Comparison of auditory and visual modalities for EEG-neurofeedback

Teresa Bucho
teresa.bucho@tecnico.ulisboa.pt

Instituto Superior Técnico, Lisboa, Portugal

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Abstract

Neurofeedback (NF) refers to the real-time self-regulation process, during which, using techniques such as electroencephalography (EEG), an individual is presented with a representation of a feature of interest of their own brain activity, so that they can consciously control it. The impact of the sensory modality used as the reinforcement signal representing the extracted features on training effectiveness is yet to be thoroughly assessed and documented. In this thesis, a NF-training system was developed and implemented and a study was conducted to compare the effectiveness of two sensory modalities, visual and auditory, on an EEG-based NF protocol targeting the individual upper-alpha (UA) band and working memory enhancement. Sixteen healthy volunteers were randomly assigned to the Visual or Auditory group, where a radius-varying sphere or a volume-varying sound, respectively, reflected the relative amplitude of UA measured at Cz EEG electrode. Both groups showed significant improvements within training sessions, but no significant improvements regarding working memory. Effects subsequent to NF training were also found beyond the target frequency and scalp location Cz, namely in the lower-alpha and theta bands and in posterior brain regions, respectively. Sample size was small and, thus, further investigation is required to determine if one of the modalities is effectively better. In this work, auditory sensory feedback proved to be as effective as visual, potentiating NF training protocols conducted under mobile conditions, which are possible due to the increasing availability of wireless EEG systems.

Keywords: Neurofeedback, Sensory modality, Individual upper alpha band, Working memory, EEG

1. Introduction

Neurofeedback (NF) refers to the real-time self-regulation process, during which an individual is presented with a representation of a feature of interest of their own brain activity, so that they can consciously control it (Thibault et al., 2016; Biswas and Ray, 2017). During the process, individuals become aware of the variations occurring in their brain activity in real-time and are able to evaluate their progress in order to adapt and achieve optimal performance (Marzbani et al., 2016). The underlying premise of NF is that through operant conditioning training and neuroplasticity mechanisms, an individual is able to control the brain activity in the desired direction, by inducing long-term training effects (Ros et al., 2014). Owing to its appealing properties like its high temporal resolution and portability, the electroencephalography (EEG) is the most studied technique for real-time NF training.

This practice is appealing to those wishing to study therapeutic applications of neural regulation (Thibault et al., 2016), especially considering that, unlike some other methods for influencing brain activity, NF is non-invasive, does not produce any known side-effects and does not prompt dependency on outside sources (Niv, 2013). Enriquez-Geppert et al. (2017) identifies the 3 main areas in which NF is applied: (i) clinical contexts, exploring its potential as a therapeutic tool for psychopathological syndromes that cause deviating brain activity in patients, e.g. attention deficit hyperactivity disorder (ADHD) (Shi et al., 2012; Mayer et al., 2016; Mano et al., 2017), epilepsy (Hurt et al., 2014; Strehl et al., 2014), pain (Martic-Biocina et al., 2017; Hassan et al., 2015); (ii) as a means to peak-performance training (to enhance cognitive performance in healthy participants), e.g. working memory; or (iii) as an instrument to explore the links between oscillations in cognition and behaviour. Upper-alpha (UA), tipically defined as the frequency band from 10 to 12 Hz, has been widely associated with cognitive performance (Klimesch, 1999) and its trainability has been previously assessed in NF studies (Hanslmayr et al., 2005; Zoefel et al., 2011; Nan et al., 2012; Hsueh et al., 2016).

Not all individuals are reasonably capable of regulating their brain activity. However, no clear criteria have been projected to help distinguish learners from non-learners and the assessment of the learning ability varies among studies (Wan et al., 2014; Vernon et al., 2009).

Although NF has proved to be beneficial for several clinical applications, a variety of procedural and theoretical factors remains unclear or smudged by disagreements in current literature (Vernon et al., 2009). One such example is the choice of the sensory modality utilized for the generation of the feedback signal, which is often grounded on practical reasons and participants specific characteristics (Enriquez-Geppert et al., 2017). The chosen feedback modality may be the key factor for a successful training and its influence on different training protocols and on the outcome of NF is yet to be thoroughly assessed and documented (Vernon et al., 2009). In fact, it is not rare that, when NF studies are designed, little care is given to how the elements of the feedback signal might affect the individuals's ability to control brain activity (Stopczynski et al., 2014). Moreover, the type of feedback is oftentimes poorly detailed, which denounces the lack of importance given to this component of NF (Fernández et al., 2016). Typically, NF applications concentrate on mapping the feedback parameter amplitude directly onto audiovisual stimulus components or, when targeted towards children, onto more complex and attractive scenarios (Stopczynski et al., 2014). Few are the studies that have investigated the effects of different feedback sensory modalities on NF training effectiveness. The most frequently explored sensory modality is the visual, although the auditory has also been studied, often in combinations of the two. Fernández et al. (2016) is, to our knowledge, the only study that has compared directly the two modalities, reporting superior results for the latter. Nijboer et al. (2008) and Hinterberger et al. (2004) have also compared the two modalities in brain computer interface (BCI). Both reported superiority of the visual feedback, although learning in the auditory group was still attained.

In recent years, there has been an increase in both the number of portable EEG systems (Krigolson et al., 2017) and in the interest on behalf of researchers in performing EEG recordings outside of the usual constrained laboratory settings (Bateson et al., 2017; Stopczynski et al., 2014; De Vos and Debener, 2014). NF studies conducted under mobile conditions (e.g. Wei et al. (2017)) might face several limitations, one being the constraints imposed by the type of sensory modality. In fact, when comparing the two most studied modalities, the auditory might be considerably more easily displayed under these conditions.

In this thesis, a NF-training system was developed and tested on a group of healthy volunteers, with the goal of comparing the effectiveness of two sensory modalities, visual and auditory, on an EEG-based protocol targeting the UA band and working memory enhancement.

2. Methods

2.1. Equipment and Signal Acquisition

The signal acquisitions took place in the NeuroLab room of the Evolutionary Systems and Biomedical Engineering Lab (LaSEEB), a research lab of Institute for Systems and Robotics (ISR), at Instituto Superior Tcnico (IST). The signals were recorded using the EEG amplifier LiveAmp (Brain Products GmbH, Germany) in the open source software OpenViBE (Inria Rennes, France), with a sampling frequency of 500 Hz, from actiCAP's 32 active electrodes (Brain Products GmbH, Germany) (based on the extended 1010 system): Fp1, Fz, F3, F7, FT9, FC5, FC1, C3, T7, FCz, CP5, CP1, Pz, P3, P7, O1, Oz, O2, P4, P8, TP10, CP6, CP2, Cz, C4, T8, FT10, FC6, FC2, F4, F8 and Fp2. The ground and reference electrodes were located at forehead over the left mastoid (on channel TP9) respectively and circuit impedance was kept below $10\,\mathrm{k}\Omega$, for all the electrodes.

2.2. NF training Protocol

This study targeted the UA band at location Cz, which has been shown to be independently trainable and to be associated with working memory enhancement (Zoefel et al., 2011). Location Cz was chosen as a compromise between posterior predominant alpha activity and frontal memory functions (Rypma and D'Esposito, 1999).

Session Design

Each training session began with a 4 min pre-baseline period, which consisted of alternating 1-minute periods with eyes open (EO) and eyes closed (EC) during which subjects were instructed to stay quiet and passively let their thoughts flow, while focusing their gaze on a white cross on the screen or close their eyes, respectively. This whole period was used to determine the individual alpha band (IAB), the minimum, maximum and threshold values of the feedback parameter during rest and reward threshold (see next sections). Subsequently, the NF training period began. This period was divided into 5 sets composed of 3 blocks each, which, in turn, consisted of 2 1-minute trials. In between blocks there was a pause of 15 seconds and in between trials the pause was 10 seconds long, while between sets the pause was at least 15 seconds long, contributing to a total training time of a minimum of about 37 minutes. In the end, a baseline identical to the first baseline was recorded (pos-baseline). To investigate the relations between motivation, sleepiness, concentration and stress and training performance, each participant filled out a questionnaire after each session (following the work of Esteves (2017)), where a numerical scale was used to assess how often the participant felt each of the aforementioned states/sensations during the session.

Individual UA Measurement

UA was determined individually for each participant, as defended by Klimesch (1999) considering the large inter-individual variability. Its measurement is illustrated in figure 1, in which the power spectral density (PSD) of both EO and EC signals are represented overlaid. PSD was estimated using the Welch method (Welch, 1967), recurring to a built-in command in Matlab (R2016b, MathWorks). A window of a length of 5 seconds was chosen, with an overlap of 10% of the window length and N equal to the size of the window. The spectra were filtered with Savitzky-Golay filter to eliminate excessive oscillations. The frequencies where the two spectra intersect mark the lower transition frequency (LTF) and higher transition frequency (HTF), which defined the lower and upper boundaries of the IAB, respectively. The UA band is then defined as the frequency interval between individual alpha frequency (IAF) and HTF. The measurement of the IAB for each participant was conducted on the pre-baseline signal taken before the first training session and on the pos-baseline of the last session in order to assess NF effects on IAF.

Online Data Pre-Processing

The EEG signal was acquired and processed by OpenViBE (Renard et al., 2010). This software allows the connection with other environments, such as the game development platform Unity (*unity3d.com*), on which the feedback display for both groups was implemented, via the lab streaming layer (LSL) system that allows the synchronization of streaming data for live analysis or recording across applications.

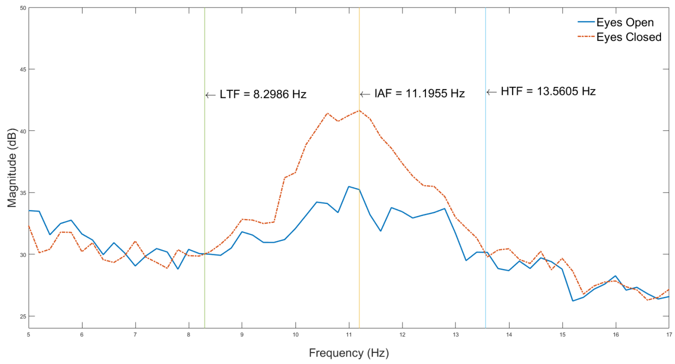

Figure 1: Superimposed spectra of EO and EC signals, illustrating the measurement of the IAB peak, LTF and HTF

The NF protocol focused on the increase of relative amplitude of the upper alpha (RAUA), computed in real-time in OpenViBE. RAUA was defined as in Wan et al. (2014), with adjustments for the UA band. It is calculated as the sum of amplitudes in the UA band divided by the total sum of amplitudes, when considering the signal from 4 to 30 Hz, as follows (1):

$$RAUA = \frac{\sum_{k=IAF}^{HTF} X(k)}{HTF - IAF} / \frac{\sum_{k=4}^{30} X(k)}{30-4} \tag{1}$$

where $X(k)$ is the frequency amplitude spectrum at frequency k, calculated by means of a sliding window fast Fourier transform (FFT). As suggested by Sterman and Egner (2006), using the amplitude spectrum instead of the power spectrum by squaring the magnitudes prevents excessive skewing and increases statistical validity.

In the online processing pipeline implemented in OpenViBE, a 2 s sliding window epoched the signal acquired in the Cz channel, shifting every 0.125 s. On each incoming windows, the spectrum amplitude was obtained by applying the FFT and two subsets of each incoming spectrum corresponding to the two frequency bands, UA and from 4 to 30 Hz, were selected and averaged across all contained frequencies. For smoothing signal fluctuations, a moving average was applied, computing the average over the last 10 epochs received. Finally, these signals were divided so as to compute the RAUA as shown in equation 1. The resulting signal was then forwarded to Unity, via the LSL system, thus provided the user with feedback which was updated every 125 ms according to RAUA in location Cz.

Baseline's signal was also appropriate to define the reward threshold. In the session 1, the threshold was set to be equal to median RAUA values registered during the EO baseline period. In the following sessions, the threshold was updated according to the participant's performance in the previous session. If the percentage of time spent above the threshold in the previous session exceeded 60% then, the new threshold was increased by 5 percentiles with respect to the same EO period in the next session. Additionally, if there was a constant increase, from set to set, of the RAUA, then the threshold was incremented by 10 percentiles. Otherwise, if that percentage was below 40%, the new threshold was decreased by 5 percentiles.

Feedback Display

Both visual and auditory feedback displays were developed in the game-engine platform Unity. The feedback parameter was streamed from OpenViBE to Unity via the LSL system. Pre-baseline RAUA values were also important to determine the values between which the feedback parameter was expected to vary, so as to being able to establish the fixed range values corresponding to the maximum/minimum size of the sphere, in the case of visual feedback, or maximum/minimum volume of the noise/piano in the case of auditory feedback. These were set to correspond to the 1^{th} percentile and 99^{th} percentile plus 20% of its value, respectively of the EO period of the pre-baseline of the first session. The addition of the +20% was introduced so as to avoid the saturation of the sphere/sound on the maximum size/volume. After being normalized according to these values, the feedback parameter was reflected as either the size of a sphere, in case of the visual display, or as the volume of a sound, in case of auditory feedback.

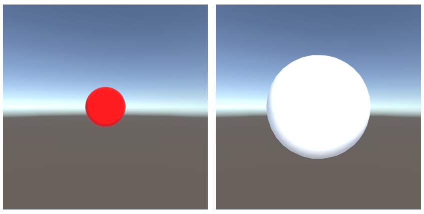

Figure 2: Visual feedback display presented to the participant when RAUA was below (top) and above (bottom) the threshold.

Furthermore, Unity also received markers from OpenViBE, which carried information about the start/end of trials and pauses. Whenever a pause period was reached, the display ceased, such that the participants received no feedback, and resumed when the next marker indicating the beginning of a trial was received.

The feedback displayed to the participants in the VIS group is illustrated in figure 2. It consisted of a size varying sphere set over a simple horizon background. The size of the sphere linearly reflected the feedback parameter (RAUA) collected at electrode location Cz. Additionally, the sphere's color interchanged between red and white, depending on whether the RAUA was below or above the predefined threshold for the session, respectively. Participants were instructed to keep the sphere as large as possible in addition to keeping it white for as long as possible. To avoid rampant fluctuations from very large to very small sizes, which could be counteracting, the sphere's radius varied more slowly, but still linearly, when RAUA was below the feedback parameter then when it was above.

Participants in the AUD group received feedback by means of a sound whose volume was modulated according to the feedback parameter. Participants were asked to keep their eyes open, while focusing the gaze on the screen, which displayed the same horizon background as in the VIS group (figure 2), but no sphere. The perceived loudness of a sound grows as a power function of sound pressure (Banaji, 2001; Stevens, 1957), implying that a subject cannot detect changes in the volume of a sound if it is modulated linearly. Therefore, there was not a linear relationship between the feedback parameter and the sound loudness (figure 3). In fact, the volume of the sound was modified to grow exponentially. In more detail, whenever the feedback parameter was below the predefined threshold, a white noise sound arose and its volume grew exponentially the lower values of the feedback threshold. Otherwise, whenever it was above the threshold, a pi-

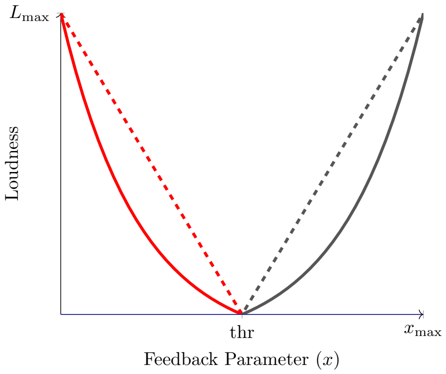

Figure 3: Modulation of Auditory feedback. thr = threshold. Red curves: perceived (dashed) and actual (solid) noise volume. Grey curves: perceived (dashed) and actual (solid) music volume.

ano music appeared with a volume that grew exponentially the higher the feedback parameter, similar to the feedback signal of (Diaz Hernandez et al., 2016). Both sounds, noise and music, were adapted to be volume matched. The piano music consisted of loop of a continuous 30 second long segment with no silent periods.

2.3. Participants

A total of 16 healthy right-handed participants with no previous NF experience, with corrected to normal vision, were randomly assigned to one of two groups: the visual group (VIS) (4 males and 4 females; ages (years): 22.5 ± 2.73) the auditory group (AUD) (3 males and 5 females; ages (years): 22.88 ± 1.25). Participants were asked to complete self-assessment health-related questionnaires (36-Item Short Form Survey (SF-36) and Hospital Anxiety And Depression Scale (HADS)) for screening. Participation was voluntary and no monetary compensation was offered. An informed written consent was obtained from participants after they were duly informed about the entire procedure, objectives, possible side effects and exclusion criteria of the study.

2.4. Design and Experimental Procedure

Both groups were submitted to the same experimental design, as the only difference between them was the feedback sensory modality. This design was inspired by the training design of the INTENSIVE group in the work of Esteves (2017). Training consisted of 4 sessions, on 4 consecutive days, at approximately the same time of the day. In the session 1, participants received all the required information concerning their participation and were asked to sign the informed written consent, fill in the health-related questionnaires (SF-36 and HADS) and complete a set of memory tests (Digit Span and N-back). Subsequently, the NF training session began, as described inDuring this period, participants were asked to remain as still as possible, avoiding body or head movements, and avoid frequent eye blinking during trials, availing of the pauses to do so if necessary. Eye closure or falling asleep were strategies not allowed. The succeeding sessions followed the same training design, except for the health questionnaires and memory tests, which were not performed. In the fourth and last session, after training, participants performed another set of the memory tests.

2.5. Data Analysis

All the components of EEG's processing, from raw EEG's data extraction to data treatment, as well as the statistical analysis, were carried out recurring to built-in functions of Matlab (R2016b, MathWorks) or its toolbox EEGLAB.

Data Quality Assessment

Data quality was assessed with the view of understanding the impact of artifacts on the feedback parameter during online NF. Independent component analsyis (ICA) was performed on segments of data acquired during pilot tests, recurring to the EEGLAB's function, RUNICA. Artifact independent components, mainly those associated with blinking, horizontal eye movements, muscle activity and bad channels, were identified visually by guidance of Chaumon et al. (2015). No considerable impact on the time-course of the feedback parameter was seen and no online artifact correction was applied. Nevertheless, participants were asked to remain still and to avoid abrupt movements. In preliminary results' analysis, variability between baselines from session to session, for the same participant, was observed to some extent. As a result, a choice was made not to normalize the RAUA values in each session by baseline values. An ICA artifact analysis on eyes-open baseline segments was conducted retrospectively, which unveiled some potentially significant differences between original and artifact-corrected RAUA time-course.

Data Extraction and Processing

All the raw data (baseline and training data) was imported to MATLAB, band-pass filtered between 4 and 30 Hz, and then re-reference to average reference. As there was an interest in studying independence and spectral changes subsequent to NF training, Morlet wavelet transform was applied to the raw EEG data, with wavelet factor fixed to 7 (Abreu et al., 2018). A moving average was then applied for smoothing signal fluctuations, as was performed in the online signal processing. The relative amplitude (RA) of each of the following bands were calculated in an equivalent way to that of equation 1, where $X(k)$ corresponds now to the Morlet wavelet transform' frequency amplitude spectrum: Theta: 4Hz to LTF; Lower alpha (LA): LTF to IAF; UA: IAF to HTF; IAB: LTF to HTF; and Beta: HTF to 30 Hz. Although the feedback parameter was computed differently during the online period, where it was computed with FFT, still RAUA variations within the time-course are comparable to the ones computed with the Wavelet transform here described.

Baseline data was then segmented into the EO/EC periods, while training data was segmented and into organized into sets, after removing all the data points corresponding to pause periods.

Training Effect Measures

The training progress was evaluated in terms of the variation of RAUA within and across the training sessions. A set of indexes was also defined with the view of evaluating the training effect, based on the methods employed in similar studies (Wan et al. (2014); Esteves (2017)). These indexes have in consideration the evolution of the training parameter, RAUA, within ($Intra$) and across ($Inter$) sessions. These are:

$IntraA1$ (Equation 2): accounts for variations of the feedback parameter within sessions, by computing, for each session (i), the mean difference between the mean of each set (j) and the mean of the first set, and then averaging across sessions:

$$IntraA1 = \frac{\sum_{i=1}^{nsessions} \sum_{j=2}^{nsets} (\bar{set}_j - \bar{set}_1)_i}{(nsessions)(nsets - 1)} \tag{2}$$

$IntraA2$ (Equation 3): accounts for variations of the feedback parameter within sessions, by computing, for each session (i), the difference between the mean of the last and first sets, relative to the mean of the first, and then averaging across sessions:

$$IntraA2 = \frac{\sum_{i=1}^{nsessions} (\frac{\bar{set}_5 - \bar{set}_1}{\bar{set}_1})_i}{nsessions} \tag{3}$$

$IntraS$ (Equation 4): accounts for variations of the feedback parameter within sessions, by computing, for each session (i), the slope (m_i) of the linear regression that fits the evolution of the learning parameter along the means of all 5 sets in that session, and then averaging across sessions:

$$IntraS = \frac{\sum_{i=1}^{nsessions} m_i}{nsessions} \tag{4}$$

$InterA1$ (Equation 5): accounts for variations of the feedback parameter across sessions, by computing the difference between the mean of the last two sessions and the mean of the first two, relative to the latter:

$$InterA1 = \frac{(\bar{S_4} + \bar{S_5}) - (\bar{S_1} + \bar{S_2})}{\bar{S_1} + \bar{S_2}} \tag{5}$$

$InterA2$ (Equation 6): accounts for variations of the feedback parameter across sessions, by computing, the difference between the means of the last two sets of the last session and the means of the first two sets of the first session, relative to the latter:

$$InterA2 = \frac{(\bar{set}_4 + \bar{set}_5)_{S4} - (\bar{set}_1 + \bar{set}_2)_{S1}}{(\bar{set}_1 + \bar{set}_2)_{S1}} \tag{6}$$

$InterS$ (Equation 7): accounts for variations of the feedback parameter across sessions, by computing the slope (m) of the linear regression that fits the evolution of the learning parameter along the means of all four sessions:

$$InterS = m \tag{7}$$

Identification of Non-Learners

Dempster and Vernon concluded, in the review of 2009, that within sessions measures may be more convenient to search for evidences of learning via NF than across sessions measures. Following these conclusions and based on experimental observations during data analysis, a choice was made to identify non-learners as those individuals for which $IntraS$ was negative.

Independence and Spatial Distribution

To answer the questions (Gruzelier, 2014a)

(1) "Is there band specificity or independence such that only the trained band is influenced?"

(2) "Is there topographical specificity such that the EEG outcome is specific to the training electrode?"

raised by Egner et al. (2004) and by Zoefel et al. (2011) as criteria for validating a NF parameter, and by Egner et al. (2004) and Gruzelier (2014b) as some of the theoretical issues in the practice of NF, the previously defined learning indexes were calculated not only for the targeted band UA and channel (Cz), but also for the theta, LA, IAB and beta bands and for all other recorded channels.

Working Memory Effects

Working memory performance was assessed by two tasks: digit span (forward and reverse) and n-back (2-back and 3-back), implemented in Presentation (Neurobehavioral Systems). Digit span tests consisted of both forward - repeating digits in the same order as they were presented - and reverse - repeating digits in the reverse order from which they were presented - order conditions. The sequences presented start with a short number of digits and increase in size in the following trials, until the maximum list length is reached or until the participant failed to accurately recollect the sequence. In N-back tests, a series of stimuli are presented to the participants, either visually or auditory, and they are required to remember the stimuli that was presented "N" times before. Two sets of N-back tests were conducted (2-back and 3-back).

Statistical Analysis

Sample size was small (8 participants in each group) and normality was not guaranteed for all the variables (assessed with Shapiro-Wilk W-test). As such, a choice was made to rely on the non-parametric tests Wilcoxon Signed Rank and Wilcoxon Rank Sum. Right-tailed tests were employed when there was an expected increase as was the case for RAUA at location Cz. Correlation between variables was assessed with Pearson or Spearman correlation. Multiple comparisons correction (MCC) were required when computing statistical analysis on topographical maps, for which the false discovery rate (FDR) method by Benjamini and Hochberg (Benjamini and Hochberg, 1995) was utilized.

3. Results

3.1. IAF

IAF in the VIS group was significantly different between the pre and pos training baselines (p = 0.031; Wilcoxon Signed Rank). The only significant difference between groups was the IAF in the pre condition (p-value = 0.0163; Wilcoxon Rank Sum). The IAF and HTF were compared with the standard values defining the UA band, 10 and 12 Hz, respectively. Significant difference was found for the pos HTF in the VIS group (p-value = 0.039; Wilcoxon Signed Rank).

3.2. Eyes-Open Baseline

Pre-baseline, pos-baseline and RAUA values registered during NF-training were compared using the Wilcoxon

Signed Rank Test, which yielded significance between pre-baseline and NF training in session 2 ($p = 0.0391$), for the AUD group. Pearson correlation tests between the six learning indexes and mean pre-baseline values resulted in no significant correlations for any of the indexes. Pearson correlation tests between RAUA values during each sessions' pre-baseline and mean RAUA of each session yielded no significant results (VIS: p-value $= 0.155$; AUD: p-value $= 0.657$) and neither did the Spearman correlation tests between pre-baseline values and session number (VIS, AUD: p-value $= 0.917$).

3.3. Training Effect on Target Location

One participant in the VIS group and two in the AUD group were classified as non-learners.

Training Effect on UA

As is clear from figure 4, there is an increasing tendency of RAUA within each session in either group. The median of the first set of each session is usually higher than the median of the first set of the previous session, which suggests a subtle carryover effect from session to session. In the AUD group a slight decrease from fourth to last sets is visible, particularly in the first 3 sessions. The effect of removing the data of the non-learner from the VIS group is reflected mainly in the slope of the third session. Removing the two non-learners from the AUD group brought the medians of the two groups closer together in all sessions.

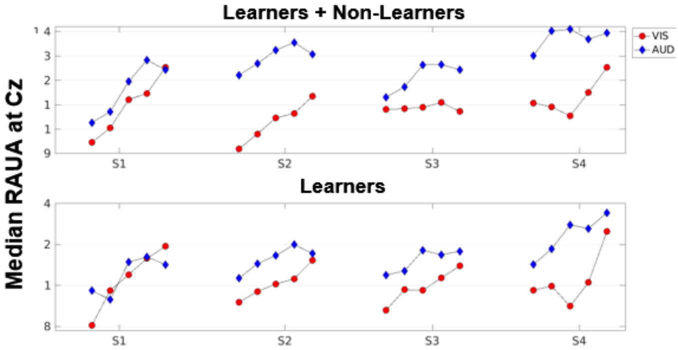

Figure 4: Evolution of the RAUA along the training period for both groups: with (top) and without (bottom) non-learners.

Training Effect on Other Frequency Bands

In figure 5, one can observe how the RA of IAB and its sub-bands have a slight, but increasing tendency along sessions, while the opposite occurs in regards to the theta band and no clear tendency is observed for beta. A similar but more obvious behaviour is seen along sets. No significant Spearman correlations were found between session number and mean RA of the session, for any of the bands. However, significant Spearman correlations were found between set number and mean RA for UA bands in some of the sessions: sessions 1 to 3 in the VIS group and sessions 2 and 4 in the AUD group. Significance was also seen in the VIS group for sessions 1 and 2 (table 1

In table 2 the results of the Wilcoxon Signed Rank test concerning the learning indexes is presented. To be noted that the significant values concern mainly within session indexes ($IntraA1$, $IntraA2$ and $IntraS$), particularly in the theta and UA band and that none of indexes related to the beta band was considered significantly different from zero. No significant changes (Wilcoxon Rank Sum test) were found between groups, regarding these indexes.

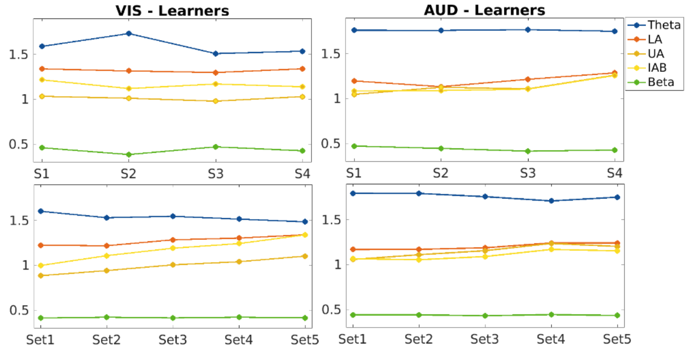

Figure 5: Medians across learners of each group of the mean RA at Cz across sessions (top) and sets (bottom), for the each of the five studied frequency bands.

Spearman correlation tests, computed between the learning indexes of the theta band and the ones of LA, UA and IAB unveiled significant negative correlations between the two bands for all indexes except $IntraA1$ of LA and theta bands (p-value $= 0.057$) and $InterA2$ between UA and theta (p-value $= 0.184$).

3.4. Training Effect on Spectral Topography

Figure 6 is a reflection of the progress of the learners in each group across sessions. Pre and pos conditions refer to the first 2 sets of the session 1 and to the last 2 sets of the fourth and last session 4, respectively. In the VIS group, training lead to a decrease of the RA of the theta band from pre to pos conditions, in central and more posterior regions. Concerning the LA band, an increase is seen, spread over the whole scalp. As for the UA, the increase is more visible in parietal and occipital regions, while beta shows a decrease in right temporal areas. In the AUD group, theta distribution is similar to that of VIS group in both conditions. As for the alpha bands LA presents a rather different distribution from that of the VIS group, since its increase is more localized on central and frontal areas, in addition to occipital. UA's increase is also more localized in occipital areas than in VIS group. As for beta, a decrease is seen in temporal and occipital left regions. Within sessions, in the VIS group, an increase along sets in IAB and its sub-bands is seen, mainly in posterior regions but spreading to central and frontal areas. Theta decreased along the session in central and posterior regions, while beta decreased in temporal regions. In the AUD group, the same pattern is observed, except for LA, which is more centrally/frontally located.

Although uncorrected for multiple comparisons, figure 7 provides an enlightening perspective on the distribution of the channels for which learning indexes were significantly different from zero. In the VIS group, uncorrected significant p-values are seen mainly for theta in central regions and for the alpha bands in central-parietal and occipital regions. Concerning across sessions indexes, $InterA2$ presents significant uncorrected p-values in frontal-central and occipital areas for the alpha bands. After correction, no noticeable significant corrected p-values were found for any of the bands nor indexes, except for some intersperse locations. In relation to the AUD group, with respect to within sessions indexes, similarly to the VIS group, theta

Table 1: p-values resulting from the Spearman correlation (right-sided for UA, two-sided for the other bands) between set number and mean RA of the studied bands, considering only learners. The last two rows refer to the Spearman correlation between set number and median of the sets means across learners and between session number and the median of sessions means across learners, respectively. Significant values (p-value $<$ 0.05) are marked with *.

	VIS - Learners					**AUD - Learners**				
	Theta	LA	UA	IAB	Beta	Theta	LA	UA	IAB	Beta
Session 1	0.233	0.083	**0.008***	**0.02***	0.233	0.133	0.133	0.175	0.133	0.950
Session 2	**0.02***	0.083	**0.008***	0.133	0.783	0.350	0.083	**0.042***	**0.02***	0.350
Session 3	0.517	0.083	**0.042***	0.083	0.350	1	0.083	0.233	0.117	0.950
Session 4	0.350	0.233	0.167	0.133	0.683	0.083	**0.02***	**0.042***	**0.02***	0.350
Med Sets	0.083	0.083	**0.008***	**0.017***	0.450	0.083	0.083	**0.042***	0.133	0.783
Med Sess	0.417	0.917	0.792	0.750	0.417	0.750	0.333	0.167	0.083	0.750

Table 2: p-values resulting from the Wilcoxon Signed Rank test (right-sided for UA; two sided for the other bands) for the learners of AUD and VIS groups. The null hypothesis is that the medians of the learning indexes across subjects for the studied bands are zero at the 5% significance level. Significant values are marked with *.

	VIS - Learners					**AUD - Learners**				
	Theta	LA	UA	IAB	Beta	Theta	LA	UA	IAB	Beta
$IntraA1$	**0.016***	**0.031***	**0.008***	**0.016***	0.156	**0.031***	0.063	**0.02***	0.063	0.844
$IntraA2$	**0.031***	**0.016***	**0.008***	**0.016***	0.156	**0.031***	0.063	**0.02***	**0.031***	0.844
$IntraS$	**0.016***	**0.016***	**0.008***	**0.016***	0.219	**0.031***	0.063	**0.02***	**0.031***	1
$InterA1$	0.469	0.938	0.289	0.934	0.688	0.688	0.219	0.08	0.219	0.156
$InterA2$	0.267	0.078	**0.016***	0.078	0.813	0.219	0.219	**0.047***	0.219	0.563
$InterS$	0.688	0.813	0.148	0.688	0.938	1	0.313	0.313	0.219	0.156

has a greater concentration of significant uncorrected p-values in the regions near the Cz channel, while LA also concentrates in occipital regions. As for UA, the distribution involves more the parietal-occipital areas, in addittion to central leads, while beta did not produce significant values, except p7 for $IntraA1$. Concerning across sessions indexes, the uncorrected p-values concentrate in central ($InterA2$) and occipital areas (all indexes) for UA, in occiptal ($InterA2$) and temporal-central regions (all indexes) for LA and in parietal and occipital areas for beta. The only significant p-values after MCC correction occurred in the UA band, particularly for within session indexes in points in central-parietal regions, but also $InterS$ in occipital areas. No significant differences were found between groups when applying the Wilcoxon Rank Sum test (two-sided), for any of the indexes in any of the bands.

3.5. Working Memory

Concerning the forward digit span test, the VIS group was able to increase their spans, whereas the AUD group was not, as median span decreased. In either case, the difference was not significant. In the reverse test, median spans increased in both groups, but this increase was only significant for the AUD group (p-value = 0.031). No significant differences in pre and pos spans existed between groups, using Wilcoxon Rank Sum test. Concerning the N-back test, improvements in median accuracy for both groups were seen in the 2-back target block, while the same was only verified for the AUD group on the distractor block. Median accuracy in the 3-back test increased for both groups in target block, but only for the AUD group in the distractor block. Concerning reaction times, VIS group's median reaction times decreased for target and distractor blocks of both 2-back and 3-back, whereas for the AUD group, median only decreased for the 2-back distractor block. None of these differences was significant and there were no significant differences between groups either, using Wilcoxon Rank Sum test. There was an increase in the median reaction times from 2-back to 3-back tests, mainly in target blocks.

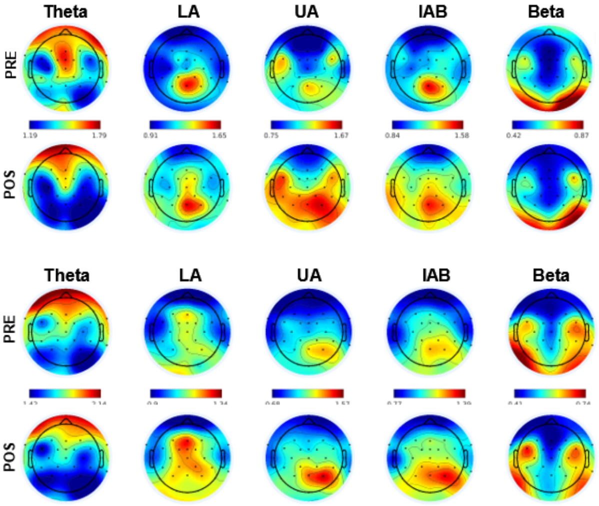

Figure 6: Median relative amplitudes topographies across learners of the VIS (top) and AUD (bottom) groups and for each frequency band. Pre: mean of the first two sets of session 1; Pos: mean of the last two sets of sessions 4. IAB includes both LA and UA.

4. Discussion

A NF-training system was developed and implemented to compare the effectiveness of visual and auditory modalities on a protocol targeting the UA band and working memory enhancement. The protocol was tested on a group of healthy participants, randomly assigned to the Visual or Auditory groups, where a sphere varied in size and sound varied in volume, respectively. Both groups were able to up-regulate their UA at Cz, more significantly within than across sessions.

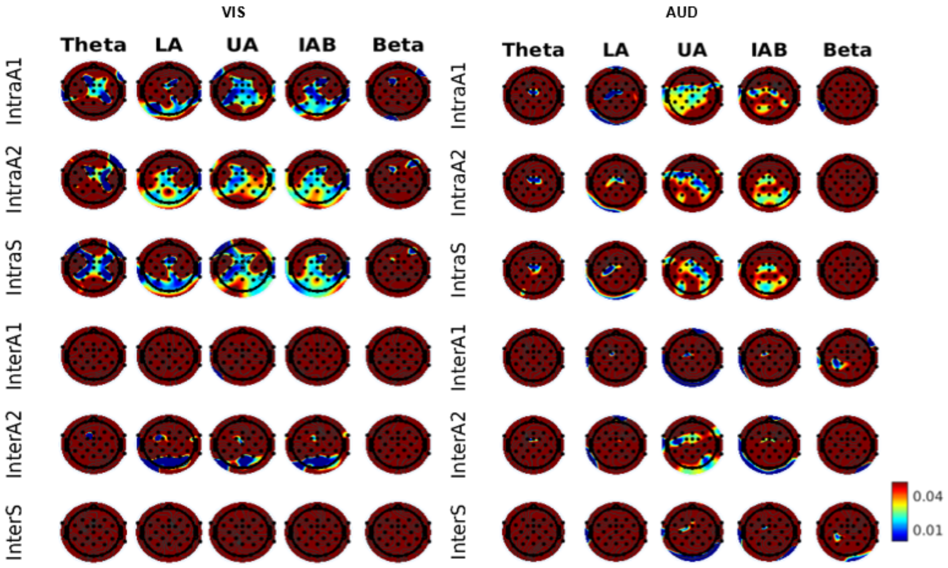

Figure 7: p-values resulting from the two-sided Wilcoxon Signed Rank test (right-sided for UA in location Cz) for the learners of each group uncorrected for multiple comparisons. The null hypothesis is that the medians of the learning indexes across subjects for the studied bands and for each channel are zero at the 5% significance level.

4.1. IAF

As predicted by Klimesch (1999), the results concerning the IAB band revealed inter-individual differences, particularly for the AUD group, whose values distributions comprised a broader range than in the VIS case. By adjusting the UA band frequency for each participant individually, one can argue that sub-optimal training was avoided (Van Boxtel et al., 2012; Zoefel et al., 2011; Hanslmayr et al., 2005), although a repetition of the results using the standard band, from 10-12 Hz, would have been useful to prove that using individually determined UA band indeed improved trainability. It must not be overlooked, however, that manual selection of LTF and HTF was often necessary, given that the crossings between EO and EC spectra were oftentimes not present.

4.2. Eyes-Open Baseline

No baseline enhancement was evident throughout training sessions, as occurred with Nan et al. (2012), but not with Zoefel et al. (2011). Nan et al. (2012) proposes that an intensive and longer training would be required in order to observe enhancement effects on individual alpha amplitude during resting condition. As no significant correlations were found between the pre-baseline values of each session and the corresponding mean RAUA, as well as between the pre-baseline values of the first session and any of the six learning indexes, one can conclude that pre-baseline values were not a predictor of training success, contrary to what Wan et al. (2014) found. Nevertheless, the fact that no artifact correction was performed on baselines must not be disregarded as it could be masking these effects. Relaxation effects during baseline measurements could affect the production of alpha differently to what occurs during training. As such, perhaps an active baseline would constitute a more appropriate condition for comparison with RAUA values during training.

4.3. Training Effect on Target Location

Training Effect on UA

A learning effect was observed for both VIS and AUD groups, as they were able to voluntarily increase their RAUA through NF training, reflected in an overall increasing tendency of the relative amplitude of this band within and across sessions. In fact, the majority of the participants in the two groups had non-negative learning indexes for the UA band in Cz location. There was a more noticeable learning effect within than across sessions, particularly in VIS group. Hanslmayr et al. (2005) and Escolano et al. (2012) also found significant enhancement of UA within the single session both studies conducted, contrary to Cho et al. (2008) and Escolano et al. (2014), where alpha and UA training, respectively, did produce effects along sessions but not within. Zoefel et al. (2011) also found progression of the UA throughout sessions and reported evidences of each training session building upon the training experiences of the previous days. Dekker et al. (2014) found long-term learning effects of the UA along the pre-baselines of each session. A linear increase was found over the first 10 (out of 15) sessions, after which a decreasing trend emerged. Although total training time per session was about 1.5 times lower (3 NF trials x 8 minutes) than in the present study, the results of Dekker et al. may suggest that the number of training sessions (four) was not sufficient for a significant effect to be observed. Importantly, Dekker et al. (2014) found a decreasing pattern from second to third (and last) trial, common to all 15 sessions, which was also hinted by the within session results of AUD group, between fourth and fifth sets. These results suggest that session duration could be reduced in future similar studies as a way to avoid exhaustion and reduced motivation as the upcoming weariness is foreseen, by removing the last set.

About 12.5% of the participants in the VIS group and 25% in the AUD group were non-learners. These percentages fall somewhat below those found in literature for similar protocols and might be indicative that non-learners might have been overlooked. The choice regarding the criterion for selecting learners could have been further sustained, for example, by evidence of learning (positive slope across session) in at least 3 of the 4 sessions.

Training Effect on Other Frequency Bands

Theta band had an opposite evolution to that of the UA band. Besides, participants had mostly negative within session indexes, which were significantly different from zero in both groups, except for IntraA2 in the VIS group. The dichotomy in these results meet the findings of Klimesch in 1999, that theta and alpha bands are related to each other albeit in opposite ways. Moreover, there were significant negative correlations found between the majority of learning indexes of theta and those of IAB and its sub-bands, in either group. Besides, the IntraS learning index for the theta band was only positive for those subjects which were considered UA non-learners, indicating that those which were not capable of increasing UA within sessions were also not capable of decreasing theta. Hanslmayr et al. (2005) suggested possible interactions between these two bands, such that one is capable of inducing changes in the other. In this 2005 study, only about half of UA responders was also considered theta responders.

IAB and LA had a similar increasing behaviour as UA. Not all UA non-learners would be considered LA non-learners. UA and LA reflect different cognitive processes (Klimesch et al., 1993). Dekker et al. (2014) reported different NF outcomes in the two bands: power decreased at the end of each session as well as at the end of the series of sessions, for the UA but not the LA. Zoefel et al. (2011) found that UA was trained completely independently of other frequency bands, since the immediate neighboring bands were not significantly affected during training. Nan et al. (2012) reported changes in bands other than the trained IAB, namely in the UA and LA, which the authors found natural, considering both bands compose the trained band, but also in delta and sigma. In Escolano et al. (2014)'s work, the authors found within sessions increase of upper beta's power and a decrease of LA and theta power, in eyes-open task-related activity and training, while the effects along sessions were positive for the trained parameter (relative UA power in fronto-central sites) in task-related activity and negative for delta power.

Considering the results obtained in present's work, by the criteria defined by (Zoefel et al., 2011), one cannot affirm total independence of UA training. However, it is remarkable that the flanking beta band was not affected and the LA band was only affected in the VIS group but not in the AUD group, suggesting that auditory feedback might promote training independence more than visual feedback.

4.4. Training Effect on Spectral Topography

The results demonstrated that training had greater effects in UA band, particularly in central locations and to some extent in more posterior regions, where alpha activity is usually predominant.

In Van Boxtel et al. (2012)'s study, it was found that alpha NF trained on central sites was associated with increased posterior alpha activity, as was also observed to some degree in both VIS and AUD groups concerning the alpha bands. In Escolano et al. (2014)'s study, across sessions effects were seen, not only in the trained parameter (UA in fronto-central sites), but also in parieto-occipital sites for UA power and in parieto-occipital sites for delta power, during task-related activity. Within sessions, trained parameter decreased, but a relative power increase was seen for upper beta in parieto-occipital sites and also an absolute power decrease in theta and LA, during task-related activity. In Egner et al. (2004)'s investigation, training of theta/alpha ratio in posterior scalp regions was associated with decreased frontal beta band activity. Hanslmayr et al. (2005) found differences UA power before and after UA training in right parieto-occipital areas for responders.

In Fernández et al. (2016)'s work, the feedback location was not fixed, as it corresponded to the lead presenting the highest abnormal ration of the target frequency bands, theta/alpha value. While the auditory group revealed increased frontal alpha' absolute power, in the visual group this increase was observed in frontal and parieto-occipital regions. Additionally, centro-parietal beta increased only for the auditory group. Such extreme alpha topographic differences between groups were not observed in the current work, except for LA in the AUD group, which was apparently more centrally located than posterior, as it was in the VIS group.

4.5. Visual vs. Auditory Feedback

The elements of the feedback display remained unchanged for all participants. To improve trainability, these elements could have been further tailored to each individual participant, for example, by allowing them to choose the preferred colors of the sphere or the sounds. Few are the studies that directly compare visual and auditory feedback modalities. Both Hinterberger et al. (2004) and Nijboer et al. (2008) found superiority of the visual modality with regards to BCI performance, even though learning was still attained with auditory feedback. Competition for attentional resources and possibly distracting "harmonies and melodies" were identified as potential reasons for the reduced auditory performance. A search of the relevant literature revealed only one study, Fernández et al. (2016), where the modalities were compared in NF performance. In this study, the auditory modality proved to be superior to the visual modality. The authors identified the higher contingency of the auditory stimulus, which reaches the brain faster than the visual, as a possible explanation as to why learning in the auditory group was better.

4.6. Working Memory

No significant changes were seen in working memory performance between pre and pos training conditions in either of the tests, except for the AUD group, in the reverse Digit Span. In Nan et al. (2012)'s study, short-term memory, increases in forward and backward digits of the alpha NF group were significantly larger than those of the control group. The authors discarded the possibility of test practice effect, considering the control group also reported improvements, although not significant. This effect does not seem likely in the present work, concerning the Digit Span test initiated with very short sequences (3 in forward, 2 in reverse), which presumably allowed the participants to get accustomed with the task at hand right from the beginning. As for the N-back task, learning effect might have had a higher impact, even though participants had the chance to practice before the actual test in the first set of tests, conducted before training. In the target blocks, there was an increase in the median reaction times and a decrease in accuracy from 2-back to 3-back tests, which is likely due to increasing task difficulty (Meule, 2017). Indeed, participants reported more difficulty in the 3-back task, which might need adjustments in future studies. Significant improvements in cognitive performance after UA training were seen in Hanslmayr et al. (2005), Escolano et al. (2011), Zoefel et al. (2011), Escolano et al. (2013), Escolano et al. (2014) and Kober et al. (2017).

5. Conclusions

A NF-training system was developed and implemented, with the goal of comparing the effectiveness of two sensory modalities, visual and auditory, on a protocol targeting the UA band and working memory enhancement. Sixteen healthy volunteers were randomly assigned to the Visual or Auditory group, where a radius-varying sphere or a volume-varying sound, respectively, reflected the relative amplitude of UA. Participants in both groups were able to up-regulate UA in electrode Cz, more evidently within sessions than across. Effects were seen to some extent in LA and theta bands, but not for the beta frequency band. Moreover, these effects were mostly centrally located, near training location Cz, although posterior effects were also seen. In any case, significant changes were not seen between the two groups and no improvements concerning working memory were reported. Although further investigation is required to determine if one of the modalities is effectively better, considering that the sample size was small, the work presented in this thesis showed that the auditory sensory modality is just as effective as the visual, potentiating NF training protocols conducted under mobile conditions, which are possible due to the increasing availability of wireless EEG system such as LiveAmp.

5.1. Limitations and Future Work

The limitations of this work include sample size, which was too small to ensure sufficient statistical power. Furthermore, no artifact correction was performed in baseline or online signals, which could have had produced a significant impact, specially in the baseline condition, and, therefore, should be taken into consideration in future work. In particular, this should allow the accurate quantification of the baseline and hence the normalization of the EEG parameter during training. No active or no-training control group was implemented to control for repetition related effects or related to the experimental setup itself. A screening session could have been conducted or resting activity could have been used as predictor of the learning ability (Wan et al., 2014) in order to detect non-learners upfront.

Other cognitive processes could have been assessed, in order to determine if training was specific to working memory processes leaving others unchanged (Gruzelier, 2014a). Other valuable analysis to be conducted in the future would be choose more posterior training electrodes (or a combination of them), to include a third training group receiving auditory feedback with eyes closed, to keep track of participants' strategies and/or instruct them on how to achieve optimal strategies, to conduct a follow-up session to assess long-term training effects, to explore if sounds or colors closer to each individual's personal preferences produce more significant effects, and to analyze the patterns of the feedback parameter and/or topographic maps during the pause periods (in between the training trials of a session), the working memory tasks, the eyes-closed baseline periods and transfer trials (participants receive no feedback but are instructed to reproduce the same strategies used during training trials).

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