DATA MINING AND THE FUNCTIONAL RELATIONSHIP BETWEEN HEART RATE VARIABILITY AND EMOTIONAL PROCESSING

Comparative Analyses, Validation and Application

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Abstract: Aims of the study are to 1-classify emotional responses in healthy and conscious brain injured subjects by Data Mining analysis of subjective reports and Heart Rate Variability (HRV), 2-compare different procedures for reliability, and 3-test applicability in patients with disordered consciousness (vegetative state). We measured HRV of 26 healthy and 16 posttraumatic subjects listening music samples selected by emotions they evoke. Each subject was interviewed and the reported emotions were used for identifing a model assessing the most probable emotion by the HRV parameters. Two macro-categories were defined: positive and negative emotions. The study matched a three-phases strategy. First, we applied several classification approaches to healthy subjects evaluating them through suitable validation techniques. Secondly, the best performing classifiers were used to forecast emotions of posttraumatic patients, without retraining. In the 3rd phase we used the most reliable decision model both for validation (1st phase) and independent test (2nd phase) in order to classify the "emotional" response of 9 subjects in vegetative state. One HRV parameter (normalized Low-Frequency Band Power) proved sufficient to forecast a reliable classification. Accuracy was greater than 70% on training, validation and test. Model represents an objective criterion to investigate possible emotional responses also in unconscious patients.

1 INTRODUCTION

Data mining techniques are used in medicine to sort significant information out of large databases in mutagenicity studies, predictive toxicology, disease classification, selective integration of multiple biological databases, etc. Application in neurology has focused on early prediction of outcome (Herskovits and Joan, 2003; Chen et al, 2008) or on the characterization of brain processing in healthy subjects and patients with disorders of consciousness (Dolce et al, 2008b; Riganello et al, 2008). Heart Rate Variability (HRV) is an emerging objective measure of the continuous interplay between the sympathetic and parasympathetic autonomic nervous sub-systems (Task Force of European Society of Cardiology and the North American Society of Pacing and Electrophysiology of Circulation, 1996); it is thought to provide information also on complex patterns of brain activation (Dolce et al, 2008a; Riganello et al, 2008; Appelhans and Luecken, 2006;). HRV abnormalities are reportedly common in psychiatric or brain damaged patients (Keren et al 2005, Cohen 2000, Draper, 2007); HRV proved a useful predictor of outcome in brain injured patients (Briswas et al, 2000; Wijnien et al, 2006); HRV spectral parameters proved able to classify the emotional responses to complex stimuli in a preliminary study on healthy subjects (Riganello, 2008).

HRV studies require quantitative approaches and large numbers of parameters are generated when the parametric and non-parametric HRV spectra are computed, in contrast with the unconsolidated knowledge of the problem and the lack of models based on physiology. In this connection, conventional statistics based on *a priori* requirements about the data distribution could generate biased results (Abt, 1981, 1983).

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In this study we compare different classification learning strategies through suitable validation techniques, such as 10folds-cross and leave-one-out validation and test on independent data set, in order to select the most reliable model to characterize and classify by HRV the emotional responses to complex stimuli. To this end, we analyzed data generated in different studies on the emotional response to music of healthy controls, conscious posttraumatic subjects and patients in vegetative state.

2 MATERIALS AND METHODS

2.1 Subjects

Three selected groups of subjects were studied:

1-twenty six healthy volunteers (14 women; mean age: 31.7±7.1 yrs., age range: 21-45 yrs.) with high-school to university education);

2-sixteen patients with no residual severe disabilities completing rehabilitation after severe traumatic brain injury (5 women; mean age: 21.6±3.0 yrs., age range: 17 to 33 yrs., grammar to high school education);

3-nine subjects (3 women; mean age: 32.5±7.4 yrs., age range: 16 to 48 yrs., grammar to High School education) in persistent vegetative state unambiguously diagnosed compliant to the international criteria as being awake, but unaware of self and environment, with no purposeful movement or behavior and no indication of processing of external sensory inputs (Dolce and Sazbon, 2002; Jennett, 2002; Giacino et al, 2002; Laureys and Boly, 2007).

None of controls or posttraumatic patients had received formal musical training. Controls, brain injured patients and the caregivers of subjects in vegetative state were informed in full detail about the study purposes and experimental procedures and the ethical principles of the Declaration of Helsinki (1964) by the World Medical Association concerning human experimentation were followed.

The procedures for data collection and the experimental setting caused no physical or emotional discomfort and the staff carrying on the experiments were instructed to discontinue stimulation and data recording whenever a subject complained or appeared to be tired or in distress.

2.2 Stimulus Conditions

Four music samples were selected following characterization by intrinsic structure and expected emotional response as indicated by the available formal complexity and dynamics descriptors. These descriptors reportedly relate music structure to self-assessed emotions and allow characterize the emotional status along a continuum from euphoria and well-being to melancholy, severe anxiety and perceived aggressive tendencies (Imberty, 1997; Tarasti, E., 1994; Nikki, 2004; Urakawa and Yokoyama, 2005) (Table 1).

Table 1: Selected music samples.

L. Boccherini: Quintet op. 11 n. 5, *Minuetto*
P.I. Tchaïkovski: 6th symphony., op. 74, *first movement*
M.P. Mussorgsky: *St. John's Night on the Bald Mountain*
E. Grieg: Peer Gynt, op 23, *The morning*

Experiments on patients and control took place at the same time of the day in a familiar environment and did not interfere with the posttraumatic patients or vegetative state subjects' rehabilitation schedule or medical/paramedical care.

Subjects were comfortably lying on an armchair, with constant 24º C ambient temperature and in absence of transient noises. They were exposed binaurally (earplugs) to the four selected music samples balanced for loudness and played in random sequence to minimize carryon effects. There was a 20-min rest between consecutive samples to avoid over-stimulation and excessive fatigue; for this purpose, the subjects in vegetative state were exposed to two music samples per day only.

At the end of each music sample, controls and posttraumatic patients were requested to report and subjectively classify their emotions, without reference to any pre-selected categories and irrespective of the emotional feeling they thought the music was intended to induce.

The distribution of the emotions expressed for each music sample was determined (Imberty, 1997; Tarasti, E., 1994). Methods are described in detail elsewhere (Riganello, 2008) where the authors have preliminary studied relationship between HRV Analysis and emotions during music listening in healthy subjects and traumatic brain injured patients. In present study authors have studied the possibility to apply the approach to the evaluation of emotional conditions of patients in vegetative state.

2.3 Heart Rate Variability

The heart beat was recorded from the beginning of the music sample and for a total of 300 beats (3',36"±24", with 83.7± 9.5 beats/min and a resulting total recording time between 3',12" and 3':55") by means of the *Virtual Energy Tester* (*Elamaya Instruments*, Milano, Italy).

The photopletismographic sensors were positioned on the third phalange of the left hand middle finger in order to minimize the subjects' discomfort consistent with the guidelines of the Task Force of European Society of Cardiology and the North American Society of Pacing and Electrophysiology (1996).

The photopletismographic signal was sampled at 100 samples/sec; the series of consecutive intervals between heart beats was analyzed in the time and frequency domains by the *HRV advanced analysis software* developed at the Department of Applied Physics, University of Kuopio, Finland (Niskanen et al, 2004). The non-parametric (Fast Fourier Transform, Welch spectrum) and parametric (autoregressive) spectra were computed (Table 2). The power spectral density from 0.01 Hz to 0.5 Hz was computed with 0.001 Hz resolution and three frequency ranges (very low frequency [VLF]: 0.01-0.04 Hz; low frequency [LF]: 0.04-0.15 Hz; and high frequency [HF]: 0.15 Hz – 0.5 Hz) were considered. A total of 35 spectral parameters were obtained from each one of each subject/patient's four recordings (Table 2).

Table 2: Clinical parameters from HRV Analysis.

Statistical Parameters	Spectral Parameters
- Mean RR interval (Mean RR) and SD (STD RR); - Mean Heart Rate (Mean HR) and SD (STD HR); - Root mean square of SD (RMSSD); - number (NN50) and percentage (pNN50) of NN intervals longer than 50 ms	- Very Low, Low and High Frequency (VLF, LF and HF), and normalized unit (nu) in FFT and autoregressive spectra - VLF, LF and HF Peak frequency in FFT and autoregressive spectra - Power Spectrum of VLF, LF, HF and Total in FFT and autoregressive spectra - % of VLF, LF, HF in FFT and autoregressive spectra - LF/HF, nuLF, nuHF, nuLF/HF in FFT and autoregressive spectra

2.4 Study Design and Data Mining Processing

The relationship between HRV and emotional response was studied in a classification task, in which every instance was represented by the subject's HRV parameters related to each music sample listening. Formulating any hypothesis about a specific relationship between heart activity (measured through HRV analysis) and reported emotions was as difficult as selecting a-priori a unique learning strategy. For such reasons we applied several classification learning procedures, such as the Decision Trees, Support Vector Machines, Rule Learners and Artificial Neural Networks all available in the open source software WEKA (Waikato Environment for Knowledge Analysis) (Witten and Eibe, 2005; Eibe, 2004).

The class label for each instance was defined by the emotions self-reported by healthy controls and traumatic brain injured patients after passive listening to each music sample. As a further step, the reported emotions were clustered into two major categories: *positive* (happiness, joy, serenity, calm, etc.) or *negative* (fear, anxiety, tension, etc.). Data Mining task was designed in three consecutive phases. In Phase 1, the most reliable classification approaches outlining a relationship between the HRV spectral parameters and the subjectively reported emotions was selected by using the healthy control group as the *training set*. Such a set included 104 instances (26 healthy subjects x 4 music samples, with 45 instances labeled as "positive emotion") and 35 attributes (the HRV parameters listed in Table 2).

The reliability of each classification method was estimated by the most suitable validation techniques (10 folds-cross and leave-one-out validation). The Classification Rule Learner (ONE-R) (Holte, 1993) and an Artificial Neural Network (Multi Layer Perceptron (Jain et al, 1996)) proved the most performing approaches at the end of Phase 1 and were entered in the study Phase 2, in which an independent test set (the traumatic brain injured patients' group) was processed without performing any algorithm retraining. Purpose of this strategy was to evaluate the model capability of correctly classifying the emotional status for new unseen data.

The independent test set included 64 instances (16 posttraumatic subjects x 4 music samples, with 25 instances labeled as "positive emotion") and the same 35 HRV parameters. In Phase 3, we applied the decision model proving reliable on both phase 1 and 2 (notably, only the ONE-R model) to classify the emotional status of patients in vegetative state listening the same music samples, only using HRV parameters selected as relevant descriptors in phase 1 and 2. The study design is summarized in Figure 1.

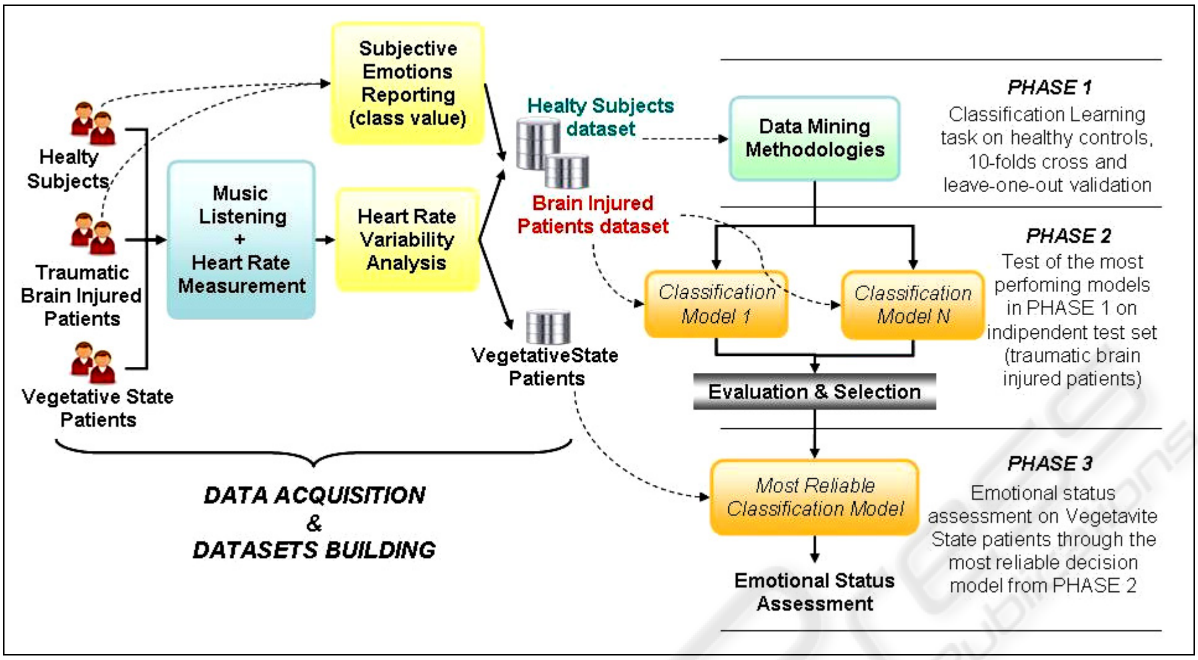

Figure 1: Outline of the study design.

Table 3: Range of nuLF for classifying emotional status.

1	2	3	4	5
[0; 29.5]	[29.5; 46.35]	[46.35;64.25]	[64.25; 72.45]	[72.15; 100]

2.5 Data Mining Procedures

ONE-R is a Classification Rule Learner that accepts a training set as input and searches for "1-rule" classifying instances on the basis of a single variable (attribute). Initially, the algorithm ranks attributes according to the training set error rate. If the attribute is numerical, the algorithm divides the range of possible values into several disjoint intervals, each one associated to a class value. In order to avoid over-fitting (i.e. intervals including only one instance belonging to one class), ONE-R allows set a parameter (the "bucket-size") that is the minimum number of instances in each interval.

We have obtained the best performing configuration for ONE-R by setting up 7 for such a learning parameter. The rule extracted from the healthy controls' group (Table 3) is characterized by five ranges of nuLF (note that nu_LF computed for each listening can belong to only one interval, so only one prediction is possible).

Multi Layer Perceptron (MLP) is a specific Artificial Neural Network (ANN) architecture also known as "feed forward architecture". It comprises at the least three different layers: input, hidden and output layers. Generally, the hidden layer can be greater than one and the number of neurons into hidden layers can also vary, where a neuron is the net "simple" processing unit. As any ANN, MLP is a mathematical/computational model based on biological neuronal networks and is commonly applied to model complex input/output relationships or to identify data patterns of distribution/ correlation. Structurally, an ANN is composed by a set of neurons linked together by a large number of (usually nonlinear) weighted connections. Each neuron is able to calculate a specific function, given the inputs and the weights on the connections are adjusted in order to minimize some criteria as the errors number. By using MLP we have obtained the best results by setting up the following net parameters: only one hidden layer with 5 neurons, Learning Rate=0.2, Momentum=0.1 and 1000 training epochs. Moreover we have previously ranked the variables by preprocessing the dataset through ONE-R WEKA Filter, which evaluates the worth of an attribute by using the ONE-R strategy. Finally, the best results for MLP were obtained selecting the first 8 ranked attributes (nu_LF, powerHF, STDRR, gender, powerVLF, peakVLF, peakLF and peakHF). The MLP architecture is showed in Figure 2.

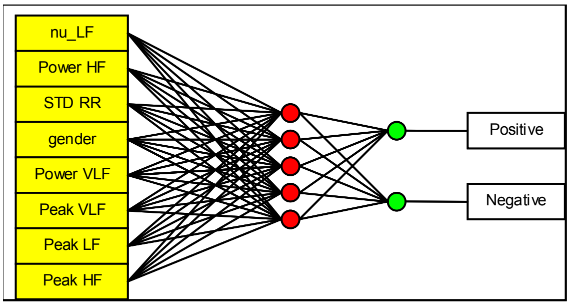

Figure 2: Multi Layer Perceptron architecture.

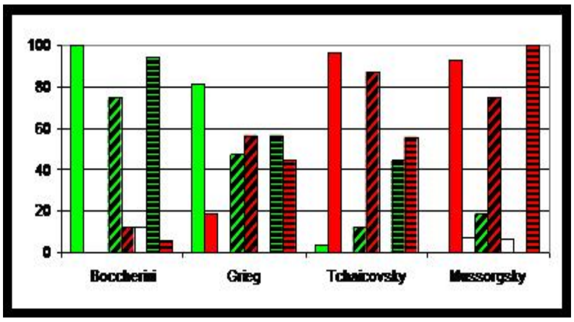

Figure 3: Distribution of self-reported emotion (positive-green, negative-red) in healthy and brain injured subject (oblique strips). In patients in vegetative state (horizontal stripes) the emotion has been extracted by Data Mining procedures (ONE-R).

3 RESULTS

Controls and posttraumatic subjects reported a variety of emotions in response to the music samples they listened to, ranging from happiness to rage and fear. The reported emotions clustered in seven categories (indifference, bother, rage, fear, sad, serenity and joy) and could be successively categorized as being "*positive*", "*negative*". In particular in the healty subjects Boccherini and Grieg induced emotions for which the positive label was applicable(100% and 81.5% respectively), as well as negative emotion were associated to Tchaicovsky and Mussorsky music's (96.3% and 92.6 respectively). Similarly, in posttraumatic subjects Boccerini induced positive emotion in the 75% of subjects while Tchaicovsky and Mussorsky' music's induced negative emotions in the 87.5% and 75% of subjects respectively. By contrast Grieg's music induced ambiguous results with 46.8% and 56.2% of positive and negative emotions respectively (figure 3). The distributions of reported emotions differed significantly across music samples (Log-likehood radio: 258.8, p<0.001), but not between patients and controls (Log-likehood radio: 2.318, p>0.05). Heart Rate increases in response to Mussorgsky and Tchaicovsky music's in 63.5% of subjects, while decreases in response to Boccherini and Grieg music's in 61.5% of subjects (ANOVA computed on HRV: F=5.074, p=0.026; homogeneity of variance p=0.4). For the posttraumatic patients, significant differences were not observed for the heart rate variation. For patients in vegetative state the heart rate trend of variation were towards decreases with Boccherini's (-1.85 ±3.9 beat/m) and toward increases with Mussorgscky Tchaicovsky and Grieg's music samples (2.9 ±7.3beat/m, 1.7±4.5, and 0.85±4.4 bea/m respetively).

With Data Mining procedures the best results were obtained by the algorithm ONE-R, that sorted out the *nu_LF* HRV spectral descriptor as the significant HRV parameter in the selected experimental conditions and for the study purpose. The algorithm allowed the best trade-off between the portion of correct sample/label association on training set (recognition) and the portion of correct sample/label association both on internal validation and an independent test set (generalization). ONE-R accuracy was 76.0% for the healthy controls' group (tenfold cross-validation: 70.2%; leave-one-out validation: 71.1%), with 69% and 81% correct classification by HRV of the emotions subjectively reported as positive or negative, respectively. Comparable accuracy estimates were obtained when the ONE-R learned model was applied to the traumatic brain injured patients' group, with 70.3% correct assessments (65% and 74% assessments of positive and negative emotions, respectively). Despite the greater accuracy of the MLP approach on the training set (82.7% vs. 76.0%, with MLP and ONE-R respectively), MLP accuracy has decreased to 50% on internal validation, with 51,6% correct attributions of the emotion relative to injured patients (Table 3). The ONE-R algorithm performed better than MLP when clustering emotions into the *negative* and *positive* classes. In this, the algorithm provides an understandable and user-friendly rule applicable in the classification of emotional conditions (Figure 2). Results comparable to (or worse then) those obtained by MLP were also observed when other classification learning approaches were used, such as Decision Trees and Support Vector Machines (personal, unpublished data).

Table 4: Accuracy, Sensitivity and Specificity on training, validation and independent test.

	Training	10Folds-cross	Leave-one-out	Independent Test
All data: ONE-R vs MLP				
OneR	75.96%	70.19%	71.15%	70.31%
MLP	82.69%	47.11%	46.15%	51.56%
Attribution of positive emotions				
OneR	68.89%	57.78%	64.44%	68.00%
MLP	68.89%	33.33%	26.67%	32.00%
Attribution of negative emotions				
OneR	81.36%	79.66%	76.27%	71.79%
MLP	93.22%	57.63%	61.02%	64.10%

The ONE-R model classified the “emotional” responses of the subjects in vegetative state by nu_LF, in the absence of any subjective classification. The results were comparable (figure 3). Boccherini’s music was attributed to the class of positive emotions in 94.4% of cases (self-classified as positive in 92.3% and 75.0% by healthy and posttraumatic subjects, respectively). The ONE-R model attributed Thcaicovsky and Mussorgsky’s music to the negative emotions class in 55.6% and 100% of cases (controls and posttraumatic patients allocated these music samples to the negative class in 96.3% and 87.5% of cases for Tchaicovsky listening, as well as 92.6% and 75.0% of cases for Mussorgsky listening respectively). Grieg’s music was classified as positive by the ONE-R model in 44.4% of cases (81.5% and 43.8% for healthy controls and posttraumatic patients, respectively).

4 COMMENTS

Data Mining techniques offer operational advantages when large datasets are analyzed, as may be the case in medicine (van Bemmel and Munsen, 1997; Robert et al, 2004; Lee et al, 2005). No underlying data distribution is requested as is conventional statistics; the variables are automatically transformed in the computational process; applicability to multivariate non-linear problems and identification of interrelationship between predictor variables are high. On the other hand, generalization is crucial when using Data Mining algorithm: full control of over-fitting requires an extensive computation, a large sample size and suitable validation techniques.

Every Data Mining approaches uses a peculiar structure to code the knowledge intrinsic to the dataset; for such reason, comparing different approaches – as in this study – may be a pragmatic strategy to extract the most reliable model applicable to new databases. In this study, the Data Mining approaches succesfully identified condition-related HRV spectral descriptors (notably the nu_LF measure) by which responses to different music samples may be classified in conscious subjects (healthy controls and posttraumatic patients) as well as in subjects with severe disorders of consciousness and no indication of sensory processing (Riganello et al, 2008; Appelhans and Luecken, 2006). When the reported subjective emotions were classified into two macro-categories, classification by ONE-R proved able to identify a “simple” relationship with good classification performance, both on training and internal validation on healthy controls. Comparable reliability has been obtained by applying (without any algorithm retraining) the learned ONE-R decision model on traumatic brain injured patients. These findings indicate that a single HRV descriptor is able to characterize the subjects’ emotional status or response. The information extracted by means of the simple “if…then” rule (ONE-R) from the healthy controls’ group was validated in the posttraumatic patients independent group. Another relevant advantage of ONE-R is that it provides a model *easy-to-understand*, while MLP is affected by the Block Box effect. The HRV approach allows to investigate brain responsiveness by non-invasive data recording techniques and widespread application in medicine, e.g. in the functional monitoring of subjects in vegetative state. A possible extension to the approach is the implementation of software tools for the HRV functional monitoring in patients whose brain processing may be relevant for diagnostic or prognostic purposes (Herskovits, 2003; Chen, 2008; Dolce, 2008b).

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