combined administration of auditory and visual stimuli (group 1) will show a significant reduction in the preoperative anxiety level (AL) compared to the groups with an isolated stimulus (group 2 and group 3) and ceteris paribus with the control group (group 4);

H2: Group 1 will show a significant reduction in systolic blood pressure (SBP) to a greater extent than the experimental conditions with an isolated stimulus (group 2 and group 3) or without stimuli (group 4);

H3: Group 1 will show a significant reduction in diastolic blood pressure (DBP) compared with the groups with an isolated stimulus (group 2 and group 3) and, ceteris paribus, with the control group (group 4);

H4: Group 1 will show a significant reduction in heart rate (HR) compared to the groups with an isolated stimulus (group 2 and group 3) and ceteris paribus to the control group (group 4).

2.2.1 Procedure

The experimental validation was conducted on patients visiting a private dental clinic for their treatment procedures (dental extraction, dental implant surgery, root canal treatment, inlay and onlay restorations). Fig. 8 details the main steps of the procedure; on arrival at the clinic, the staff greeted the patient and invited him to take part in the experimental validation, with the purpose to improve the service offered by the clinic (pre-recruitment). Afterward, a staff member accompanied the patient to a private waiting room, invited him to sit, and give written informed consent. Patients could withdraw at any time. Once assessed the eligibility to the experiment, the patient was randomly assigned to one of the four groups; then a first questionnaire consisting of 6 questions, was submitted in order to measure the pre-surgery anxiety level [34]. Once completed the questionnaire, the staff measured the patient's blood pressure (systolic and diastolic) and heart rate (pre-stimulation parameters). After this pre-stimulation phase, the subject switched to a dental treatment unit (stressor), in an adjacent room, and he sat down in the dental chair in the correct position, as per best practice. General room illumination provided by our device was at 500 lux as per national and international requirements and standards for optimum illumination [35]. The device had previously been positioned, above a cabinet, behind the dental chair, to ensure low sensory stimulation and avoiding direct exposure to the colored light stimulus. The staff member informed the patient of five to ten minutes waiting before surgery start and then left him alone, exposed in vivo to the stressor of the operating room environment for 10 minutes. After this time period, he came back apologizing because the doctor was still occupied in another treatment and the surgery would be delayed by some minutes.

The "waiting period" was equal to 20 minutes in total, during which stimuli were or not administered to the patient, according to the experimental conditions. Once completed the stimuli administration phase, and before the dental intervention, the staff asked to compile for a second time the administration questionnaire (to assess post-stimulation anxiety levels) and to record the physiological parameters (exposure parameters).

Note that the experimental procedure ended before dental intervention; details about eligibility, data recorded and stimuli administration are given in the following sections.

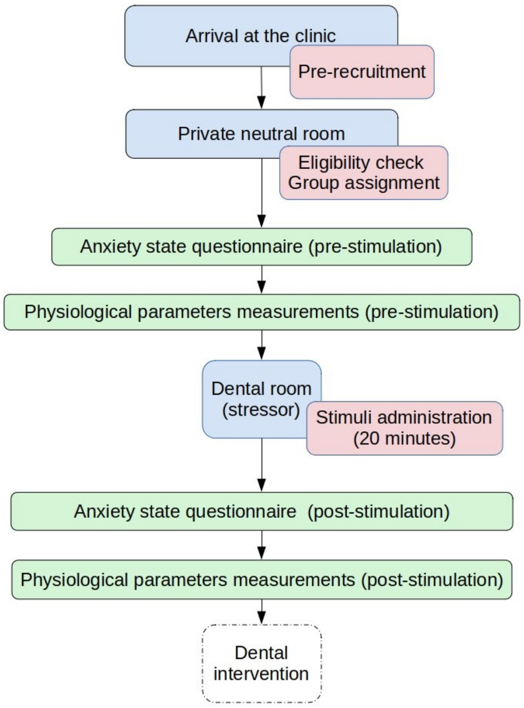


Fig. 8. The diagram shows the procedure adopted for the experimental validation of the device. In light blue/red, the main involved places/phases; in light green, the data collection moments. Dental intervention is not part of the experiment.

2.2.2 Participants

Two hundred and twenty adult surgical patients (76 female and 144 male, average age 43) were enrolled in the present study as volunteers, without any monetary reward. Based on anamnesis, inclusion criteria were: 1) normal visual acuity (natural or o corrected by using corneal lenses); 2) normal auditory acuity 3) no history of ophthalmologic (such as congenital color vision deficiencies), auditory, psychiatric and neurological disorders. Patients with manifest difficulties in speaking and understanding were excluded. Patients who were unwilling to fill the questionnaires or those who partially fill the questionnaires were excluded. Pregnant patients, pediatric patients, patients having systemic diseases, and those taking anxiolytics or antidepressants were excluded too. Participants were randomly assigned to one of the four groups (55 per group); note that the sample size corresponds to the minimum size required to ensure the statistical significance of the tests performed in section 3 (α = 0.05, power of at least 80% to detect an effect size even of small entity (d = 0.2)). The four groups are essentially homogeneous to each other in terms of gender (χ^2 (3) = 3.37; ns) and age (F (3, 216) = 0.732, ns).

2.2.3 Stimuli

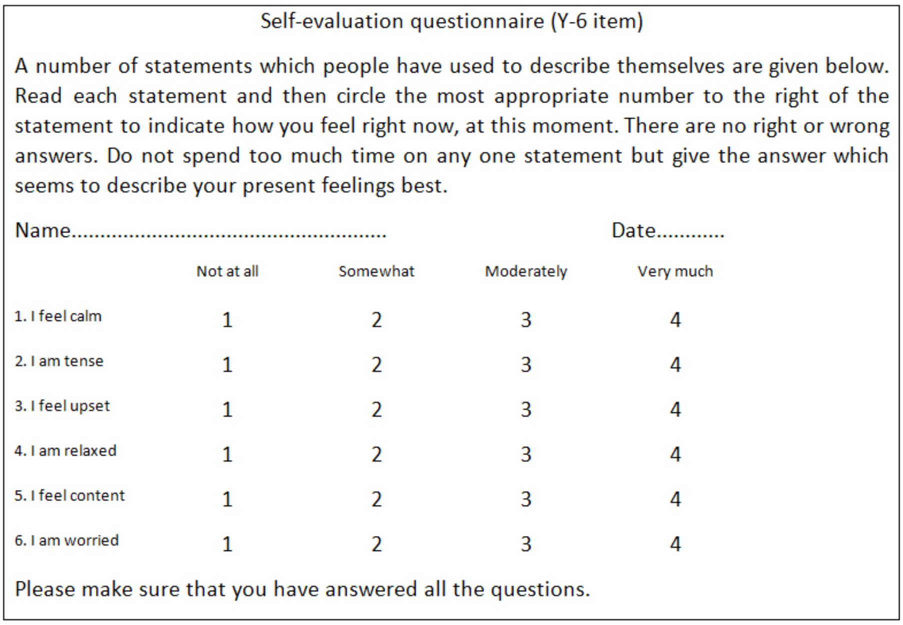
The selection of appropriate auditory stimuli has been one of the main difficulties in the preparation of the experimental materials. In clinical practice, there are two approaches in music selection: a patient-centered approach, in which the patient selects the music, and the experimenter-centered approach, in which music is selected by the experimenter [36]. To preserve the objectiveness of empirical evidence, the external validity, and the generalizability of our study, we have opted for the experimenter-centered approach, establishing some objective criteria that relaxing music must have. The tempo of the music is the most important factor [37], it should fall between approximately in the range 60-80 beats per minute, the same pace as the heart at rest [38]; beat should be constant and regular, with a 4/4 time signature; melodies should be strong and secure because melodies that are weak and less obvious are not conducive to relaxation [39]. Finally, the patient should not be distracted by words, thus leading to the exclusion of music with lyrics [2]. Based on these criteria, we have selected a relaxing piece of music at 60 bpm. (Elemental Healing Sounds); in order to ensure standard and homogeneous reproduction of the stimuli the system was set to the pre-recorded audio mode and the maximum volume level was set at 60 dB [40]. Most of the studies that used music to reduce pre-operative anxiety revealed that the optimal listening time was 15 to 30 minutes; this timing fits satisfactorily to the duration of stimulus administration (20 minutes) set in our experiment.

Concerning the visual stimuli, as reported in the theoretical framework, we have narrowed the search area to short-wavelength colors, specifically blue and green colors. Primarily because they are considered calming and relaxing in comparison to longwavelength colors, which are considered arousing (Arousal-based theory), secondly because they are correlated with positive meanings through learned associations, (Context-based theory). In the choice between blue and green color, we have selected the last one because it is reported effective in anxiety and other pathological conditions; green color induces relaxation, improves anxiety symptoms and has a calming effect [19] [41] [42]. On the contrary, the blue color, under certain brightness conditions, is twice more activating compared to green [43].

In terms of wavelengths, we have thus set up a scenario limited to the green light color, mapping the absolute maximum of the spectrum in a range between 520 and 560 nm.

2.2.4 Data recorded

An anxiety-state questionnaire (Table 2) was used to assess the patient's anxiety levels, before having a dental surgery treatment (Pre-operative Anxiety-state) and after stimuli administration (Post-Stimuli-administration Anxiety-state). We used a six-item short-form of Spielberger State-Trait Anxiety Inventory (STAI), instead of the STAI full form. The six-item short-form of the STAI produced scores similar to those obtained using the full form of the STAI but retaining several advantages (time-saving, maximization of response rates, minimization of response errors and unanswered items) and thus improving the validity and generalizability of findings [34].



Self-evaluation questionnaire (Y-6 item)

A number of statements which people have used to describe themselves are given below. Read each statement and then circle the most appropriate number to the right of the statement to indicate how you feel right now, at this moment. There are no right or wrong answers. Do not spend too much time on any one statement but give the answer which seems to describe your present feelings best.

Name.. Date...........

	Not at all	Somewhat	Moderately	Very much
1. I feel calm	1	2	3	4
2. I am tense	1	2	3	4
3. I feel upset	1	2	3	4
4. I am relaxed	1	2	3	4
5. I feel content	1	2	3	4
6. I am worried	1	2	3	4

Please make sure that you have answered all the questions.

Tab. 2. Pre-treatment questionnaire based on six-item short-form of Spielberger State-Trait Anxiety Inventory. Each question admits only one of the four answer options.

Physiological responses were taken through a non-invasive, reliable, and accurate method; specifically, blood pressure (systolic and diastolic) and heart rate were recorded using Omron HBP-T105, a clinically validated blood pressure device [44].

During measurements, the patient (quietly and no moving), followed the indications provided, placed the right hand with the palm facing upward, to align the artery position mark, on the cuff, with the brachial artery.

3. Results

3.1 *Sound-to-color conversion*

Figure 9 shows the result of the conversion algorithm for a short excerpt (20 seconds) of the piece of music adopted in the experiment. On the left column, the original signal in the time domain (top) and the corresponding color (bottom) computed in the green scenario.

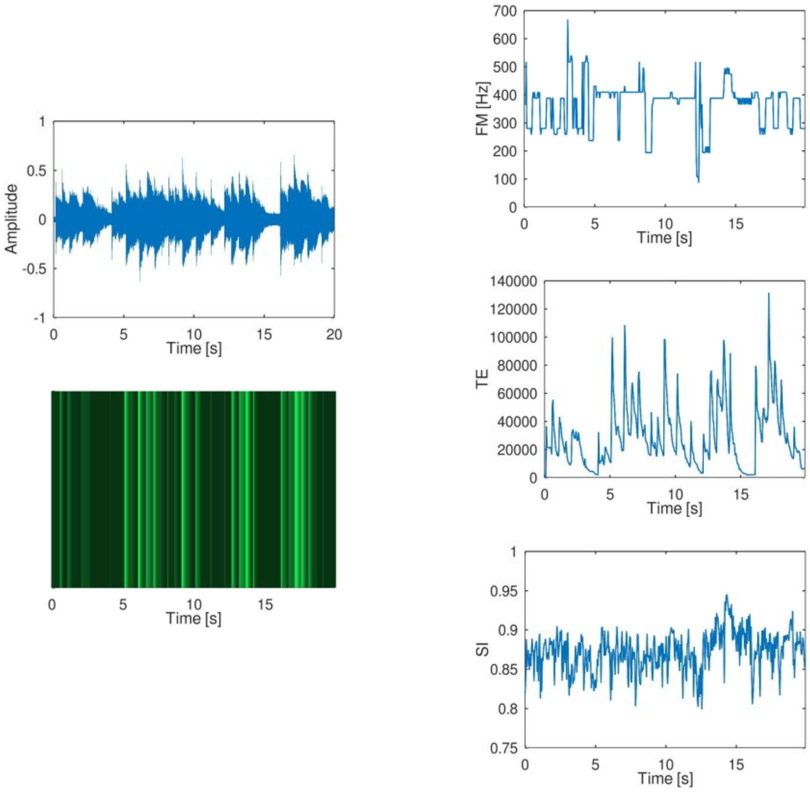


Fig. 9. Result of the sound-to-color conversion. Color is represented with vertical bars that proceed from left to right, according to the time axis. For the meaning of FM, SI, TE plots (left column) refer to section 2.

On the right column, some intermediate results; note that the total energy of the spectrum TE (bottom) is relatively small, due to the low volume level adopted in the experiment. Also note, that for this simple and relaxing music track, the reference frequency FM (top) fluctuates in a relatively small range.

3.2 *Data recorded*

STAI measures were derived as per Marteau and Bekker's methodology [34]; values are in the range 20-80.

Pre and post-stimulation physiological data were directly recorded from the Omron HBP-T105 device; systolic and diastolic measures are expressed in mm Hg while heart rate in bpm. As an example of the data collected, Fig. 10 shows the distribution of the heart rate (HR) index. Note that values do not follow a normal shape.

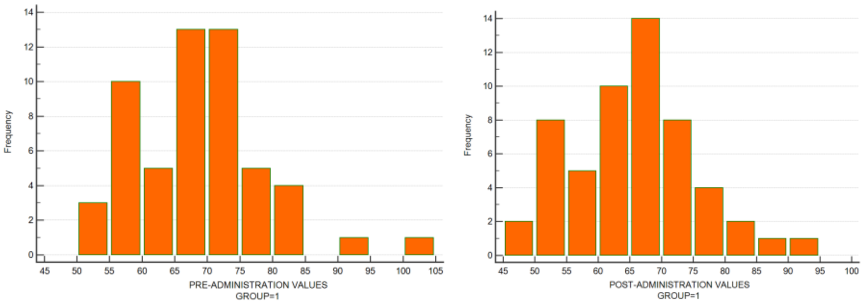


Fig. 10. Distribution of the HR index for group 1 (55 participants); (left) pre-stimulation phase, (right) post-stimulation phase.

Table 3 shows some descriptive statistics of the results. Rows correspond to dependent measures, while columns correspond to stimulation groups.

	(group 1) Combined Stimulation		(group 2) Auditory Stimulation		(group 3) Visual Stimulation		(group 4) Absence of stimulation	
	Pre	Post	Pre	Post	Pre	Post	Pre	Post
AL, STAI	38 34-43,75 (9,75)	34 30-40,50 (10,5)	37 32,50-43,75 (11,25)	34 29,25-42,75 (13,5)	36 32-44 (12)	36 30-43 (13)	35 29,25-44,75 (15,5)	34 30-43,75 (13,75)
SBP, mm Hg	115 108-124,75 (16,75)	113 103,50-121 (17,5)	114 107,25-121,75 (14,5)	110 105,25-119 (13,75)	119 108-126 (18)	119 108-125,75 (17,75)	114 108-121 (13)	116 108,25-123 (14,75)
DBP, mm Hg	70 65-78,75 (13,75)	66 62,25-76 (13,75)	72 65-78 (13)	70 63-77,50 (14,5)	72 65-80 (15)	74 67,25-80 (12,75)	72 67-79 (12)	73 68-79,75 (11,75)
HR, bpm	69 60-72,75 (12,75)	66 57,50-71 (13,5)	68 63-74 (11)	66 60,50-71 (10,5)	67 60,50-71,75 (11,25)	69 64-72 (8)	69 60-74,75 (14,75)	70 60,50-77,50 (17)

Tab.3. Summary of data recorded in the pre and post-stimulation phase. For each group/data set: median, Q1-Q3 percentiles, and InterQuartileRange (IQR) are displayed. AL = anxiety level; SBP = systolic blood pressure; DBP = diastolic blood pressure; HR = heart rate.

3.3 *Statistical analysis*

Statistical analysis of the recorded data was primarily aimed to test the hypothesis system previously described; in other words, to check whether the combined administration of auditory and visual stimuli applied to group 1 would show a significant decrease of the recorded psychophysiological data.

To this purpose, we first proceeded to the computation of difference distributions for each group/data type (post values – pre values, 16 subsets in total) and then checked the normality of these distributions. According to the D'Agostino-Pearson normality test, we rejected the normality. Table 4 shows descriptive statistics of difference distributions; median values are apparently increasing going from the leftmost column (group 1) to the rightmost column (control group) for all types of data recorded.

	DELTA			
	(group 1) Combined Stimulation	(group 2) Auditory Stimulation	(group 3) Visual Stimulation	(group 4) Absence of stimulation
	-4	-2	-1	-1
AL,	(-5; -2)	(-3; -1)	(-1; -1)	(-2; 0)
STAI	3	2	0	2
	-4	-3	-1	1
SBP,	(-4,75; -3)	(-4; -2)	(-1; 2)	(-2; 4,75)
mm Hg	1,75	2	3	6,75
	-3	-2	-1	1
DBP,	(-3; -2)	(-3; -1)	(-1; 2)	(-1; 3)
mm Hg	1	2	3	4
	-3	-2	-1	0
HR,	(-4; -2)	(-3; -1)	(-2; 3,75)	(-1; 2)
bpm	2	2	5,75	3

Tab. 4. Descriptive statistics of difference distributions (post - pre-stimulation phase). For each group/data set: median, Q1-Q3 percentiles, and InterQuartileRange (IQR) are displayed. AL = anxiety level; SBP = systolic blood pressure; DBP = diastolic blood pressure; HR = heart rate.

This effect is graphically more evident in the plots of Fig 11, better summarizing the character of the 16 distributions considered; note that each plot corresponds to four distributions, one for each group involved in the experiment.

We thus considered each type of data recorded (corresponding to a plot or likewise to a single row of Table 4) and compared the four groups to check whether samples originate from the same distribution; we opted for a non-parametric equivalent of the one-way between-subjects ANOVA, the Kruskal–Wallis test. Note that the sample size of the group (55 samples) was sufficient to detect a medium effect size, for α=0.05 at power=0.80 [55].

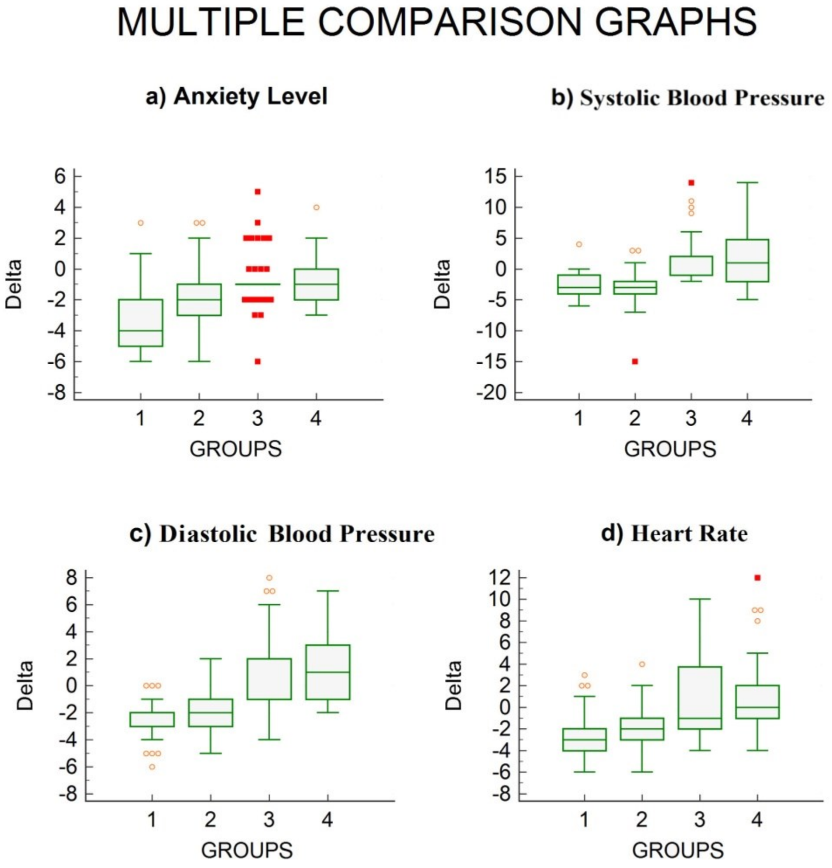


Fig. 11. Descriptive statistics of difference distributions (Delta = post-stimulation values - pre-stimulation values). Boxplots indicate median values, first-third quartiles (Q1, Q3); whiskers indicate the lower-upper adjacent values [Q1-1,5 x IQR : Q3+ 1,5 x IQR]. Outliers are indicated by red circles (outside values) and filled squares (far out values). (a) Anxiety level - the negative delta percentages express an improvement in conditions. The anxiety level is dropping, and the group with the best positioning is group 1 (Combined Stimulation). (b) Systolic Blood Pressure - group 1 (combined stimulation) and group 2 (auditory stimulation) show similar performances in reducing Systolic Blood Pressure. Although the auditory stimulation has a very remarkable performance, the combined one retains its prerogative concerning the response variables

examined. (c) Diastolic Blood Pressure - the performances of group 1 and group 2 are similar. Furthermore, we observe that this response variable, compared to the others, seems to be less sensitive (in terms of negative delta percentages reached) to the different types of treatment. (d) Heart Rate - Group 1 has the best positioning; the response variable Heart Rate decreases significantly by the combined treatment.

Table 5 shows the result of the Kruskall-Wallis test; note that a significant result indicates that at least one of the considered distributions significantly differs from the others but doesn't say anything about between-group differences.

In order to analyze in deep these differences, we proceeded with post-hoc tests [45] [46]; more in detail we proceeded by pairwise comparisons with the Conover-Iman test using the rank sums.

Kruskal-Wallis test

Manipulated variables	Test statistic	Corrected for ties Ht	Degrees of Freedom (DF)	Significance
AL	53,5979	56,0606	3	P<0,000001
SBP	102,3323	104,4565	3	P<0,000001
DBP	107,5814	110,9055	3	P<0,000001
HR	66,5944	67,7950	3	P<0,000001

Tab. 5. Summary table of the Kruskal-Wallis test, calculated on difference values between post and pre-administration measurements. AL = anxiety level; SBP = systolic blood pressure; DBP = diastolic blood pressure; HR = heart rate.

ANXIETY LEVEL

Group	*n*	Average Rank	Different (P<0,05) from Factor nr
(1) Combined stimulation	55	65,23	(2)(3)(4)
(2) Auditory stimulation	55	96,95	(1)(3)(4)
(3) Visual stimulation	55	140,10	(1)(2)
(4) Absence of stimulation	55	139,72	(1)(2)

(a)

SYSTOLIC BLOOD PRESSURE

Group	*n*	Average Rank	Different (P<0,05) from Factor nr
(1) Combined stimulation	55	54,66	(2)(3)(4)
(2) Auditory stimulation	55	81,70	(1)(3)(4)
(3) Visual stimulation	55	155,02	(1)(2)
(4) Absence of stimulation	55	150,62	(1)(2)

(b)

DIASTOLIC BLOOD PRESSURE

Group	*n*	Average Rank	Different (P<0,05) from Factor nr
(1) Combined stimulation	55	59,13	(3)(4)
(2) Auditory stimulation	55	74,17	(3)(4)
(3) Visual stimulation	55	146,58	(1)(2)
(4) Absence of stimulation	55	162,12	(1)(2)

(c)

HEART RATE

Group	*n*	Average Rank	Different (P<0,05) from Factor nr
(1) Combined stimulation	55	65,83	(2)(3)(4)
(2) Auditory stimulation	55	86,83	(1)(3)(4)
(3) Visual stimulation	55	142,01	(1)(2)
(4) Absence of stimulation	55	147,34	(1)(2)

(d)

Tab. 6. Summary table of the Conover-Iman test: (a) AL = anxiety level; (b) SBP = systolic blood pressure; (c) DBP = diastolic blood pressure; (d) HR = heart rate.

Table 6 shows the results of the Conover-Iman test; note that sub tables depict a very similar behavior for all types of data recorded. In particular, groups 1 and 2 seem to significantly differ from all other groups, while groups 3 and 4 do not show statistical differences. The consequences of these findings are better analyzed in the next section.

4. Discussion

In pairwise comparisons of STAI, SBP, and HR (see Table 6a, Table 6b, and Table 6d), post hoc analysis shows that the experimental condition with the combined administration assumes statistically different values compared to the experimental conditions with the administration of a single stimulus and the control condition (absence of stimuli) ($P<0.05$). Conversely, there is no statistically significant difference in values between groups 3 and 4.

In practical terms, considering STAI, SBP, and HR, data say that group 1 statistically differs from groups 2, 3, and 4. This effect can be better appreciated by looking at a specific set of measures; for example, looking at the STAI values, median delta values are -4 for group 1, -2 for group 3, and -1 for groups 2 and 1; we can thus argue that the hypothesis H1 is true and that the combined administration of auditory and visual stimuli (group 1) shows a significant effect in the reduction of the preoperative anxiety level.

The median delta values of SBP and HR present comparable trends; we can thus argue that the hypothesis H2 and H4 are also true and that, again, data support the assumption that a combined administration of auditory and visual stimuli produces a measurable effect.

It is worth noting here that statistical results do not allow to draw any conclusion about the relationship between groups 3 and 4 (they could be different or not); on the other hands, they support the hypothesis that a difference exists between groups 1 and 2 and, ceteribus paribus, between groups 2 and 3.

In summary, experimental results not only confirm the previous authors' findings of music effectiveness in decreasing preoperative anxiety levels [2] [3] but also show that the relaxing effect of the auditory stimulus (relaxing music 60-80 bpm) is amplified by pairing a calming visual stimulus (green light in a range of ~ 520–560 nm). Moreover, while the combined administration (group 1) turns out to be more effective than a simple auditory stimulation (group 2), single visual stimulation (group 3) cannot be considered effective compared to the control group (group 4).

Several factors may have influenced this latter result; for example, the heterogeneity of conditions related to a field experiment and the presence of confounding variables may have played a fundamental role in attenuating the effect of the main visual stimulation. Furthermore, it is worth noting that a difference that does not emerge in the experiment does not imply that such a difference does not exist. However, our interpretation of the results is closely related to the way the experiment was designed, considering the visual signal as an "addition" to the audio signal. Consequently, the use of a single visual stimulation, somewhat orphaned of the audio track, probably induced a perceptual bias that obscured the actual relationship between group 3 and group 4.

Concerning pairwise comparisons of diastolic blood pressure (Table 6c), post hoc analysis shows that the experimental condition with combined administration is yet statistically different from the control condition. However, there is no statistically significant difference in the values between groups 3 and 4 and the values between groups 1 and 2. In other words, measures of DBP do not draw to a full acceptance of hypothesis H3 because the combined administration (group 1) cannot be considered more effective than a simple auditory stimulation (group 2). Hypothesis H3, however, can be partly accepted because significant differences yet emerge between groups 1 and 2 on one side and groups 3 and 4 on the other. From this perspective, the results further confirm the anxiolytic effect of a simple auditory stimulus with respect to the control group.

5. Conclusions

Audio-visual stimulation (AVS) is nowadays considered a promising method of non-drug treatment of functional disorders and in the reduction of pain and anxiety.

However, the way listening to music is accompanied by visual stimulation is a topic largely unexplored and left to the creativity of researchers. This study proposes a novel algorithmic approach for this type of cross-modal stimulation and shows the applicability of the algorithm by implementing a fully functional portable device exploiting a low-cost architectural platform. The effectiveness of the device is demonstrated through the collection and the statistical analysis of psychophysiological parameters strictly related to the state of anxiety.

Experimental results show that the proposed cross-modal stimulation seems to be the most performing solution to reduce anxiety levels, to a greater extent than the other experimental conditions with isolated stimuli or without stimulation. This is a substantial novelty compared to the reference literature, in which the combined administration of auditory (relaxing music) and visual stimuli (calming colors) to reduce preoperative anxiety in adults has poorly been studied.

Physiological parameters such as SBP and HR responded to the treatment in the way we expected; the lowering effect obtained with cross-modal administration was superior to that observed under the other experimental conditions. In contrast, diastolic blood pressure did not completely confirm our hypotheses, as diastolic blood pressure followed a similar trend compared to the systolic blood pressure but statistically not significant.

These encouraging results, in testing the device, should be considered in light of the limitations of the study, which, although designed as a randomized controlled trial, is not a clinical trial. For example, the study was conducted on a selected and homogeneous population, excluding complex patients and pediatric subjects, in whom dental anxiety occurs in a particularly intense form [47]. Some others points have been intentionally neglected; for example a single relaxing piece of music was used, rather than offering a wide selection or allowing patients to use their preferred genre or artist. Moreover, the visual stimulus was always dependent on the music, making somehow controversial the administration of the visual stimulus alone, “orphan” of the original audio piece. Finally, the skills and motivations of the professionals involved in the experiment and the organizational standards of care adopted were very high and hardly comparable to real medical environments. We also have not tested the device in other than the proposed surgical environment, neither compared the strength of the device with respect to other types of cross-modal administration [7] [48] [8]. These aspects will be thus included in future research activities.

In summary, our first goal was to show that the combined administration of relaxing sounds and soothing light stimuli can be performed in accordance with scientific criteria and a reproducible processing of the soundtrack. The result of our study not only confirmed the findings of previous authors on the properties of music in reducing preoperative anxiety levels [2] [3] but also showed that the relaxing effect of the auditory stimulus (relaxing music 60 bpm) is enhanced by pairing it with a calming visual stimulus (green light in the range [520-560 nm]).

Among non-pharmacological interventions, such a device could be a safe option for preoperative anxiety management in adult patients undergoing dental surgery or facing more complex surgical procedures for severe diseases in a hospital context. Furthermore, these experimental results could be of great interest to a large audience of technicians and medical staff, especially in the quest to create increasingly comfortable hospital environments. Hopefully, this study will also set some key milestones in the scientific use of AVS, encouraging the development of new soundtrack processing models, better expressing the potential of cross-modal stimulation, and useful to maximize specific effects, like relaxation or arousal, on patients requiring some help to control stress or anxiety related to medical treatments.

Compliance with ethical standards

The authors have no financial interest in the material used in this study. All experimental protocols were in accordance with the ethical standards of the institutional research committee and in accordance with the Helsinki Declaration.

The experiments involved only healthy subjects in non-invasive procedures. All participants received detailed information and provided written informed consent to participate in the study.

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