Fourth LACCEI International Latin American and Caribbean Conference for Engineering and Technology (LACCET'2006)
"Breaking Frontiers and Barriers in Engineering: Education, Research and Practice"21-23 June 2006, Mayagüez, Puerto Rico

Analyzing a psychiatric domain using KDSM methodology

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ABSTRACT

A KDSM methodology for analyzing repeated very short-serial measures in a psychiatric ill-structured domain is introduced. This methodology is based on a combination of clustering based on rules with some Inductive Learning (Artificial Intelligence) and clustering (Statistics) techniques. This proposal focuses on results obtained on a real application of this kind of data, where common statistical analysis (time series analysis, multivariate…) and artificial intelligence techniques (knowledge based methods, inductive learning) of such data are often inadequate because of the intrinsic characteristics of those domains.

Categories and Subject Descriptors

[**Data mining in medicine**]: Design of a methodology for knowledge discovery in domains where repeated very short-serial measures are presented.

General Terms

Measurement, Design.

Keywords

Knowledge Discovery, Repated Serial Measures, ill-structured domains.

1. INTRODUCTION

A great quantity of medical information is obtained from domains without structure and when it would be necessary to make a decision about what is good knowledge and what is not is a very difficult problem. These kind of domains are included in what is named by Gibert1 as ill-structured domains (ISD). Some of their features are: *heterogeneous data*, *additional knowledge of the domain*, and *partial and non-homogeneous knowledge*.

The application presented here fits on the definition of an ISD. Moreover, it presents some additional particularities such as some repeated serial measures. Therefore, finding a consistent methodology to handle them, extracting useful information from them, and being able to find profiles in this kind of data is the goal of this work.

The structure of the paper is as follows: Firstly, an explanation of the application domain will be found in section **2**. Section **3**, introduces the material and methods. In section **4** the problem is introduced. In section **5** the methodology to solve the problem is introduced. Section **6** give important results of the KDSM application to this domain. Finally, section **7** draws some important conclusions about this work and points to various directions for future work.

2. APPLICATION DOMAIN

Electroconvulsive therapy (ECT) is a complex procedure in which several electroshocks (ES) are applied. In each electroshock, an electrical current through the brain is applied in order to induce an adequate seizure (convulsion) necessary for a therapeutic response. Nevertheless, the biological processes that take place in the brain related to its efficacy are still unknown. The standard practice of selecting electrical stimulus parameters and monitoring the multiple responses of each patient optimises the therapy, but the neuropsychological effects of ECT are still criticised and are the reason behind much of the anti-ECT feelings2. Several aspects of cerebral functioning may be affected by ECT, such as orientation, attention, calculation, recall and memory3. Cognitive functioning generally returns to normal six months after treatment, but some patients complain that they never regain their previous memory at all 2.

Until now, psychiatrists have treated ECT (the set of all the ES applied to a single patient over the treatment period) as a whole, analysing its neuropsychological and psychophysiological effect before and after the entire therapy.

Many studies have focused on the physiological response to electroshock (ES), such as heart rate, blood pressure, electrocardiographic effects, cardiac enzymes, electroencephalographic effects, and hormonal response. These studies have all been important in understanding the ECT processes, such as the seizure threshold, or vagal and adrenergic response; and on the technical advances of the application. Many of these processes are related to each ES and not with a global therapy (ECT). The monolithic entity "ECT" was valid in relation to the therapeutic efficacy but not for its cognitive effects3. As a consequence of this, cognitive impairment should also be studied as an individual effect of each ES.

The present study shows the psychophysiological effects of Electroconvulsive Bilateral ECT after each ES. In order to achieve this, we made repeated measures of simple and choice time reaction tests (visual and auditory) in 13 patients. However, to date, a formal technique to analyse psychopsysiological effects of ES does not exist and there have only been a few studies on the effects of ECT on psychophysiological parameters, such as the reaction times (RT) directly related with memory loss3. The reaction time is understood as the period of time between a stimulus and some kind of reaction observed on the patient. The effects of ECT on both visual and auditory reaction times were studied (Figure 1).

The study analysed repeated very short serial measures of different types of reaction times following the application of ES, formal profiles and the identification of the attributes which have a direct influence on them (and, in consequence, on the cognitive state of the patient), as well as the establishment of a methodology for these kind of domains.

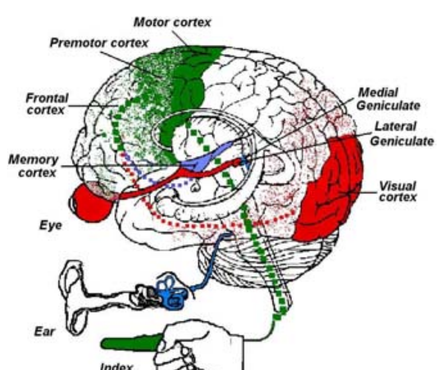

Figure 1. The brain's pathways and its cortical areas.

3. MATERIAL AND METHODS

3.1 Subjects

The subjects were 13 inpatients from Bellvitge Hospital. Patients were selected according to DSM-IV criteria for a major depressive disorder, a schizoaffective disorder or schizophrenia. All patients agreed, by means of a written consent form, to participate in the study and to receive ECT. Only 11 completed treatment, because one patient had an incomplete baseline psychophysiological assessment and treatment; was stopped on another patient following agitation after the second and third ES.

The average age was 47.3 years old (23 - 82 years). There were 6 men and 7 women. In the Study, 5 patients (38.5 %) did not finish primary education (<8 years of schooling); 6 (46.2 %) had primary education (8-12 years of schooling); and 2 (15.4 %) completed secondary school education (>12 years of schooling). Also, 6 patients had DSM-IV criteria for schizophrenia; 6 for major depression; and 1 for a schizoaffective depressive disorder. The mean duration of illness (affective or schizophrenia) was 120 months (1-402 months), the average number of episodes of illness was 4.85 (1-12 episodes) and the duration of an episode was 128 days (19-390 days). On admission, all patients, schizophrenic or affective, showed a severe psychopathology, 23.8 (15-41) measured by HAM-D17 (Hamilton Rating Scale for Depression), and 51.2 (25-75) measured by BPRS (Brief Psychiatric Rating Scale). The majority of the patients showed normal results in somatic anamnesis and exploration, routine haematologic and biochemical tests, chest X-ray and ECG. There was no presence of previous alcohol, drug abuse or dependence disorders, but 7 patients were smokers.

No further serious illnesses were present such as a neurological, gastroenterical, cardiovascular or pulmonary disease, endocrine dysfunction, vitamin deficiency, or abnormal serology. One patient suffered from asymptomatic asthma and one from asymptomatic hepatitis B. The average risk level for anaesthesia (ASA) was 2 (1-3). Five patients had received ECT (2-8 years previously).

3.2 Treatments

A total of 86 electroshocks from the 11 patients in the study were examined. Electrical stimulations were administered three times a week during the first week, and twice a week thereafter. A square-wave, brief pulse stimulus device (Thymatron DGx device, Somatics Inc, Lake Bluff, Illinois) was used, following medication with intravenous thiopental sodium (1.5 mg per kilogram of body weight) and intravenous succinylcoline (0.5 mg per kilogram). All subjects were given 100% oxygen through a mask. The standard bifrontotemporal (bilateral) placement of electrodes was used for all the patients. Electrical stimulations were adjusted according to the age of the patients (5% of total energy (25,2 mC) to 100% (504.0 mC)) so as to produce an adequate seizure and then monitored by two prefrontal-mastoid channels (right and left) of EEG (Dualgraph two channel monitor-recorder Thymatron DGx). Seizure time, seizure energy index, postictal suppression index and seizure concordance index were measured. The average number of ES was 7.23 (5-12) and the mean total energy applied throughout therapy to each patient was 1776 mC (630 –5090 mC). Continuous oxygen saturations were monitored from the patient's index finger using an Engström Eos portable pulse.

3.3 Psychophysiological measures

A Vienna Reaction Unit II (RG- version 7.00)4 was used to determine the reaction time. Stimuli are presented via a panel fitted with a red lamp and a yellow lamp (wavelength: 635 and 585 nm) and an audio tone with a frequency of 2400 Hz. For reaction input a push button is provided below the two lamps. The rest button below the reaction button is a touch button, which is sensitive to contact.

This set-up allows for the application of different sets of stimuli to measure the reaction time (median) using the Sternberg paradigm5: Simple auditory reaction time was recorded in response to a simple auditory stimulus (tone) shown at irregular intervals (S6) and simple visual reaction time was recorded in response to a visual stimulus (yellow light), also shown at irregular intervals (S5).

Visual reaction and categorization time was recorded, in response to the association of visual signals (yellow and red light), which were randomly presented at irregular intervals among other irrelevant signals (S7). Visual and auditory reaction-categorization time was recorded, in response to the association of one visual signal (yellow light) and one auditory signal (tone), which were also presented randomly among other irrelevant, associated or not, signals (S8) (Figure 1). In every test, 32 stimuli were presented. All stimuli lasted 1 second at intervals of 1 to 1.5 seconds. The studied variable was the median of reaction-time (milliseconds). The number of correct reactions were also studied. The test was run several times; after an initial learning step, the day before the first ECT (baseline) at 10AM, 12AM, 02PM, 08PM and at 10AM (next day) and then following each treatment at intervals of 2, 4, 6, 12 and 24 hours post-ES. These times intervals were aleatory, given that there are no previous studies focusing on the global cognitive impairment, only studies analysing orientation and memory in the initial 2 hours post-ES.

3.4 Procedure

Except for Lorazepam, of which 3 mg was allowed per day, all psychotropic drugs were stopped at least 5 days before electroconvulsive therapy and were not prescribed again until 1 week after the therapy was completed. Smoking was also avoided 12 hours before each ES. The measures were recorded before the onset of ECT and after each ES.

4. PROBLEM

The representation of a series of patients (i_1 .. i_n) in which ni occurrences of a given event *E* (electroshock) take place at different time points (E_1…E_n) is shown in Figure 2. Connected to each electroshock occurrence, there exists an attribute of interest *Y* (RT) which affects the behaviour of the patient.

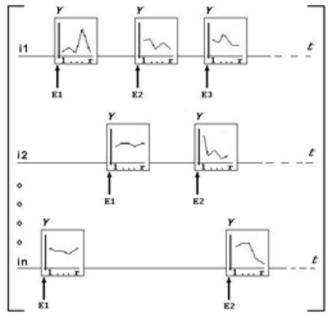

Figure 2. Patients (i_1 .. i_n) and electroshocks (events E)

Hence, a certain small number of measures of Y is taken for each patient and for each occurrence of electroshock (*E*). In this particular case, such a number is fixed (*r*) for all the occurrences of *E* and the time points where *Y* will be measured are also fixed. This measure is performed during the first 24 hours after the application of each ES, in particular after 2h, 4h, 6h, 8h, 12h, and 24h. Measuring this attribute is of special interest for the study of the side effects resulting from a ECT.

Such a scenario generates information structured by two matrices:

— The matrix X contains a set of quantitative or qualitative characteristics X1…XK for each patient.

— The matrix Y contains a sequence of measures of RT at all the fixed time points for each occurrence of E.

It should be specified that the measures points are the same with respect to the occurrence time of all the electroshocks for all patients.

The measures of RT may be graphically represented by very short curves (r is too small) apparently independent among them. In fact, each patient is independent of the others. As a consequence, the amount of events and the instant at which they occur may differ from patient to patient with no other underlying pattern. Nonetheless, all the events which occurred on the same patient are affected by his/her characteristics which result in all the measures relative to a single patient being under this common influence from the patient.

Therefore, in the matrix Y, a single patient may be acts as a blocking factor, defining packets of curves which are not independent between them at all. A block is thus constituted by all the measures which follow any occurrence of each electroshock on the same patient. The number of measures is the same after each electroshock and the measures are equally distributed along time, considering the electroshock occurrence as the starting time point. In particular, a set of repeated very short serial measures with a blocking factor is going to be analyzed.

The purpose of this research is to find the characteristics of the patients, among X1…XK which are related to the temporal evolution of the RT. This is not a trivial situation, because of the features relative to the patient are represented by a single row in matrix X, and the measures of RT placed at random in the time line are represented in certain rows of the matrix Y. So, first of all it is necessary to look for a way of manipulating matrices X and Y together.

Such situations are not exceptional in the medical field, and they have been a subject of formal study in other fields. In the context of temporal series, a method commonly used in such cases is either the reduction of each block of series to a single series which summarizes the whole set, either using the mean at every time point (thick line, see Figure 3), or the reduction of every series to small set of independent indicators such a mean area or a mean tendency per series6. This would allow the measures of RT to be reduced to a single row for each patient, and the matrices X and Y would become compatible and would enable a classical analysis. However, in a number of cases if the average measures for each patient is built, too much relevant information (Figure 3) will often be lost since variability depends both on each event and individual effect. Using such a transformation, the conclusions from the study may be very far from reality. Nevertheless, this mean can give an idea of a patient's general evolution trend, which will be useful afterwords. In fact, there is a significant change from patient to patient curves, and from test to test. So, it is difficult to find a general pattern from specific patient curves.

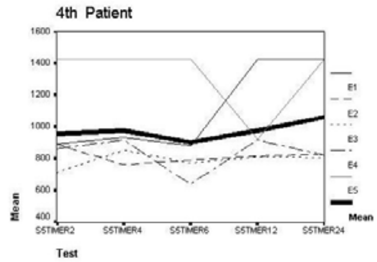

Figure 3. Curves of test S5 from 4th patient.

Figure 3 shows lines joining the reaction times on a simple visual test (S5) measured at 2, 4, 6, 12 and 24 hours after every ES applied to the 4th patient. This patient receives an ECT of 5 electroshocks and each curve represents his/her RT evolution.

Furthermore, there is no standard quantity of ES to be applied to a patient. Thus, reducing patient's information to only one record in the database is not the proper way to proceed. Therefore there is an interest in maintaining all the curves of all the patients in the same database, but taking into account this patient effect for the analysis.

5. KDSM METHODOLOGY

Next, a first approach of the methodology is presented and it will be described, in Section 6, on the basis of a certain experience with a concrete real application.

1. Extraction of a baseline matrix Y0 from matrix Y (serial measures).
2. Hierarchical clustering of the patients using Y0.
3. Use of attributes of patients features to interpret the classes obtained.
4. Rules induction from comparison between classes and patients features attributes.
5. Construction of a matrix of differences D for measuring the effect of a given ES occurrence.
6. Clustering Based on Rules of matrix D with a knowledge base KB (rules induced in step 4).
7. Interpretation of resulting classes.

All details of KDSM methodology can be found in Rodas et. al.8

6. RESULTS

According to the considerations exposed in Section 4, determining if there are different patterns on reaction time curves and their relationship with the characteristics of patients has great interest. In addition, it has been justified that matrices X and Y are not directly mergeable. So, the analysis will be done by the steps presented in Section 5.

6.1 Baseline Reaction Time measures analysis

We analysed the baseline reaction time in all categories: simple auditory (S6) and visual (S5) reaction time, visual reaction and categorization time (S7), visual and auditory reaction and categorization time (S8). These baselines were very heterogeneous and were first of all classified by means of a hierarchical clustering. The clustering technique clearly indicates the initial varying conditions of the patients (Figure 4). By studying the distribution of the other variables in each class, the factor of Age is extremely relevant (Figure 5). This result indicates that young and elderly patients have different responses on reaction times. The influence of age on the Reaction Time has been considered in literature3.

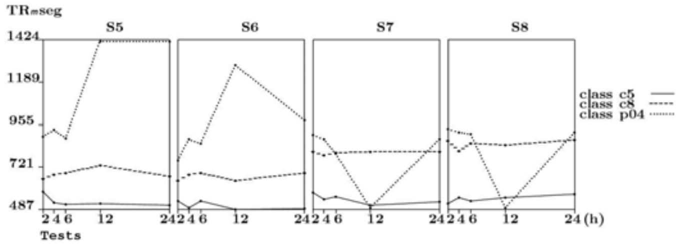

Figure 4. Three classes curves for tests S5 to S8.

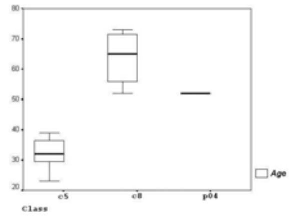

Figure 5. Multiple Boxplot of Age.

6.2 Effects of electroshocks

Initially, the curves corresponding to each patient show no uniform association with the application of ES (Figure 3), but rather a great variation between patient, ES and reaction time was found. However, by controlling the age variable, based on the baseline curves, and dividing the patients into young and elderly, the differences were considerably reduced.

Therefore, in order to study the effect of each ES on the reaction time, a new database with the reaction time differences was obtained with the new curves now representing the differences between post-ES and pre-ES. The analysis suggests four classes of curves (Figure 6). In two of these classes the differences between before and after ES are positive, one of young patients and the other of elderly patients. This means that the reaction times are slower after the ES, and would therefore be considered bad reactions. We have called those classes cy48 (Young increase) and cm33 (Elderly increase). The other two classes correspond to those patients with faster reaction times after ES. The differences between before and after ES are negative, in other words, they are good reactions. We have called those classes cy50 (Young decrease) and cm31 (Elderly decrease).

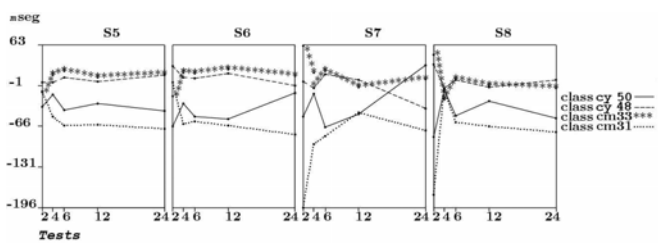

Figure 6. Four class curves for tests S5 to S8.

For each patient, elderly or young, the psychophysiological response after some ES applications was slower whereas after other sessions of ES, the psychophysiological response was faster. Furthermore, faster responses were associated with fewer errors for simple reaction times but not for complex reaction times.

7. CONCLUSION AND FUTURE WORK

Based on the real life application mentioned before, the KDSM methodology was designed. It allows one to discover new knowledge using repeated serial measures on a set of patients.

Application of KDSM to the measurements on ECT provided very satisfactory results, from a psychiatric point of view. It has been seen that the curves of RT on each patient, are not inherent to the patient, nor to the global observation of all the therapy. On the contrary, every patient may react in a different way in each ES session. In view of these results, experts think that this is due to some causes either external or internal to the patient but which can be or not present in each ES session. For the moment, these causes are not well identified, though there already are some hypotheses with which the psychiatrists are starting to work. This is clearly new knowledge in the area of psychiatry that has modified the way how research is carried out in this field. This work is in progress at present.

With the results obtained, one is able to say that it is possible to efficiently handle this kind of information by our KDSM methodology which has allowed the identification of knowledge which is novel, useful, and relevant in the area of the application, according to the classic requirements of KDD7.

As a future work, it is interesting to see the kind of relation between others patients' variables and the last classification. The next step will be the establishment of a definitive methodology for solving the problem formulated in Section 4.

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