Decision support system for the Classification of Epilepsies and Epileptic Syndromes for children

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ABSTRACT: In Medicine, Information Technology has often been used to assist doctors in their diagnostic procedures, especially whenever there are problems of differential diagnosis in diseases. Methods from the domain of Artificial Intelligence give us the opportunity to formalize the medical knowledge and standardize various diagnostic procedures, in specific domains of Medicine and store them in computer systems (Knowledge Base). In the present research, we have developed a Decision Support System (DSS) for the disease of Epilepsy during childhood, when certain epileptic syndromes present difficulties in diagnosis and laboratory tests do not lead to specific results. The development of this specific DSS is based on the «International Classification of Epileptic Syndromes and Epilepsies», as is proposed by the «International League Against Epilepsy». In order to check the effectiveness of this diagnostic system we examine cases of patients with epileptic seizures. The results from the application of the Expert System is being compared with the diagnoses proposed by an experienced doctor.

INTRODUCTION

Artificial Intelligence in Medical applications have been proposed various well known methods, in order to formalize the medical knowledge, to standardize the diagnostic procedures in specific domains and to effectively store them in computer systems [5, 4, 18, 20]. In practice, the computerized diagnostic systems take advantage of this wide stored information (named Knowledge Base), which «do not forget» and in a way through inference mechanisms, they mimic the doctor's procedure of thinking, by assisting him in conclusion making [16].

In the present study, we have developed a decision support system on the knowledge domain of Epilepsy during childhood, where certain epileptic syndromes present difficulties in diagnosis and laboratory tests do not lead to specific results. The aim of this system is to help the doctor classify properly each patient case according to the «International Classification of Epileptic Syndromes and Epilepsies» [12, 13] as is proposed by the "International League Against Epilepsy" (ILAE). The present medical knowledge of this domain, the bibliography and the classifications occasionally processed and proposed by ILAE, give us the convenience to formalize the data and the factors that affect the diagnosis of epilepsy and to handle them properly, in order to get useful conclusions.

The International Classification proposes more than 50 diagnostic categories for epilepsy and epileptic syndromes. More than 100 different factors (lab and EEG findings, symptoms, clinical data) affecting the diagnosis should be examined, in order to include all these diagnostic categories in a decision support system for epilepsy.

We propose a diagnostic methodology that analyzes the initial problem for the diagnosis of epilepsy in smaller sub-problems. Each such sub-problem examines the possibility that only a limited number of diagnostic categories can be concluded. Thus by creating separate diagnostic sub-systems we reduce the complexity of the diagnostic procedure. The system's inference engine follows a decision tree that is developed based on the inputs given by the user. By interfacing the decision tree in the diagnostic procedure of the system, it is possible to determine more explicitly the range of potential diagnostic classes.

As undoubtedly the most significant factor for the diagnosis of Epilepsy is the seizure type observed on the patient [12, 13], the first level of the decision tree starts the branching, based on this specific information. For the assessment of the epileptic seizure type, another separate diagnostic system has been developed. The decision tree is extended, based on explicit data and eventually the "leaves" of this decision tree are the various diagnostic sub-systems that could lead to conclusions. Concerning the implementation of the smaller diagnostic sub-systems typical "backwards-chaining" techniques have been used and the "Knowledge Base" of them is consisted of rules [4]. The final aim of the used methodology is to minimize the searching time for the proper rules stored in the Knowledge Base of the system that could lead to right conclusions.

THE EPILEPSY

Epilepsy is a chronic illness characterized from recurrent seizures that cause sudden but revertible changes in the brain operation [2]. According to ILAE there is a fundamental difference between seizures and epilepsies. Epilepsy is a chronic disorder and seizure has a beginning and an end. So ILAE has periodically published different classifications for both seizures and epilepsies (and epileptic syndromes) [12, 13]. The international clasiification describes 4 main classes of epilepsies:

1. Localization related (focal, local, partial) epilepsies
2. Generalized epilepsies
3. epilepsies and syndromes undetermined as to whether they are focal or generalized, and
4. Special syndromes

The genetics of epilepsy are not always straightforward. Epilepsy in most cases is caused by acquired damages of brain cortex (sympormatic) but brain predisposition to seizures is also a good reason for the appearance of the disease (idiopathic).

Prevelance rates of epilepsy have been reported from many countries, but there are significant diferences between studies. Nevertheless most studies point a prevalence of 0.5% in the general population [2].

The diagnosis of epilepsy primary is made on the basis of the type of the epileptic seizure observed. Other fundamental factors that influence the diagnosis of epilepys are brain scans (CT and MRI), electroencephalograph (EEG) measures and various clinical data.

METHODOLOGY

The implementation of such diagnostic support system inevitable follows the traditional development of any other software. That is we have to work out the basic stages of analysis, design, construction and proofing, namely the “life cycle” [19, 11]. More specifically a typical implementation of knowledge based system, usually includes the development of three rudimental sub systems, (a) the knowledge base, (b) the inference engine and (c) the user interface [16].

Attempts to develop computer programs that can diagnose medical condition began many decades ago [14] and various implementation methodologies have been proposed. However, there is no commonly accepted philosophy to guide the development of medical decision support system [11].

Taking into account the clinical data, the results of laboratory tests and the EEG findings, various implementation stages were organized, for the construction of the specific DSS for Epilepsy. In this implementation, related bibliography [6, 7] and the international classifications of ILAE [12, 13] were very helpful. Studies have been shown that the international classification as it proposed by ILAE, despite its incompleteness, it has very good practical application with satisfactory results [17, 1].

Combining the two major philosophies (traditional and knowledge base implementations), the development of the DSS for epilepsy, has been elaborated in the following stages:

- Identification of the most important data, to structure the Knowledge Base (analysis stage)
- Development of Knowledge Base and design of Inference Engine (design stage)
- Software development on the computer (construction stage)
- Testing the diagnostic system (proofing stage)

<u>Identification of the most important data</u>

In this initial stage, investigation of all the factors and data that can influence the epilepsy diagnosis is done. This recording is based on the related bibliography according to expert doctor conviction. From that investigation and taking into account the various diagnostic categories (types of epilepsies and epileptic syndromes) proposed by the international clasification of ILAE the most significant data were selected. More specifically for the diagnosis of epilepsy more than 100 different factors were estimated and they were placed amomg 3 grours:

A. Clinical data

The epileptic seizure type, the primary indication for the diagnosis of epilepsy, estimated according to the descriptions in the classification for epileptic seizures, as proposed by ILAE [ILAE.1]. In this classification there are 19 different categories. Apart form the seizure type, various findings related to the epileptic seizure are estimated. These are the severity (slight, intermediate, severe, status), the focus (frontal, temporal, parietal, occipital, with multiple focus, unknown) and the diffusion (focal, diffuse, both) of the epileptic seizure.

In addition to the epileptic seizure type, data concerning the pregnancy and delivery status, the family inheritance, the behavior, the neurological estimation, the psychomotor development and (if applicable) the school performance are also estimated gradated from 1 to 5 (1:normal, 2:suspicious, 3:slight pathological, 4:pathological, 5:sever pathological). Gradation zero (0) has the meaning that there are no information available (unknown situation).

B. Laboratory findings

Findings extrapolated from laboratory scans such as MRI and/or CTI, and the focus and/or the diffusion observed through them, could affect the diagnostic procedure. These two factors also have to be evaluated by the system. The results from the digital scans are gradated from one to five again and the localization has the values focal, diffuse, both and not traceable.

C. EEG findings

The EEG finding were classified in four (4) main categories. Each category was sorted in subcategories, that correspond in specific EEG descriptions related to epilepsy and that can help and guide the doctor in her/his diagnostic procedure. The main categories are:

- Non specific abnormal EEG patterns, as widespread intermittent slow abnormalities and bilateral/focal persistent findings (3 sub-categories),
- Abnormal EEG patterns - epileptic paroxysmal as spikes, polyspikes, sharp waves, spike wave complex, small sharp spikes, polyspikes of multiple Spikes etc (12 sub-categories),

- Specific EEG patterns, as hypsarhythmia, rolantic spikes, typical neonatal EEGs etc (26 sub-categories in total) and
- Epileptic findings in specific recordings as during sleep, photostimulation, hyperventilation, during seizure, longtime recording, video recording etc (9 sub-categories).

Analyzing the above significant data we conclude to the rules that govern the knowlegde base of the system. The last procedure in this stage was the theoretical application of these rules to check the correctness of each one of them.

Development of Knowledge Base and design of Inference Engine

For a successful Decision Support System, a detailed depiction of the knowledge domain for a given issue is not enough: the system's appropriate exploitation is also a prerequisite. Hence, the conclusion inference engine developed for the software in question aims at the full exploitation of the knowledge stored in the system, in order to come to useful results. Due to the complexity of the issue, it was obvious that a trifling analysis and a subsequent examination of the rules concerning the Knowledge Base, following some known methodology for conclusion inference would be inadequate. Thus, a methodology that is described below was adapted.

The initial problem of diagnosis was further divided into smaller diagnostic sub-systems, to which the software is led, following a decision-tree. This decision tree is evolved according to the user's choices during the operation of the software, based on the values given to the data that are initially input. With the intevention of this decision tree in the function of the inference engine, it is possible to define the diagnostic problem with greater precision. As a result, the range of potential conclusions is limited. For instance, when the patient is younger than 40 days (neonate), the system should search for data leading to specific diagnoses of epilepsy, which are exclusively present at neonates, while examining the application of the respective rules and rejecting the data, which would not lead to diagnoses of epilepsies for neonates.

The start of the decision tree is based on the accurate definition of the value concerning the most important data, which is seizure in the case of the diagnosis of epilepsy. For that reason, an initial diagnostic system has been constructed, aiming at the aid on the right classification of seizure. Concerning the development of this initial diagnostic system examined here, the system disposes its own Knowledge Base, which is rule-based and results in the type of seizure, through the backward chaining technique. The conclusions stem from this initial sub-system will primarily lead the course of the decision tree, which finally ends up in smaller diagnostic sub-systems. When we analyze the diagnostic problem in that way, we create small, independent diagnostic sub-systems with a limited Knowledge Base, through less complicated reasoning. Those sub-systems are more easily implemented. Besides, they result in sets of potential diagnoses and make use of the backward chaining technique (**Figure-1**). This hierarchical formulation aims mainly at the minimization of the time spent on the search of the appropriate rules, which would lead us to the right diagnosis.

There are three levels of certainty grading, concerning the conclusions inferred from the diagnostic system («absolute certainty», «great possibility» and «possibly»), once we decide on a given diagnosis. In the cases where we also experienced seizures of epilepsy in the past or where the patient is under medical treatment, the system recommends to the user not to take the result proposed into account, while in some cases it also suggests more than one diagnosis (differential diagnosis). For instance, in cases of mild, focal seizures during childhood, it is not possible to detect clinical findings and the neurological evaluation is ambiguous. As a result, classification of the diagnosis under one of the focal epilepsies proposed by the international classification (idiopathic or symptomatic) is very difficult, even if we have distinct results by the electroencephalogram. In those cases, the experienced system proposes alternative diagnoses. The latter is implemented by creating connections among the smaller diagnostic sub-systems.

Testing the system

In the present phase, the diagnostic system implemented went through controls and some cases of patients were examined, in order to evaluate the diagnostic precision of the system and make potential improvements. Initially, the user-doctor inputs data to be used by the system, in order to propose the type of epileptic seizures, which is compatible with the international classification [12]. Then, a number of historical, clinical and laboratory data, such as the features of the electroencephalograph, are also input and the diagnostic system asks the user for other data as well, according to the case, through a series of appropriate questions. For instance: it asks for the extent or the intensity of the seizure, or for data on the conditions of incidence, etc, in order to be led to a distinct diagnosis. The result of the diagnosis suggested always complies with the categories of epilepsy described in the international classification.

The material gathered consists of 71 cases of epilepsy for children up to 15 years old. From those cases, 34 concerned girls and 37 concerned boys. Concentration of the data was made from patients of the General University Hospital of Heraklion, Crete, after a specific authorization issued by the Faculty of Medicine, always respecting the patients' anonymity.

As metioned before, in the classification of epileptic syndromes and epilepsies as proposed by ILAE [13] the different types of epilepsy organized in four (4) primary categories:

- Localization-related (focal, local, partial) epilepsies and syndromes
- Generalized epilepsies and syndromes
- Epilepsies and syndromes undetermined whether focal or generalized
- Special syndromes (situation-related seizures)

Further analysis of localization related and generalized epilepsies as proposed by ILAE gives us 9 main sub-categories:

- Localization-related, Idiopathic
- Localization-related, symptomatic with simple partial seizures
- Localization-related, symptomatic with complex partial seizures

- Localization-related, symptomatic with secondary generalized seizures
- Generalized, idiopathic
- Generalized, cryptogenic or symptomatic (in order of age)
- Generalized, symptomatic
- Epilepsies and syndromes undetermined whether focal or generalized
- Special syndromes (situation-related seizures)

The variety of diagnoses that come from the above-mentioned material covers the whole range of the 9 main categories of the international classification. More specifically, distribution of the 71 diagnoses, which were made by an expert children's neurologist according to the international classification, for the cases of the sample, is shown on **Table-1**.

When we used the diagnostic system that we had constructed, in order to make diagnoses for the 71 cases of the material's patients we came to the following results, after comparing the conclusions of the system with those of the expert children's neurologist:

- In 61 cases, the diagnoses were identical with those of the neurologist. The respective rate of success is 86%.
- In 5 cases, the diagnoses were different form those of the expert neurologist (percentage of error 7%) and
- In 5 more cases, the diagnoses were similar (7%).

CONCLUSIONS

The results we came to, after we input the diagnostic system we constructed with the data of the case-sample, in order to verify its diagnostic ability, were very encouraging. The conclusions inferred by the diagnostic system were identical with those of the expert doctor for 61 cases (rate 86%). Furthermore, if we take into account that in 5 cases we had similar, well-accepted results, then the percentage of accuracy for the program reach 93%.

As far as the 5 mistaken results are concerned, one of the cases regarded a patient who had been treated and his electroencephalograph had changed form. This means that we did not have a clear picture of initiation of the disease, which would probably lead the software to a safe diagnosis. In three cases, the diagnoses proposed by the international classification, as well as by the software were different than those proposed by the expert neurologist, due to incompatibility of the clinical findings. Finally, in a patient's case, the diagnostic system could not come to any diagnosis, due to an ambiguity of the clinical picture of the seizures and due to the impact of drugs to the situation. In general, the diagnostic system we constructed led to the right diagnosis for the majority of the cases. Thus, this may constitute a very useful, auxiliary diagnostic tool.

The methodology we have used for developing this specific system is deemed easily applicable for similar problems of medical diagnosis, where implementation of a decision tree is possible. That tree will be based on specific, well-established events, which will allow us to draw a safe course of the tree. The evolution of a decision tree stops, where uncertainly of the conclusion starts, thus limiting the range of research for right results. Furthermore, existence of significant data, such as the type of seizure in the case we examined, offers us the opportunity to create a decision tree, which results in smaller, independent problems of diagnosis. For the evolution of those smaller diagnostic sub-systems, the use of different technologies is possible as Bayesian [5, 21], ANN [3] or rules [4]. Since those systems are independent, each of them can be implemented through different methodologies. The current operational systems and working environments offers an infrastructure, which facilitates on-line connection and sharing of a common decision tree, thus creating a bigger, hybrid diagnostic system.

About the evolution of the specific system, the nodes of the tree refer to questions to the user and the course of the tree is based on the user's answers. Besides, a different way to get answers is the use of diagnostic sub-systems or the reception of automatic, digitalized results of laboratory instruments and equipment.

The international classification of epilepsies and syndromes is an indispensable tool for every doctor who deals with epilepsies. Observations and diagnostic procedures offered by that tool to the doctors facilitate their task largely, as it is pointed-out by the present study. It can play an important role to the standardization of medical knowledge, which is so significant for implementing respective systems of automated diagnosis. Nevertheless, the international classification presents some weaknesses and limitations, as it is pointed out by researchers who have tried to classify cases of epilepsy based on that classification [17, 1, 8]. This has been justified by factors such as the quality of clinical information on the patients' seizures, as well as by internal weaknesses of the international classification, such as the unclear distinction among diagnostic categories. Besides the aforementioned studies, another example is Manford at al, who did not manage to categorize 190 out of 814 patients with a newly diagnosed epilepsy [15]. For those reasons, the revision of that classification system has been recently suggested [10, 9].

It is certain that no matter how accurate and rational the diagnostic ability of the experienced system may be, it is always a result of series of finite data analyses, so the treating doctor should always have the last word. Nevertheless, he can always refer to it, in order to verify the diagnosis. The software's results can be of consultative character. A very efficient role of the specific diagnostic system is certainly that of an educational tool for students of medicine or doctors in the period of their specialization, as its development has been based on the international classification of syndromes and seizures.

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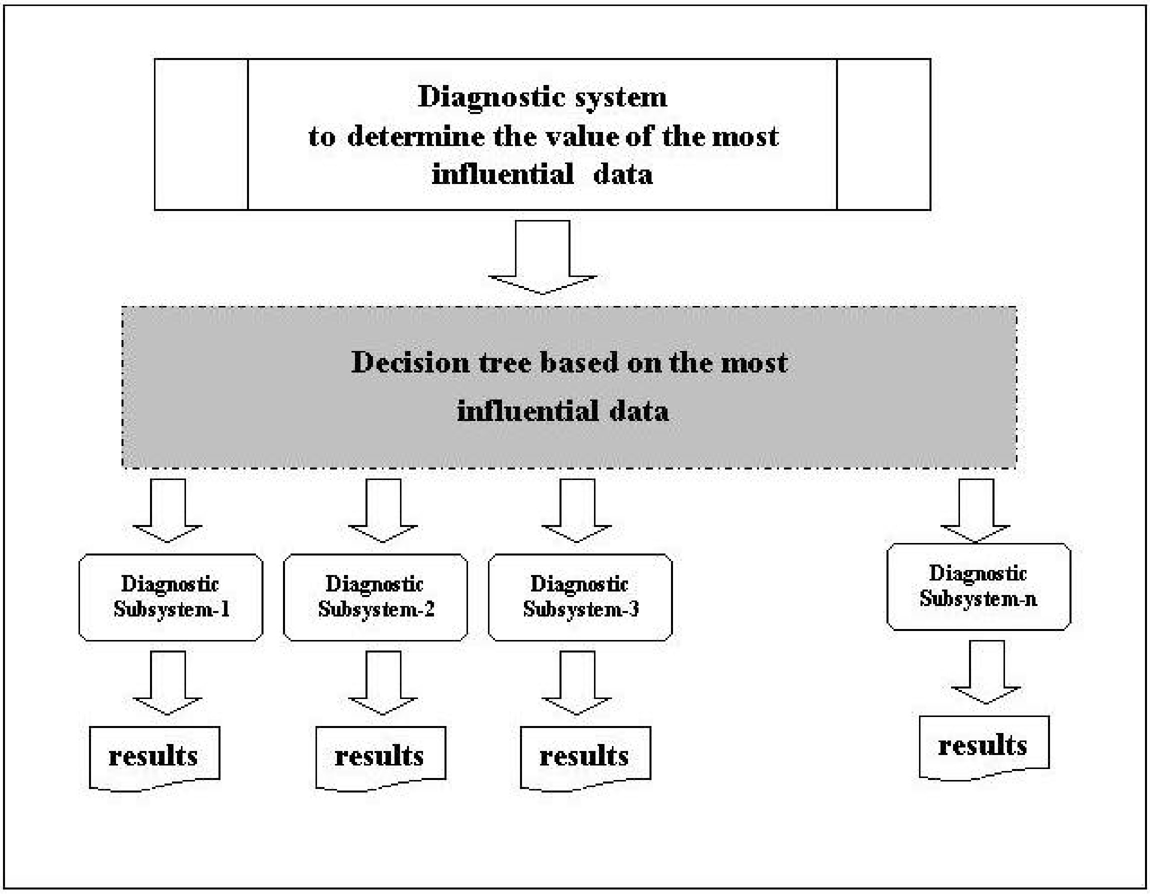
Table –1

#	Epilepsy type / Epileptic Syndrome (expert's diagnosis)
15	Generalized idiopathic epi with no specific discreteness
10	Special syndromes, situation-related seizures (febrile convulsions)
8	Localization-related, Idiopathic, benign childhood epilepsies with centrotemporal spikes
5	West Syndrome - infantile spasms, Blitz-Nick-Salaam Krampfe (generalized cryptogenic./symptomatic)
4	Localization-related, symptomatic with secondary generalized seizures arising from temporal lobes
4	Undetermined epilepsy without unequivocal generalized or focal features (epilepsies and syndromes undetermined whether focal or generalized)
3	Localization-related, symptomatic with simple partial seizures arising from temporal lobes
3	Localization-related, symptomatic with secondary generalized seizures arising from parietal lobes
2	Localization-related, symptomatic with complex partial seizures arising from temporal lobes
2	Localization-related, symptomatic with secondary generalized seizures arising from frontal lobes
2	Localization-related, symptomatic with secondary generalized seizures arising from multiple lobes
2	Localization-related, symptomatic with secondary generalized seizures with locus of onset unknown[1]
2	Lennox-Gastaut syndrome (generalized cryptogenic./symptomatic)
2	Neonatal seizures, epilepsies and syndromes undetermined whether focal or generalized
1	Benign psychomotor epilepsy (localization-related, idiopathic)
1	Localization related, symptomatic, simple partial seizures arising from occipital lobes
1	Localization related symptomatic, complex partial seizures arising from parietal lobes
1	Childhood absence epilepsy – pyknolepsy (generalized idiopathic)
1	Juvenile absence epilepsy (generalized idiopathic)
1	Epilepsies with myoclonic-astatic seizures (generalized cryptogenic/symptomatic)
1	Epilepsies during diseases affecting CNS (generalized symptomatic specific syndromes)

[1] Diagnostic category proposed by Dreifuss [20].

Figure-1


Diagnostic system
to determine the value of the most
influential data
Decision tree based on the most
influential data
Diagnostic
Subsystem-1
Diagnostic
Subsystem-2
Diagnostic
Subsystem-3
Diagnostic
Subsystem-n
results
results
results
results