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# Management and Evolutionary Analysis from Behavioral and Cognitive Measures

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In this paper we present the basis of a tool for managing and assessing the evolution of subjects (patients) with central nervous systems alterations. This tool takes into account behavioral data, combined with neurophysiological measures obtained from a specific hardware designed to capture evoked potentials. Evoked potentials are used to measure electrical brain activity in response to visual, auditory or somatosensory stimulus. The stimuli, which are sent to the brain through each of these senses, evoke minute electrical signals that can be interpreted. These neurophysiological measures have been used in countless cases, but it is necessary to implement formal- based software capable of providing the therapist storage and management methods of these signals, taking into consideration behavioral data, fused as an efficient way of obtaining a knowledge base for decision making. Particularly, in this paper we emphasize the use of a certain type of cognitive component (P300) as a neurophysiological measure to assess, objectively (analyzing its evolution over time), the effectiveness of clinical treatments designed to improve impulsivity and lack of concentration in ADHD subjects (Attention Deficit/Hyperactivity Disorder).

*Key words:* Cognitive measures, evoked potentials, neurophysiological measures, health informatics, density-based averaging.

*Gestión y Análisis Evolutivo a partir de Medidas Cognitivas y Comportamentales*. En este artículo se presentan las bases de una herramienta para la gestión y evaluación de pacientes con alteraciones en el sistema nervioso central. Esta herramienta tiene en cuenta datos comportamentales, combinados con medidas neurofisiológicas obtenidas a partir de un hardware específico, diseñado para la captura de potenciales evocados. Los potenciales evocados se utilizan para medir la actividad eléctrica cerebral que se genera como respuesta a estímulos visuales, auditivos o somatosensoriales. El estímulo, que es enviado al cerebro a través de estos sentidos, evoca señales eléctricas que pueden ser interpretadas. Estas medidas neurofisiológicas se pueden utilizar en numerosos casos, aunque es necesario implementar una herramienta software basada en métodos formales y capaz de proporcionar al terapeuta mecanismos de almacenamiento y de gestión de las señales, tomando además en consideración medidas subjetivas, fusionándolas de una forma eficiente como forma de obtener una base de conocimiento para la toma de decisiones. En particular, en este artículo enfatizamos el uso de un cierto tipo de componente cognitivo (el P300) como medida neurofisiológica útil para evaluar, de forma objetiva (analizando su evolución a lo largo del tiempo), la efectividad de un tratamiento clínico diseñado para mejorar la impulsividad y la falta de concentración de sujetos TDAH (Trastorno por Déficit de Atención e Hiperactividad).

*Palabras clave:* Medidas cognitivas, potenciales evocados, medidas neurofisiológicas, informática médica, media basada en densidad.

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In this paper, our main goal is the design of a web-based tool for managing and analyzing the evolution of subjects with alterations in the central nervous system.

This tool is powered by clinical, contextual data and neurophysiological measures that are obtained from a specific hardware designed to obtain evoked potentials.

As an example of target population, we propose an application domain focused on patients who show the well-known Attention Deficit/Hyperactivity Disorder. This disorder is a common condition in childhood with neurobehavioral pathology that causes in the subject attentional alterations, impulsivity and motor over activity, symptoms that have significant implications in their development skills, learning ability and social adjustment (Barkley, 2006).

From the approximation of Cognitive Neuroscience, researchers have studied its relation to the Executive Control Network, with the possibility to planning-training sessions so as to carry out an intervention and get cognitive behavioral improvements in this population. By performing programmed cognitive tasks, it has been demonstrated that the subjects experienced a qualitative improvement in their attention capability (Tang & Posner, 2009). However, this improvement is discernible only from a behavioral point of view. With the idea of assessing the effectiveness of this type of training with physiological measures, we have designed a web-based tool for editing, managing and analyzing heterogeneous data, making special emphasis on managing neurophysiological signals (evoked potentials) over time as a mechanism through which an evolutionary study of these subjects can be carried out.

Clinical evidence shows that the combination of these different kinds of information into a structured visual representation significantly helps the experts in the assessing process. Centered in this fact, expert and formal knowledge has guided the development of the tool. Formal aspects are based in the proposal presented in Angelov & Yager (2013), where the authors introduced a new data-fusion operator that consists of an averaging method weighted by the density of each evoked signal.

The remained of the paper is organized as follow. In Section 2 we present, briefly, the main concepts of evoked potentials, the P300 component, and its relationship with the Attention Deficit/Hyperactivity Disorder, the fundamental basis of our proposal. Technical aspects of hardware/software are presented in Section 3. Section 4 is focused in the main software uses, presenting the formal aspect of the tool, based on a density-based operator. Finally, Section 5 presents the summary and main conclusions of the paper.

## *Evoked potentials, the P300 component, and ADHD*

One of the main issues in psychology is the human cognition, and for its study, this discipline has used different techniques (Quevedo-Blasco et al., 2016;

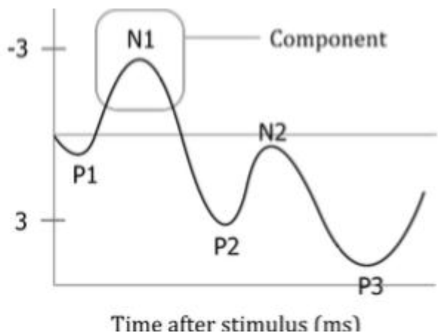
Sternberg, 2015). We want to make emphasis on a specific technique that has been widely used: evoked potentials (EP) (Kutas & Dale, 1997; Sirvent-Blasco et al., 2012).

EPs are fluctuations in the electroencephalograms voltage (EEG) caused by sensorial, motor or cognitive events. It has been observed that, after the presentation of a certain type of stimulus or after the performance of a particular task, there are constant changes in the EEG (Chiapa, 1989). These changes take the form of peaks or valleys and they can inform us about the underlying cognitive processes.

In our case, the function includes portions of the recorded brain electrical activity, sensitive to a specific experimental manipulation that is considered as a response of a particular process, or group of processes, which we call components. These components will be the main focus when studying our software tool, in special the

P300 (or simply P3) component (see figure 1).

*Figure 1*. Evoked potential components




It is especially important to use the cognitive component (or wave) called P300 which is an element with an established pattern that usually appears, at about 300 ms, to unexpected stimuli that are relevant to the task to be performed by the subject. Its amplitude is modulated by the degree of expectation that the subject shows to a certain stimulus. The P300 is considered as an index of working memory in which the amplitude tells us about the allocation of attentional resources, and its latency is a measure of stimulus evaluation time.

The main features of this component are: it often appears with unexpected stimuli that are relevant to the task to be performed by the subject; its latency varies depending on the difficulty of the task and its amplitude is modulated by the degree of expectation that the subject has from a particular stimulus.

There are previous data in literature that show that the P300 component can be used as an objective measure or index of the clinical effectiveness of methylphenidate (Jonkman et al., 1997). So, having a tool that helps the therapist to keep track of their patients (visualizing the changes in latitude and amplitude of P300) in order to test the clinical effectiveness of drug treatment in some cognitive disorders (impulsivity, lack of concentration, etc.) can be very helpful.

As a target population, it is proposed an application domain focused on patients who show the Attention Deficit/Hyperactivity Disorder (ADHD).

Cognitive impairment is sometimes correlated to changes in the P300 component; the waveform can sometimes be used as a measure of several treatments effective- ness in neurocognitive rehabilitation. Moreover, it has been suggested to be used as a clinical marker. There is a wide range of uses for the P300 component in scientific research, ranging from the study of depression (Hansenne et al., 2000) to anxiety disorders (Boudarene & Timsit-Berthier, 1997), Alzheimer disease (Howe et al., 2014; Polikar et al., 2008) and also, it has been proposed its use in brain-computer interface (Iscan & Dokur, 2014; Jin et al., 2012; Mayaud et al., 2013).

As already mentioned, we are interested in using the evolution of this component in the study of ADHD as it can be related to a variety of cognitive activities such as selective attention, orienting response, probability of stimulus and decision making. The common element in these activities is the active processing in relation to the subject of the information provided by the stimulus. The amplitude of the P300 is not affected by the physical properties such as modality or intensity, but it is highly psychologically influenced by variables such as frequency of occurrence of the target stimulus, the task difficulty, the inter-stimulus interval and the distribution of care resources. Moreover, the P300 latency is considered to be a measure of the evaluation time of the stimulus received by the subject, which indicates the timing of mental events before the answer is selected or produced. If latency is prolonged, the time spent in processing the information is greater (Sangal & Sangal, 2006).

*Technical aspects of hardware/software*

The different condition, physical and contextual, of patients justifies the need of providing multiple sources of signals to provide experts with the needed information to make decisions. These signals can be processed online to control devices or can be stored for a posterior intelligent analysis phase. The hardware system used in the experiments has been designed as a non-invasive brain-computer interface (Shalk et al., 2004). Usually, the used system showed an important lack of flexibility, as there are no tools to store and compare brain signals along the time dimension, essential in the evolutionary analysis of patients.

The system designed to monitoring the signals was built using a customized EP device to capture evoked potentials with an auditory and visual stimulator system component. This hardware measures the voltages between electrodes placed in head positions, which have been specially selected for each kind of study. These signals, which result from neural activity, are greatly attenuated by different tissues that separate the point where they have been originated from that where the potential is measured, reducing them to a few microvolts. However, and with the aim of build and hardware-independent application, the software tool accepts as an input a signal generated with different devices as a float-based array.

The web application is entirely done using a free-set of languages designed for dynamic web development, accessing to a centered database using the appropriate techniques to obtain that is known as Rich Internet Application (RIA) (Abolfazli et al., 2014). This application consists of two distinct modules: (1) the management system of subjects and (2) the graphical editor for signal processing.

The subject management system implements all the management functions required by the application: add/remove/modify subjects in the system, insert/remove tests, subject and graphics search, statistics visualization, etc. Therapists that make use of the application must firstly ask the system administration for a login and a password.

The most important part of the application is the graphical editor, which shows the graphs of evoked potentials that is where the therapist may interact with graphical components, improving the evolutionary analysis and monitoring of tests conducted over time. These graphical components are updated in the database in an asynchronous way, allowing the therapist to continue working while the system, automatically, updates changes to the database.

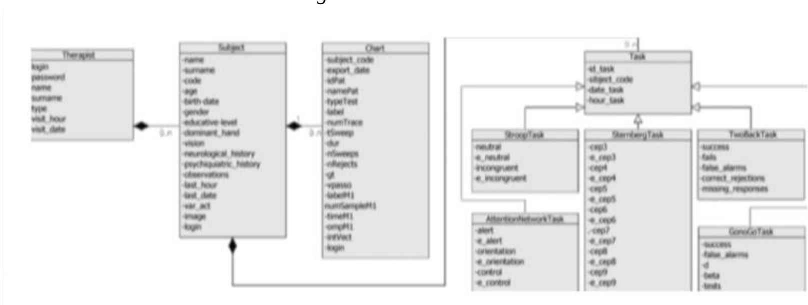
This part of the application is implemented by using the library JSX Graph (Dynamic mathematics tool). JSX Graph is a multi-platform library for interactive geometry, function graphing and efficient data display in web browsers. It uses SVG (Scalable Vector Graphics), VML (Vector Markup Language) and canvas (HTML5). With these software technologies, the application is accessible from any computer (or mobile device) that has a standard web browser, regardless of its geographical localization.

The application has been designed centered in a database structure, which constitutes the core of the tool. Basically, the key entities of the database are: Therapist, Subject, Chart and Task. Briefly, the system allows storing data related to subjects that have received care from a particular therapist; it can be a neuropsychologist of neurophysiologist professional, or an interdisciplinary team with both professional profiles.

For each subject, in addition to storing the personal data and other clinical information of interest, the software enables the recording of the results obtained in different sessions of EP capture (see figure 2). The main goal is that the evolution of the patients gets to be assessed objectively, showing any improvement after the administration of a rehabilitation therapy.

Alternatively, with the intention to conduct further studies to show any correlation between the neurophysiological data and the behavioral one obtained after the completion of cognitive tasks, the system allows to store data about different cognitive tasks used during the process assessment and the rehabilitation of cognitive functions as Working Memory (Sternberg type Task, Task 2-Back and Go-NoGo task) and Attention (Attention Task-Network and Stroop tasks). This is a very important aspect to lead the therapist to obtain useful patterns using, for example, pattern-mining techniques (Guil et al., 2013; Marcano-Cedeño et al., 2013). The aim is the building of a knowledge-base formed by patterns as the basis of an automatic evolutionary diagnosis system.

*Figure 2*. Database scheme

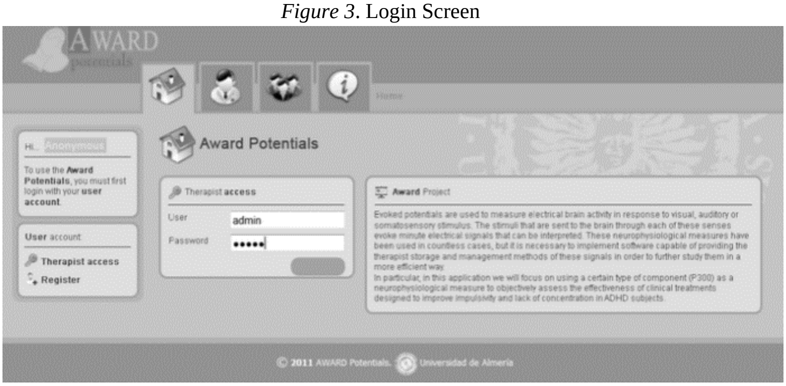


*Software aspects and theoretical background*

We have divided the use cases (obtained after the requirements engineering phase) of this software in 6 sections:

Application User Account: Anonymous users can request a Therapist account in this application. Once the user account is requested, they must wait for an administrator user who will accept or decline the request (see figure 3).

*Figure 3*. Login Screen



Manage new therapists: This use covers the actions that the administrator therapist user can perform with the incoming requests of anonymous users. This user can accept and decline the applications obtained.

Session Management: This item includes actions to login and logout the system (start and end of sessions).

Manage subjects: A Therapist can perform several actions related to associate subjects in the database. These actions include: searching subjects (standard or advanced search), creating a new subject, a subject updating (personal data, media...) and removing a subject (see figure 4).

*Figure 4*. Search subject form

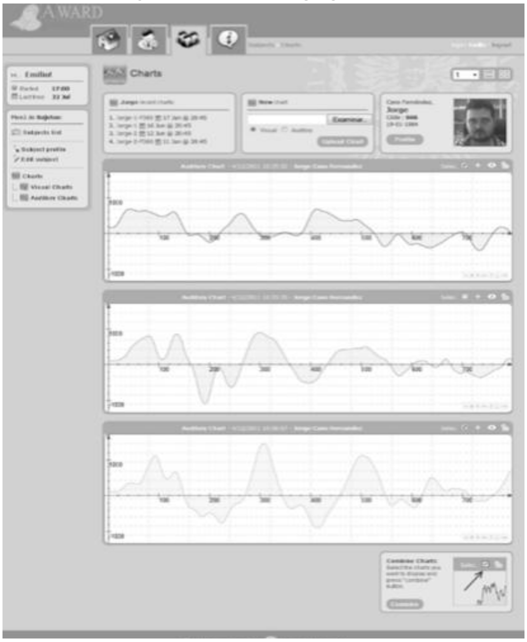

Edit charts: The main functions of the system are responsible for editing charts obtained from the evoked potential tests. Charts can be edited individually, or grouped, if the therapist needs to perform some kind of comparison between different tests carried out in different periods of time.

Edit simple chart: The therapist edits a chart which is only intended to get results without making evolutionary comparatives or showing any information about cognitive components. The editing panel shows different features or use cases such as: label editing (add, delete and save in the database), calculation of areas or changing the chart display (evoked potential, cognitive component, or combined).

Edit multiple charts: If the therapist wants to perform an evolutionary analysis of a patients test or just want to see a potential associated with his cognitive components and perform several actions with them, we can do it using this feature by showing the difference between charts and measuring distances in an interactive way.

Manage charts: A therapist, after selecting a specific subject associated with him/her, can view and manage the different charts (captured along the time) that belong to a given subject. The user can also combine different graphs (the sequence of signals recorded during the treatment phase) in order to view and edit them together (see figure 5). In this software aspect, a new density-based data fusion operator, named DbA (Angelov & Yager, 2013), has been used. DbA is a OWA-kind operator (Yager & Alajlan, 2014) where the constraint that imposes order between data is omitted.

*Figure 5*. Chart managing screen



The basic, and useful, underlying idea of fusing the input-streams of signal samples is to obtain the average graph that synthetize the evolution pattern of a certain subject. The meaningful cognitive measures associated with this average signal (for example, P300), combined with the different behavioral measures, form the associated pattern of the subject i, that is, $P_i$. The set of patterns, one per patient or set of similar patients, could be used as the core (knowledge base) of a classification-based diagnosis system (one rule per class type classification problem).

So, the pattern *Pi* is defined as the pair formed by the set of behavioral measures and the average cognitive component, that is, *Pi={bm, cm}*, where *bm={bm1,bm2,...,bmn}* and, in our case, *cm={P300}* (other cognitive components, as N100 or N200, could be taken into account (Sumich, Castro & Kumari, 2014).

The selection of the DbA (Density-base Averaging) operator, instead of the use of a simple arithmetic averaging, relies on the fact that the importance of each signal, *Sj*, is not the same. In real-domain, variability is a factor that must be taken into account, specially when we are dealing with neurophysiological measures.

Basically, DbA is a weighted averaging operator, where the weights of each signal is represented by its relative density. Each patient, characterized by its pattern *Pi*, has associated a set (stream) of signals ($SP_i=\{S_1, \ldots, S_t\}$) registered during a certain period of time. As we said before, each input-stream is formed by a float- based array of length 1000 representing brain activity during a session with a span of 1000 ms. That is, $S_j=\{a_1, a_2, \ldots, a_{1000}\}$. The number of samples (*t*-value) depends of the treatment and could vary significantly from one patient to another.

The arithmetic expression of DbA operator is presented in (Angelov & Yager, 2013) and could be adapted to our case as follows:

$$\overline{S_{P_i}} = \sum_{i=1}^{t} w_i S_i \text{ , } where\ w_i = \frac{\delta_i}{\sum_{j=1}^{t} \delta_i}$$

$\delta_i$ is a density function defined as: $\delta_i = \frac{1}{1+\frac{1}{t}\sum_{j=1}^{t}(d_{ij}^2)}$,with a Cauchy type of kernel and a distance measure ($d_{ij}$) like, for example, Euclidean or Cosine distance.

Once $\overline{S_{P_i}}$ is computed (in an on-line, real-time fashion), therapists can determine the average cognitive measure in a graphical way, determining which amplitude is related to the averaged cognitive P300 measure, value that must be selected following an expert-based criteria.

## CONCLUSIONS

The paper has presented a web-based tool to monitoring and analyzing the evolution of behavioral and cognitive measures as an objective test to check the effective-ness of rehabilitation treatments, both pharmacological and/or neuropsychological, or a combination of them. The tool provides different functionalities that make possible its use for therapists with a small learning curve.

This paper has focused on a particular case, where the objective measures are of behavioral nature combined with the P300 measure, a neurophysiological component widely used in clinical context as a cognitive marker, closely related to working memory and attentional processes. The tool has been implemented by using dynamic web technologies, and this enables, in a formal way, the possibility to manage clinical, contextual and temporal information essential to acquire know- ledge, to track the evolution of patients from the set of tests performed over time and to keep track of the diagnostic conclusions which have been obtained.

The software tool has been designed and assessed in collaboration with the Neuropsychological Assessment and Rehabilitation Center at the University of Almería. Initially, this tool emerged because of the need to carry out an empirical study about the evolution of a group of ADHD-diagnosed children which was provide with a neurocognitive rehabilitation plan, taking neurophysiological measures as cognitive markers. The absence of useful tools designed to manage and analyze both neuropsychological and neurophysiological data was decisive in the proposal and further development of the proposal.

Finally, we want to highlight the possibility of adding the necessary functionality to incorporate another objective measures, like those studied in Lin, Yang & Su (2013), with the aim of having a more complete understanding of ADHD in children.

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