Decision Support Systems (DSS) as tools to diagnose Epilepsies in children.

K. M. Vassilakis, Sifis Micheloyannis, Manolis Marakakis
Technological Educational Institute (TEI) of Crete and University of Crete, medicine

Emails: kostas@cs.teiher.gr, mmarak@cs.teiher.gr and mixelogj@med.uoc.gr

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ABSTRACT

Artificial Intelligence in Medical applications has 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. The computerized diagnostic systems take advantage of this wide stored information (Knowledge Base), which «does not forget» and in a way through inference mechanisms, they mimic the doctor’s procedure of thinking, by assisting him in conclusion making.

We developed a decision support system to help the diagnosis of Epilepsy in childhood, where certain epileptic syndromes present difficulties in diagnosis and differential diagnosis. 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» as is proposed by the “International League Against Epilepsy” (ILAE). The existing medical knowledge and the classification proposed by the ILAE, give 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.

Initially, the user-doctor inputs medical information used by the system, in order to propose the type of epileptic seizures, which is compatible with the international classification. Several clinical and laboratory data, as well as the features of the electroencephalograph, are also inputs. 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 implementation of such diagnostic support system inevitable follows the traditional development of any other software: We have to work out the basic stages of analysis, design, construction and benchmarking, namely the “life cycle” of a software system. The proper construction process of knowledge based systems, usually includes the development of three rudimental sub systems, (a) the knowledge base, (b) the inference engine and (c) the user interface. The implementation contains the phases of (1) feasibility analysis (2) conceptual design, (3) knowledge acquisition, (4) knowledge representation and (5) validation of the system.

Trying to combine the two major approaches (conventional and knowledge base) of software construction, we decide the methodological framework supporting the DSS development and assessment to include four distinct phases: namely: (A) Identification of the most important data, to structure the knowledge base (analysis stage). (B) Development of knowledge base and design of inference engine (design stage). (C) Software development on the computer (construction stage). (D) Testing the diagnostic system (benchmarking)

We used the diagnostic system in more than 100 cases of children with seizures. We had the following results in comparison to the diagnosis of the expert children’s neurologist:

In 85.2% of the cases, the diagnoses were identical with those of the neurologist.

In 6.6% cases, the diagnoses were different from those of the expert neurologist

In 8.2% cases, the diagnoses were similar, acceptable by the specialist.
1. INTRODUCTION

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 Artificial Intelligence (AI) have supported a wide variety of clinical and medical decision making [Buchanan84, Shortliffe87, Szolovits88]. Furthermore, AI methods have contributed towards the formalization and representation of medical knowledge both formal and informal. Formal connotes knowledge embodied in textbooks and well-established procedures while informal indicates context and subjective elements.

This article presents the research results from the development and assessment of a medical decision support system (MDSS). This system aims to support medical doctors in the diagnosis of epilepsy (including seizure type) with special emphasis on childhood episodes. Diagnosis of Epilepsy during childhood is difficult, because individual laboratory findings and symptoms are often inconclusive. Classification of epileptic syndromes is done according to the «International Classification of Epileptic Syndromes and Epilepsies». This classification is proposed by the “International League against Epilepsy” (ILAE) [ILAE81, ILAE89]. ILAE nomenclature, procedure and standards are extensively used in system modeling presented herein.

International classification includes more than 50 diagnostic categories for epilepsy and epileptic syndromes. More than 100 different factors (lab and EEG findings, symptoms, and clinical data) affecting epilepsy diagnosis should be assessed and effectively incorporated in a decision aid system, in order to distinguish between different diagnostic categories of ILAE.

We organize the article in sections. The first section reports epilepsy and discusses salient clinical aspects underlying system’s development and assessment. The next section presents the development methodology of the system that is implementation stages, system’s architecture, clinical cases representation and modeling of inference. Next, we summarize results in the “Assessment” section. Finally, we conclude the article by discussing the work performed so far and pointing to areas for further research.

2. THE EPILEPSY

Epilepsy is a chronic illness characterized from recurrent seizures that cause sudden but revertible changes in the brain operation [Ballis98]. According to ILAE there is a fundamental difference between seizures and epilepsies. Epilepsy is a chronic disorder while epileptic seizure is an acute phenomenon that has a beginning and an end. ILAE publishes periodically different classifications for seizures, epilepsies, and epileptic syndromes [ILAE81, ILAE89]. Causation of epilepsy is not always straightforward. Epilepsy in most cases is generated by acquired damages of brain cortex (symptomatic). However, brain predisposition to seizures is also a good reason for the appearance of the disease (idiopathic). The last international classification of ILAE [ILAE89] includes four main classes of epilepsies, namely:

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.

Prevalence rates of epilepsy have been reported from many countries, but there are significant differences among various studies [Cockerell96]. Nonetheless, most studies point a prevalence of 0.5% in the general population [Ballis98]. It is estimated that in England there are more than 300.000 with active epilepsy and over than 1.000.000 people with a history of seizures [Cockerell96]. The prevalence of epilepsy is bigger in children and elderly people (over 60), while the incidence is much bigger (75%) in children and in those under 20 years old [Cockerell96]. It has been estimated that 2-4% of children in Europe and United States before 4 years, have the experience of at least one epileptic seizure usually during fever [Hauser94]. Proportionally epilepsy affects more male than female population. Epilepsy may be a life-threatening condition, but there no documentary studies about that.

Diagnosis of epilepsy is achieved based on the type of the epileptic seizure observed. Various clinical data such as motor / physic/ somatosensory symptoms, impairment of consciousness, absence etc can help doctors to define the seizure type. On a second stage electroencephalograph’s (EEG) findings are also interpreted to clarify the seizure type, mainly by figuring out the focus and often they are very helpful for the diagnosis and the differential diagnosis of epilepsies. The epileptic seizure type and the electroencephalographic findings are the main diagnostic criteria used by the classification of epilepsies according to the international classification. Furthermore, very helpful for the diagnosis of epilepsy are the coexisting miscellaneous clinical data, patient’s demographics, as well as laboratory findings such as Computerized Tomography (CT) and Magnetic Resonance Imaging (MRI) [Cockerell96].
3. METHODOLOGY

The implementation of such diagnostic support system inevitable follows the conventional development of any other software. That is, we have to work out the basic stages of analysis, design, construction and benchmarking, namely the “life cycle” of a software system [Sommerville95]. On the other hand, a typical construction process of knowledge based systems, usually includes the development of three rudimental sub systems, (a) the knowledge base, (b) the inference engine and (c) the user interface. The implementation contains the phases of feasibility analysis, conceptual design, knowledge acquisition, knowledge representation and validation of the system [Parsaye88].

Attempts to develop computer programs that can diagnose medical condition began many decades ago [Ledley59] and various implementation methodologies have been proposed. However, there is no commonly accepted philosophy to guide the development of a medical decision support system [Healthfield93].

Our methodological framework combines the two major approaches of software construction, conventional and knowledge base. It includes four distinct phases, namely:

1. Identification of the most important data, to structure the knowledge base (analysis stage).
2. Development of knowledge base and design of inference engine (design stage).
3. Software development on the computer (implementation stage).
4. Testing the diagnostic system (assessment).

![Diagram of MDSS development framework]

3.1 Analysis

The proposed MDSS exploits the history, the clinical data, the laboratory tests and the EEG findings of the patient. We identified more than 100 different factors which support knowledge representation and modeling. These factors have been figured out by taking into consideration the diagnostic categories, the types of epilepsies, the epileptic syndromes and ILAE classifications [Dreifus89, ILAE89]. We divided these factors into the following four groups, motivated by clinical practice.

3.1.1 Patient demographics

This group includes pregnancy and delivery status and family inheritance. Demographic data are assessed using scales ranging from 1 to 5 (where, 1: normal, 2: suspicious, 3: slight pathological, 4: pathological, 5: sever pathological). Zero (0) indicates lack of information (unknown situation).

3.1.2 Clinical data.

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

Apart from the data related to the seizure, other clinical findings should be considered as well. That is, the behavior, the neurological estimation, the psychomotor development and (if applicable) the school performance of the patient. These are assessed using scales ranging from 1 to 5. Zero (0) again indicates lack of information (unknown situation).

3.1.3 Laboratory findings.

Laboratory findings encompass MRI and/or CT readings. Readings are summarized using a five point’s scale in proportion to the seriousness, while localization takes one of the following values: focal, diffuse, both and not traceable.

3.1.4 EEG Finding

EEG findings are very important for the diagnosis of epilepsy and they contain very helpful information for the classification of a patient case. They are sorted in four (4) main categories. Each category is in turn codified in subcategories. These subcategories correspond to specific EEG descriptions related to epilepsy and that could help and guide the doctor in her/his diagnostic procedure. Main 4 EEG categories are:

1. non-specific abnormal EEG patterns, as widespread intermittent slow abnormalities and bilateral/focal persistent findings (3 sub-categories),
2. abnormal EEG patterns - epileptic paroxysmal as spikes, polyspikes, sharp waves, spike wave complex, small sharp spikes, polyspikes of multiple spikes etc (12 sub-categories),
3. specific EEG patterns, as hysparrhythmia, rolantc spikes, typical neonatal EEGs etc (26 sub-categories in total) and
4. epileptic EEG findings in specific recordings as during sleep, photostimulation, hyperventilation, during seizure, longtime recording, video recording etc (9 sub-categories).

Analyzing the above, significant for the task, data we conclude specific rules that govern the knowledge base of the system. The last procedure in this stage was the detailed theoretical examination of these rules by firing them on sample data, in order to check their correctness.

3.2 Design

The inference mechanism that has been developed for the software in question aims at the full exploitation of the knowledge stored in the system, in order to derive precise results. A simple inference mechanism would be inadequate due to the complexity of the problem. Thus, the methodology described below was adapted.

Initially, for each diagnostic category reported in the international classification of ILAE, we have developed a corresponding set of rules that could derive conclusions for that category. That way the knowledge base (KB) is partitioned into sets of rules. For each KB partition an independent diagnostic sub-system has been developed. These diagnostic sub-systems are easily implemented and make use of the backward chaining technique. We have developed more than forty-five (45) such KB partitions in our system. There is one KB partition, for each diagnostic category (epilepsy type). Examining a patient case, the inference engine of the system should evaluate sequentially each such KB partition in order to derive the diagnostic category that fits the specific case. Guiding the inference engine to process all the implemented KB partitions creates the assumption that all the diagnostic categories, proposed by the international classification, are active hypotheses. However, this process is time-consuming, and eventually costs to the overall performance of the system in real life application of the system. It is also possible to derive confusing suggestions, as the examination order of the KB partitions is critical to the system complexity [Musen97].

We have created clusters of hypotheses based on unexceptionably criteria arising from the input data [Szolovits88]. We have done that in order to reduce the number of hypotheses and to avoid a possible wrong sorting, of the KB partitions. Observations concerning the type of the epileptic seizure, the findings of EEG and the age of the patient could help a lot for the formation of these clusters. This applies especially for the diagnosis of epilepsy in childhood [Dreifus89, Cockerell96]. Therefore, each implemented cluster contains a number of diagnostic categories (active hypotheses) that are characterized by similar symptoms. In other words, cluster contains a subset of KB partitions. A decision tree is used by the inference mechanism in order to derive these clusters of active hypotheses. Examination of the critical data is taking place in each node of the decision tree. Finally, the inference engine of the system explores each hypothesis in the concluded cluster. That is, the
The inference process is driven by the data. It reaches at the most precise conclusions by using the decision tree, i.e. clusters. The aforementioned methodology is shown in Figure-2.

The root of the decision tree is based on the determination of the seizure type, which is the most important data in the case of the diagnosis of epilepsy. For that reason, a separate diagnostic sub-system has been constructed, which classifies the epileptic seizure through interaction with the user. The conclusions of this first sub-system will initially direct the course in the decision tree.

The aim of this hierarchical handling of the knowledge base is to make the reasoning less complicated and more rational. This hierarchy introduces three levels of abstraction when a case is examined. The first level concerns the seizure type. The second level concerns the concluded cluster. Finally the third level of abstraction concerns the evaluation of the rule partitions existing in the concluded cluster. In sort, the steps of the diagnostic mechanism of the system are the following:

1. Decide about the epileptic seizure type (consult the separate decision support sub-system).
2. Based on the results of the previous step and according to the input data, follow the decision tree to get the proper cluster of active hypotheses.
3. Examine the rule partitions for all the active hypotheses in the cluster.
4. If the system gets results, it will propose conclusions.

The design of this methodology aims mainly at the minimization of the time spent for the search of the appropriate rules. This results in less complicated reasoning to the right diagnosis.

Construction (Operational characteristics)

During this stage the formalized knowledge base and the designed inference engine are implemented. In addition, a prototype has also been implemented in order to verify the analysis and design concepts of our methodology.

The operational environment of the diagnostic support system is the well-known MS-Windows (any edition). Initially, the user-doctor inputs patient’s data in order to decide about the type of epileptic seizure. The system derives epileptic seizures which are compatible with the international classification [ILAE81]. Next, historical, clinical and laboratory data, such as the features of the electroencephalograph, are also given to the software. The diagnostic system most probably asks the user for additional data as well, according to the patient case. For instance, it may ask for the extent or the intensity of the seizure, or for the conditions of incidence, etc, in order
to be led to a distinct diagnosis. The data are given to the system through menu driven lists of all alternatives, that in order to eliminate data entry mistakes. The result of the diagnosis suggested always complies with the categories of epilepsy described in the international classification.

There are three levels of certainty grading, concerning the conclusions inferred from the diagnostic system: «absolute certainty», «great possibility» and «possibly». In the cases where the patient has experienced epileptic seizures in the past or where she/he is under medical treatment, the system recommends to the user not to take the proposed result into account. In some other 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. 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 these cases, the system proposes alternative diagnoses.

4. ASSESMENT & RESULTS

A set of patient cases were examined using the diagnostic system, in order to examine the completeness of the knowledge base, to ascertain the correctness of the inference engine, to evaluate the diagnostic precision of the system and to make potential improvements. The diagnoses of the system were compared with those pronounced by expert child neurologist.

The collected material consists of 122 cases of epilepsy for children up to 15 years old. From those cases, 56 concerned girls and 66 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. The whole range of the main categories of the international classification of diagnoses is covered by the above-mentioned material.

Processing the material by the system, we got the following results:
- in 104 cases (85.2%), the diagnoses were identical with those of the neurologist,
- in 8 cases (6.6%), the diagnoses were different from those of the expert neurologist,
- in 10 cases (8.2%), the diagnoses were similar to the specialist (acceptable by him).

Thus, the results of the DSS were adequate in 93.4% of the cases. The system seems to perform better in localization related cases of epilepsy. In this case, 89.1 % of its diagnoses were identical to those of the neurologist while in 9.1% of the cases were adequate. The worst results were obtained in cases of undetermined epilepsies (focal and generalized). In these cases only 66.7% DSS diagnoses were identical to those of the neurologist. In the cases of generalized epilepsy we got 83.3% correct (identical to neurologist) DSS diagnoses. Finally, in cases of special syndromes we got 87.5% correct DSS diagnoses. Initial results were published in [Vassilakis01, Vassilakis02].

5. CONCLUDING REMARKS

We have developed a decision support system to help the diagnosis of epilepsies and epileptic syndromes in childhood. We used it with promising results in 122 cases belonging to a large variety of these diseases. Eight (8) cases were misdiagnosed by our system. Two children were included, which had been receiving treatment for a long time. The EEG findings in these cases were inadequate. In five cases the diagnoses were compatible with international classification of ILAE, but different from those of specialist. Finally, in one child, the DSS could not lead to diagnosis due to the ambiguity of the clinical picture.

Another diagnostic system called Epilepsy Expert was developed by Leena Korpinen [Korpinen93]. It is one of the first known Decision Support Systems for the diagnosis of epilepsies. Korpinen’s diagnostic system combines decision tree techniques and hypertext facilities. It contains four independent subsystems (modules) that the user can choose from, to enter information about the patient. It can be characterized more as an advisory system that the user could consult, since it contains a lot of text data. Emphasis is placed on the presentation of the diagnostic alternatives in textual mode. The performance of Epilepsy Expert was 72% correct 8% partly correct and 20% incorrect diagnoses. The module of the Epilepsy Expert, developed using hypertext techniques, was rather successful giving results close to the experts in 80% of the cases, while the other modules proved to be weaker [Korpinen94]. Our system has better performance than Epilepsy Expert and it is especially designed for children. Our objective was to construct a system which uses information not confined to symptoms and is endowed with more precise diagnostic abilities.

Our MDSS uses pure knowledge based techniques and introduces a new methodology to address this medical problem. It begins with the introduction of seizure type observed, thus helping the user to choose from the entries of the international classification. Then the software attempts to narrow the set of hypotheses, by taking into account the EEG findings and posing relevant questions to the user. Our methodology decomposes
diagnosis into a set of smaller size sub-diagnoses. Thus, diagnosis size and complexity are reduced with no loss in diagnostic accuracy. We placed particular emphasis in designing a decision system which can reach a correct diagnosis on its own, rather than allowing the user to choose between alternatives.

Decision making in medicine involves uncertain and vague knowledge. Future improvements of this system should deal with this kind of knowledge. We should see patient’s data, that is patient history, clinical data, laboratory tests and EEG findings, to be enhanced with doctor’s belief about the contribution of each one to the diagnosis. For instance, let’s take the clinical findings “seizure focus” and “seizure severity” of epileptic seizure. Each specific value for “seizure focus”, i.e. frontal, parietal, occipital, multiple, temporal and unknown, will weigh differently for each type of epilepsy where it is applicable. Similarly, each value of “seizure severity”, i.e. slight, intermediary, severe, status and unknown, has a different contribution to the type of epilepsy where it is applicable. The reasoning of such a decision system will depend on the certainty factors that have been assigned to medical attributes which affect the decision process. The new approach may have rules of the following form:

\[
\text{if } (\text{Seizure} = i a 1)^{CF=0.7} \land (\text{Seizure\_focus} = \text{temporal})^{CF=0.8} \land \ldots \text{ then } (\text{Epilepsy\_type} = 1.1.A)^{CF=c}
\]

Each expression in the assumption of a rule is associated with doctor’s believe about the weight of the corresponding medical attribute (data). The above rule expresses the belief of a doctor about the contribution (weight) that the patient’s “seizure type” (for a specific value) and “seizure focus” (for a specific value), etc, may have when the epilepsy type is “1.1.A”. Note that “c” is a real in [0, 1]. The final percentage for the derived epilepsy (conclusion of the rule) can be calculated using techniques such as certainty factors [Buchanan84, Parsaye88, Rowe88, Rich91].

In addition, our system can be enhanced with a knowledge base maintenance component. This component should allow a specialist, i.e. doctor, to perform the following operations on the knowledge base (KB): (1) Extending the KB with new rules, (2) retrieval in graphical form any rule from the KB, for reviewing purposes and (3) modification of any rule of the KB.

In general, our diagnostic system drives to the right diagnosis for the majority of the tested cases. Thus, this may constitute a very useful, auxiliary diagnostic tool. Such knowledge-based systems are very helpful for the diagnosis and the differential diagnosis of epilepsy, especially during childhood, where there are many epileptic syndromes that make difficult the doctor’s decision.

The diagnostic ability of a MDSS is always a result of series of limited data analysis, no matter how accurate and rational it is. So the treating doctor should always have the last word. Nevertheless, he can always refer to such a system, in order to verify her/his diagnosis. The system’s results can be of consultative character. A very useful application of the specific MDSS is as an educational tool for students of medicine or child neurologists during their formative period. That because its development has been based on the international classifications of ILAE and the system formally approximates the medical human thinking by considering multitude parameters to reach a diagnosis.
REFERENCES


