Clinical Web Environment to Assist the Diagnosis of Alzheimer’s Disease and other Dementias

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Abstract: In this article we present a web application for an interactive and modular virtual clinical environment, (EDEVITALZH), which constitutes an essential part of an intelligent system of neural computation to assist the diagnosis of Alzheimer’s disease and other dementias (SICONMID3), based on the HUMANN neural architecture. By using EDEVITALZH, it is possible to pre-diagnose dementia, to give a probable diagnosis of Alzheimer’s disease and differential diagnosis of dementias in a more reliable and flexible way in primary care as well as in specialised centres, due to its use in a telemedicine format.

EDEVITALZH presents a Global Clinical Protocol for Dementias (GCPD) implemented using a web interface supported by a three level modular architecture (data, diagnosis and communication security) that allows rigorous and easy data handling, as well as undertaking a previous analysis before diagnosis and comparative studies of patients regardless of their actual location and geographical position. EDEVITALZH permits the fusion of heterogeneous data, enabling data introduction to be processed and analysed ranging from the purely numerical to the imprecise sentences of natural speech, normally associated with clinical records and/or of histopathological interpretations, including multidimensional and multi-parameter signals.

Key-Words: Web Environment, Internet, Artificial Neural Networks, Diagnosis of Dementias, Alzheimer’s Disease.

1 Introduction
The progressive inversion of the population pyramid means an increased presence of illnesses whose incidence is positively associated with growing old. There exists a significant prevalence of dementia syndromes, 5-10% of people over 65 years old. The figure rises to 25%, if the cognitive deterioration of the elderly is considered to be an early stage of dementia.

We still have an insufficient knowledge of the causes of Alzheimer’s disease and other dementias. Over 30% of dementias remain unexplained.

Using the diagnostic criteria actually in use, the ante mortem diagnosis of “probable Alzheimer’s disease” is currently confirmed post-mortem in 80-90% of cases only in specialized centres. The diagnostic certainty has not been evaluated for non-Alzheimer dementias. In addition to this a reliable biological marker of Alzheimer’s disease...
is not expected to be found in the foreseeable future [1, 2] meaning an accurate diagnosis can only be obtained from a pathological post-mortem study. Therefore we find ourselves considering diseases that are not able to be detected easily or with certainty. We think that the key is in the use of new methods to assist in diagnosis that exceed the classic Newtonian reductionist lineal analysis of cause and effect that has been used in medicine during centuries and that take into account all the possible data that could characterise a dementia, from numerical data to the imprecise sentences of natural speech, normally associated with clinical records and/or of the histopathological interpretations, including multi-dimensional signs and multi-parameters. The suitable approach is that of the artificial neural networks (ANNs).

EDEVITALZH covers these aspects. It will facilitate the handling of the SICONMID3 [3] prototype. It will provide the possibility of the developed system being used in telemedicine. It will be able to be used for conveniently and rigorously performing the clinical protocol for DCL, Alzheimer-type dementias and other cortical dementias. It will allow computerised medical records to be set up, creating a data base of the patient’s medical records. EDEVITALZH can be used for allowing analysis to be carried out prior to the diagnosis with the possibility of providing pre-diagnosis, conducting evaluation studies of the evolution of the dementia and carrying out online consultations with other colleagues in different geographical locations. Finally, EDEVITALZH is an expandable system.

The most relevant aspect of our proposal is that any patient with dementia, or any potential patient will not be without adequate medical attention, without a correct diagnosis and finally without the appropriate treatment due to lack of human and/or clinical resources.

2 EDEVITALZH Modular Architecture
EDEVITALZH has been implemented using a web application model, basing this on the advantages that it provides:

1 It is not necessary to install specialised software in the computers that will be using EDEVITALZH. Any computer or workstation, regardless of its operating system, can access the application using a web browser. Thus, the Internet use extends the possibility of its utilization on health centres, specialised centres and hospitals.

2 The information is centralized and is always available for consultation from anywhere; that is to say the information can be visualised, analyzed and processed by different people simultaneously in different geographical areas.

EDEVITALZH is made up of three first level blocks (Fig. 1): 1) Data Module and User Interface, 2) Diagnosis Module, and 3) Communications, Security and Information Privacy Module.

![EDEVITALZH Modular Architecture](image)

This logical structural separation also allows a physical separation; different parts of the system can be located in different places. For example, the same diagnosis module can operate with various data modules at the same time. Furthermore, thanks to its modular character, its complexity and the cost of the system hardware and software are reduced. This is thanks to the diversity of the modules that make up EDEVITALZH and that are in constant communication to share information.

Each one of these blocks is expandable, so that they accept future expansions at the request of the specialist, with the minimum impact on the working of EDEVITALZH during this change.

2.1 Data Module and User Interface
The Data Module uses all the procedures and functions related with the database system activity. All data consultations, insertions and modifications will be undertaken using the tools provided by this level.

The corresponding lexical/syntactic data interpretation and codification for insertion will be undertaken. It will
again be interpreted when the consultation requires a sample of the stored user data.

Communication is achieved by using the web application interface, that is to say, with the logged user, receiving and offering information.

The web application interface implements the Global Clinical Protocol for Dementias (GCPD). Using a structure of forms and reports, it allows the user to interact with the GCPD and the diagnosis system.

GCPD reflects the specific data of interest channelled towards the detection of Alzheimer’s disease and other dementias while at the same time, it helps to indicate the steps to take, in a schematic way, correlating the clinical and therapeutic parameters.

GCPD consists of different sections: 1) Personal Data, 2) Social Data, 3) Reason for consultation, 4) Habits, 5) Family history, 6) Intercurrent Diseases, 7) Clinical Records, 8) Drugs, 9) Diagnosis. Each one of these contains relevant or interesting data related to the subject in question.

EDEVITALZH data model is a realistic computer representation of the clinical protocol. It defines structurally how it stores, connects and manages the information of cases on the database management system. It can be found represented by the EDEVITALZH forms and reports structure. The data model entities largely correspond to the GCPD sections. These entities maintain connections that make up the scheme of entity-interrelation.

EDEVITALZH web interface (Fig. 2) has been designed using the ORACLE Application Server. We selected this technology because:

1. It allows the creation of web applications based on robust and secure components.
2. It stores all types of documents, such as images, reports, presentations and any other information needed by the user, allowing work with the information to be versatile and agile.
3. It allows information sharing among users, meaning that EDEVITALZH is an application that harnesses workgroup.
4. It integrates a large number of technologies and services on the same workplace, reducing development and implementation costs.
Data Module can be found integrated into the ORACLE Application Server, which includes all the necessary processes for the information handling, as well as simple and advanced search methods adapted to EDEVITALZH need. Other enlargements are possible using the design of adaptable modules based on ORACLE’s Portlets and PL/SQL. Our data model implementation was carried out on a ORACLE Database 10g database server.

2.2 Diagnosis Module
The diagnosis process will be performed by an HUMANN-based computational neural system. HUMANN is a biologically plausible unsupervised feed-forward modular neural network. It consists of an input layer and three modules hierarchically organised in the neural processing with different neurodynamics, connection topologies and learning laws [4, 5].

HUMANN implements the two last stages of the general approach of the classification process, the template generation, and the discrimination (labelling), in a transparent and efficient way.

The main causes of its biological plausibility are its adaptive character, its modular functionality and it has connection structure with two types of synaptic connections present in the biological neural network, namely the active synapses and the silent synapses, [4, 6]

The adaptive character of HUMANN is essentially embodiment in the labelling module, because of its dynamic dimension. This characteristic is implemented by two neural mechanism, a) neural elimination, b) neural generation.

They perform refinement processes in the neural circuits, and they are present in the human brain and in the brain of some birds [4,5]. We are able to consider this system as an ontogenic net, capable of adapting its dimension to the characteristics of its environment.

2.3 Security and Privacy Module
The Communications Security and Privacy Module group together all the services in favour of the EDEVITALZH system security. We approached the structure on the basis of a User Hierarchy, Information Security and Communications.

Our proposal for the rights hierarchy is established determining three types of user:

ADMINISTRATIVE-type User: With authority to carry out supervisory and control activities. In this way, this user type can undertake management tasks and the application maintenance (backups, events logs analysis, grant permissions to users, etc).

RESEARCH-type User: With authority to undertake study and analysis activities in the Diagnosis Module. This user will have at his/her disposal a quasi-development environment, where it will be possible to undertake studies and modify the way the neural net works.

The Research user type, when using selection tools, will be able to decide what data model fields are necessary so that the neural network generates a precise diagnosis.

Due to all of this, it will be possible to analyse and deduce which are the GCPD elements semantically relevant to the diagnosis generated, which permits the GCPD redefinition and reduction in size.

For the diagnosis generation, it is necessary to build a collection of standards which will make up the HUMANN information domain.

EDEVITALZH provides two transmission methods: 1) Transfer by demand, and 2) Planned transfer.

The transfer by demand allows the researcher to request the transmission of the collection of standards to the Diagnostic Module. The planned transfer automates the task of transmitting the collection of standards without the need for any human action, in planned determined intervals of time.

The minimum unit of information for interchange will be constituted of text files, made up of vectors of information to be pre-processed and analysed by HUMANN. The files will be transmitted by http protocol using SSL security. In this way, HUMANN acts as a research user, accessing the data it requires and transferring them to its control with the needed security measures.

DOCTOR-type User: With authority to undertake information consulting, insertion and/or modification activities. This user has, at his/her disposal, his/her own information on the database, concerning his/her patients and personal documents (clinical reports, statistics, graphics etc)
The Doctor user type can share information with other users, in the way that with EDEVITALZH, the doctor has the possibility of opinions and criteria comparison with other professionals, at any time and in any geographical location.

Concerning communications, computer systems are in continuous compromise in all what relates to their operation and the data they manage. With the object of increasing the system security, and from the perspective of EDEVITALZH as a distributed application supported in computer networks, our project incorporates a system for intrusion detection based on hierarchical and modular unsupervised neural nets (ANNs-based IDS), [7].

Our ANNs-based IDS is an intelligent system for intrusion detection, capable of monitoring and analysing user activities in a local and remote mode, inspecting user behaviour and the information traffic sent and received, detecting potential intrusion attempts, attack or virus infections in the network where the application is running.

Our ANNs-based IDS is capable of detecting any type of attack, new or known (or still unknown) protecting the information and systems that stores it, in an effective way against illegitimate users or processes; it will take immediate and effective actions, minimizing and/or avoiding the incidence of these harmful and illegitimate actions.

The incorporation of ANNs-based IDS to EDEVITALZH provides security and privacy to communications transfer, controlling the net systems with the object of avoiding intrusions, service denial (DoS), exploitation, etc.

3 Infrastructure EDEVITALZH

EDEVITALZH runs under an ORACLE technology-based software architecture; this is an ORACLE Database as a database management system (DBMS) and ORACLE Application Server. ORACLE Application Server is a collection of services grouped together to a HTTP server to give connectivity and support to the different technologies ORACLE incorporates, i.e. Java.

EDEVITALZH allows multiple web application servers, although it only permits one unique database (multiple instances of the same could exist) for the entire system.

It is necessary to ensure the infrastructure availability and the working application 24x7. To allow fault tolerance, the use of redundant configurations is required [8] (Fig. 3), all system components –application servers, database servers, network load balancers, routers, etc).

If the data load grows, an option will be to install an ORACLE data cluster (RAC) [8], which would provide an adequate scalability and fault tolerance. EDEVITALZH is a scalable application, from one-server tier configurations, to reaching structures of \( n \) servers per tier.

Studies have been made on the possible occurrence of catastrophes and the level of effect this would have on EDEVITALZH. Electric current failure, fires, floods and other natural phenomena such as earthquakes or storms could destroy the system; this could however only happen if there does not exists a system replica at another place not affected by the problem.

In any case, EDEVITALZH incorporates planned back up techniques that allow information on the database copies to be made on magnetic tapes, hard disks or any other information saving device adequate for the process.

Finally it is very important to minimize EDEVITALZH system down time. The system should not be allowed to fail due to disk errors.

The use of redundant disk arrays (RAID) proposed by Patterson et al. [9] allows the combination of disks of reduced size and cost in vectors of disks able to reach the performance of a high cost storage unit. This also permits a high level of tolerance against failures.

In the majority of situations where EDEVITALZH is being used, the use of RAID architectures gives good results.

In favour of possible scalability, it should be mentioned that there are other more sophisticated storage systems.
DAS, SAN, or NAS are possible schemes to study for those structures that require efficiency on storage and maintenance of large volumes of information.

4 Conclusions
The clinical web environment concept proposed represents an important advance in the area of telemedicine. Its technical specifications make its implantation viable in any personal or professional area, thanks to the minimal resources required: a computer or workstation with an Internet connection and a web browser.

The complex EDEVITALZH mechanical processes are hidden to ensure a user friendly and rigorous interface, with control and access security, that helps to undertake a more efficient and disciplined work. The information is centralized and always available for consultation. It can be visualised, analyzed, and processed by different people, simultaneously and at different geographical areas. This interface also gives access and control of the HUMANN neural architecture, core of the intelligent system of assistance to the diagnosis.

The area of development at a research level will allow the analysis and GCPD study in depth, as well as the implementation of different configurations of HUMANN with the aim of producing precise diagnosis and obtain an optimum GCPD.

EDEVITALZH is a versatile system due to its application in clinical medicine and research, its character of dynamic expansion and for the possibility it gives of its distribution in different parts in different places.

EDEVITALZH ensures the integrity and security of the clinical information incorporating an intelligent system for the intrusion detection, our ANNs-based IDS. EDEVITALZH also uses methods of data protection such as users and rights hierarchy.

We also propose different analysis to ensure the constant availability of the system to maintain it protected not only against computing risks but also against other occasional ones. With the use of EDEVITALZH and SICONMID3, the diagnostic work of the doctor will be more accurate, agile, and patient dedicated, allowing the optimization of time and resources. All what is needed is a centre specialised in Alzheimers disease and other cortical dementias that are not Alzheimer, with experts, and Internet workstations connections to allow the possibility of undertaking highly reliable diagnosis, in real time, while parallely being able to work with different patients in different geographical locations that are being studied by other doctors using EDEVITALZH.

After all that has been stated in this paper, we conclude the most relevant aspect of the effect of this proposal is that it will ensure that no patient with dementia or with the potential to have it, will go without the adequate medical attention, without a proper diagnosis and finally, without the appropriate treatment to alleviate their condition, due to lack of human and/or necessary clinics resources.

References:

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