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Music and Emotion: an EEG connectivity study in patients with disorders of consciousness

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Abstract— **Human emotion perception is a topic of great interest for both cognitive and clinical neuroscience, but its electrophysiological correlates are still poorly understood. The present study is aimed at evaluating if measures of synchronization and indexes based on graph-theory are a tool suitable to study and quantify electrophysiological changes due to emotional stimuli perception. In particular, our study is aimed at evaluating if different EEG connectivity patterns can be induced by pleasant (consonant) or unpleasant (dissonant) music, in a population of healthy subjects, and in patients with severe disorders of consciousness (DOCs), namely vegetative state (VS) patients.**

In the control group, pleasant music induced an increase in network number of connections, compared with the resting condition, while no changes were caused by the unpleasant stimuli. . However, clustering coefficient and path length, two indexes derived from graph theory, able to characterise segregation and integration properties of a network, were not affected by the stimuli, neither pleasant nor unpleasant. In the VS group, changes were found only in those patients with the less severe consciousness impairment, according to the clinical assessment. In these patients a stronger synchronization was found during the unpleasant condition; moreover we observed changes in the network topology, with decreased values of clustering coefficient and path length during both musical stimuli.

Our results show that measures of synchronization can provide new insights into the study of the electrophysiological correlates of emotion perception, indicating that these tools can be used to study patients with DOCs, in whom the issue of objective measures and quantification of the degree of impairment is still an open and unsolved question.

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I. Introduction

Among stimulus paradigms used to explore emotion perception, music is a complex auditory stimulus able to induce a powerful effect on emotions, feelings, and mood states [1] [2].

Music masterpieces usually evoke defined affective states, and consequently are appropriate to analyze the neural correlates of the emotion perception [3] [4]. Moreover music can be used as complex stimulus in order to study responses in patients with severe impairment of consciousness, for which most of the 'communication channels' with external environment are strongly impaired.

Few recent studied [5],[6] on healthy subjects has addressed the issue of quantifying EEG modifications induced by musical stimuli, showing that changes in spectral properties or coherence, mainly in the theta and delta bands, were linked to the different emotional content of the stimulus

To the best of our knowledge, no study have been performed until now to evaluate changes in the global cortical connectivity pattern induced by music. Moreover, despite the large use of musical stimuli in rehabilitation of patients with severe disorders of consciousness (DOCs), no study has addressed the issue of quantifying objectively the effect of different types of stimuli on the brain activity in patient with DOCs.

There is increasing evidence that synchronization of oscillatory brain activity in various frequency bands may be one of the key brain mechanisms during cognitive tasks [7]; in fact most of the brain's cognitive functions are distributed within and across different specialized brain areas that require a coordinated interaction. Therefore, the study of functional and effective connectivity can provide important insight into the neural correlate of emotion perception.

The present study is aimed at evaluating if different EEG connectivity patterns can be induced by two different musical excerpts, in patients with severe DOCs, namely in patients in vegetative state, defined as a condition of wakefulness (the patient spontaneously opens the eyes) but of unawareness (the patient is unconscious or not responsive to the environment) [8], and in a population of healthy controls. The stimuli consisted in a pleasant (consonant) musical piece, and in a modified unpleasant (dissonant) version of the same piece.

The EEG network changes were quantified by means of a multivariate measure of effective connectivity , the Partial Directed Coherence [9]. The network properties were studied using indexes based on graph theory: density,

clustering coefficient and path length; these measures are assumed to be able to characterize different properties of the network topology, corresponding to brain functions, such as integration and segregation.
The main objective of this study was to evaluate whether such a methodology can provide an objective tool able to study and quantify the complex neural correlate of emotion perception, and to evaluate if it can be suitable to study brain activity in patients with DOCs, with the goal of providing objective parameters capable of better characterize the severity of the impairment in these patients.

II. METHODS

A. Subjects and Musical stimuli

The study involved 6 healthy subjects and 5 brain-injured patients with a clinical diagnosis of persistent VS, observed at Coma research Center (CrC) of Besta Foundation, Milan. The severity of impairment was clinically evaluated by a quantitative scale, the Revised Coma Recovery Scale (CRS) which were repeatedly administered by trained neuropsychologists and neurologists.
Subjects were presented with two categories of musical pieces differing in their degree of dissonance. The stimuli were based on previous fMRI and EEG studies [5], [10]: a consonant piece, J. S. Bach: Rejouissance (BWV 1069), used as pleasant stimulus. Dissonant (i.e., unpleasant) stimuli were electronically manipulated counterparts of the consonant excerpts, obtained by playing simultaneously with two pitch-shifted versions of the same excerpt, the pitch-shifted versions being a tri-tone below and one tone above the original pitch (sound samples of the stimuli are available at http://www.stefan-koelsch.de/Music_Emotion1). The two versions were identical in their dynamic outline, their rhythmic structure and tempo, and their melodic contour, and only the difference between consonant and dissonant version can contribute to different neural effect. The order of stimuli presentation was randomly varied between subjects in order to avoid any sequence effect.
The present study was approved by the Ethics Committee of Carlo Besta Neurological Institute Milan, Italy. Written informed consent was obtained from controls or the patients' legal representatives. All patients and controls did not have any professional musical training.

B. EEG recordings and Analysis

EEG and polygraphic channels (EOG, ECG, sub-mental EMG) were recorded in a dimly lit room using Ag/AgCl surface electrodes (impedance <5 kΩ) placed in accordance with the 10-20 International System, and acquired at a sampling rate of 256 Hz using a computerised system (Micromed SpA, Mogliano Veneto,TV, Italy) using the linked ear-lobe as reference. Before the analysis, the EEG epochs were filtered using a digital 1-120 Hz (12 db/octave) band-pass filter followed by a 50 Hz notch filter to suppress the noise of the electrical power line. Moreover, the EEG data were normalised by subtracting the mean value and dividing the result by the standard deviation.
The first half (30 s) EEG section during each musical stimulus was considered for the analysis, and compared with 30 s of artifact-free EEG recorded at resting condition.
The connectivity pattern was thus estimated in three condition, rest-pleasant-unpleasant. For each condition, the EEG signals were divided into 15 non-overlapping 2 sec length epochs. All of the 19 EEG derivations were simultaneously used as inputs for a multivariate autoregressive (MVAR) model, the order of which was determined using the multichannel version of the Akaike (AIC) criterion as a guideline, and fixed at 10; the goodness of the identification was verified by means of a 'portmanteau' chi-squared test.
The MVAR coefficients estimated for each epoch, were then averaged , and the mean PDC spectra was then estimated for each condition. The statistical significance of the non-zero PDC values at each frequency was estimated using a bootstrap approach based on phase randomisation and the Theiler algorithm [12].
All of the data were pre-processed and analysed using a custom-written toolbox in Matlab (Mathworks Inc., Natick, MA, USA), which also contained modified functions from the Biosig toolbox [11].
The Five traditional EEG frequency bands were considered for the study (delta, 1-4 Hz; theta 4-8Hz; alpha 8-13 Hz; beta 13-30; gamma 30-80). For each of these bands, the area under the PDC thresholded curve was considered, in order to obtain the adjacency matrix, and related graphs. A graph is an abstract representation of a network consisting of vertices (the EEG electrodes) and edges (the connection between two vertices).
A graph can be binary, meaning that a connection between vertices either exist or do not exist, or weighted, in which the a certain weight can be assigned to an edge that reflects the strength of the relation between the two vertices . In this study weighted graph were used, considering as weight the PDC area.
The graph can be characterized by different indexes, able to describe the global properties of network. Three indexes were considered : mean density, clustering coefficient and characteristic path length [13].
The mean density represents the average number of connections ingoing and outgoing from each node, divided by the total number of possible connection.

$$k_{in}(i) = \frac{\sum_{j \in V} a_{ij}}{n} \qquad (1)$$

The mean value was obtained averaging the density between all the vertices.
The clustering index Ci of a vertex i is the probability that its neighboring vertices are also connected to each other. The

clustering coefficient C of a graph is the averaged Ci over all vertices.

$$C = \frac{1}{n}\sum_{i\in V} C_i = \frac{1}{n}\sum_{i\in V}\frac{2t_i}{(k_i - 1)} \qquad (2)$$

With t_i number of triangles around a node i.
The characteristic path length L is defined as the average shortest path length between all pairs of nodes in the network

$$L = \frac{1}{n}\sum_{i\in V} L_i \frac{1}{n}\sum_{i\in V}\frac{\left(\sum_{j\in V} d_{ij}\right)_i}{1-n} \qquad (3)$$

It is well know most of the graph parameters are influenced by the average degree, even if the precise kind of relation is not well known (see [14] for a comprehensive overview).
For this reason, the clustering coefficient and the path length were normalized, in each temporal condition, with respect to the average density.
Statistical assessment of difference between the stimuli conditions were calculated by means of the Wilcoxon test..

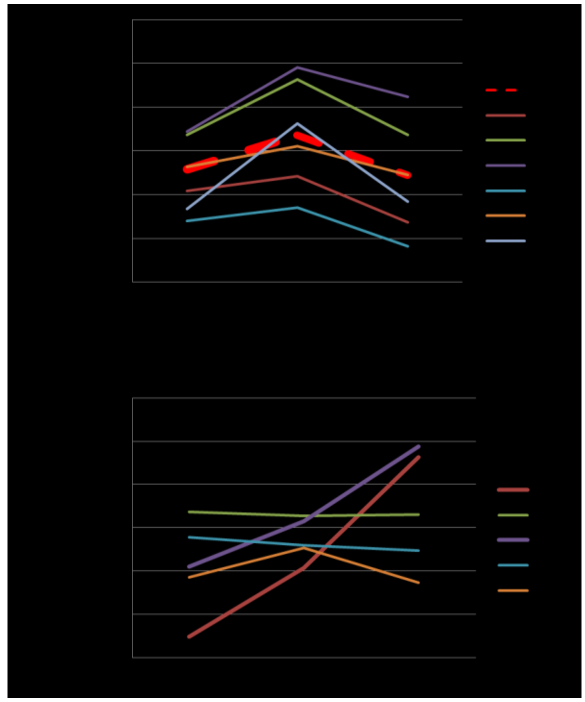

Figure 1. Global density values of the six control subjects (A) and the 5 VS patients (B), during the three stimulus conditions.

III. RESULTS

The global density, calculated for all the subjects during the different stimulus conditions (pleasant, unpleasant and rest) showed differences both in patients and healthy controls, mainly in delta and theta frequency bands. Since the strongest changes was observed in theta band and it is well known that this band is involved in cognitive tasks, the results will be presented for this frequency range only.
As far the healthy subjects, we found that the pleasant musical stimulus was able to induce an increase in the number of connections with respect to the resting condition (pleasant: 0.083±0.01; rest: 0.075±0.008; p=0.02). On the contrary, no changes were detected during the unpleasant condition (unpleasant: 0,072±0,01). (Fig 1 A).
In VS patients, on average, no difference were found between the three condition. In fact we observed two different change patterns. Two out of five patients, namely patients #1 and patient #3, showed clear differences in the mean density degree values induced by the musical stimuli. This two patients were those with the higher value of the CRS index and with a better response to auditory evoked potentials, findings that suggest a less severe impairment of consciousness. However, in these patients the changes induced by the musical stimuli were opposite to those of the controls, namely no changes between the resting and the pleasant conditions, and an increase of connectivity during the unpleasant stimulus. In the three remaining patients the two musical stimuli did not change the density values (Fig. 1 B).

According to these findings, we further characterized the topological changes of the networks in the two patients who showed a response to the stimuli, by means of the clustering coefficient and path length indexes.
Fig 2 showed the normalized clustering coefficient (A) and path length (B). Interestingly we found that, once the influence of the network degree has been removed, the controls group did not present, on average, any changes in the three conditions. On the contrary, the two patients had a similar pattern, characterized by a path length and a clustering coefficient value strongly higher that the controls during resting condition. These values decreased during the musical stimuli, reaching the minimum in the unpleasant condition.

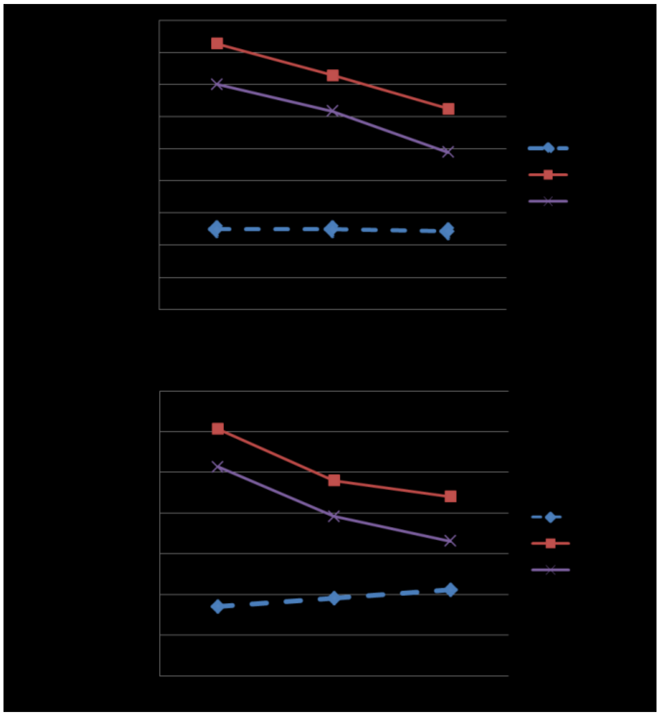

Figure 2. Comparison of Path length (A) and Clustering coefficient (B) between average controls (dotted line) and the two VS patients responding to the stimuli.

IV. CONCLUSION

This study was aimed at evaluating whether a methodology based on synchronization measures and indexes derived from graph theory can capture the neural correlate of emotion perception, as induced by musical stimuli, and to evaluate if it can be suitable to characterize the severity of impairment in patients with DOCs

In healthy subjects, we observed an increase of synchronization, as indicated by higher mean density values, in delta and theta bands during pleasant musical excerpts with respect to unpleasant music and rest. Previous studies [5],[6] reported a significant increase of theta power during listening to pleasant music and suggested that the activity in this band may have a role in emotion processing. Our data further support this finding, and also suggest that during listening to pleasant music there is an increase in connectivity, and thus in information flow and integration, among cortical regions.

As far the VS group, we did not find any changes induces by music, neither pleasant nor unpleasant, in three patients with the most severe brain damage, as described by the CRS scale; in the remaining two patients we found an increased connectivity elicited only by dissonant music. Contrarily to the controls, the VS showed changes in the network topology, as described by clustering coefficient and path length indexes, in both pleasant and unpleasant condition. This suggest that, even in the absence of changes in the mean degree, a rearrangement of the network topology can took place in response to this kind of stimuli.

The very limited number of patients make our results very preliminary and does not make possible any interpretation of these findings; from a pure speculative point of view we could hypothesize that strong emotional stimuli can elicited, in patients with severe brain damage, different brain responses with respect to those observed in controls. Further studies are needed to better characterize these differences, possibly involving other forms of DOCs.

Our results indicated that advanced signal processing techniques can detect changes in synchronization and in network topology during emotional music listening, both in controls and in patients with DOCs and therefore they appear to be appropriate methods to understand the circuitry/system rearrangement associated with DOCs.

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