Expert System for Epilepsy with Uncertainty

Emmanuil Marakakis¹, Kostas Vassilakis¹, Emmanuil Kalivianakis¹, Sifis Micheloyiannis²
¹ Science Department, Technological Educational Institute (TEI) of Crete, ²School of Medicine, University of Crete
Heraklion, Crete, Greece
[mmarak, kostas]@cs.teicrete.gr, mkaliv@venus.cs.teicrete.gr, mixelogj@med.uoc.gr
http://www.cs.teicrete.gr

Abstract
This paper presents an expert system which derives differential diagnosis about epilepsy cases in childhood, according to international classifications. This expert system is intended to be used as a consultation system by neurologists. The physician specialist can update the knowledge base of the system through a user friendly interface. Uncertainty is handled by using weights and certainty factors. Meta-rules drive the reasoning process of the system. The initial evaluation results of the system are very promising, i.e. 83.3% successful diagnosis.

Keywords: Expert systems, meta-rules, uncertainty, and epilepsy.

1. Introduction
Epilepsy is a chronic disease characterized from recurrent seizures that cause sudden but reversible changes in the brain operation. Classification of epilepsy cases, according to international classifications, during childhood is difficult because individual laboratory findings and symptoms are often inconclusive.

This paper presents the development of an expert system which diagnoses medical formal diagnostic categories of epilepsy. The diagnosis of epilepsies by our system follows the classification of epileptic syndromes and epilepsies of International League Against Epilepsy (ILAE) [1]. Our expert system is called HIPPOCRAT-EES (HIPPOCRATes Epilepsy Expert System - Hippocrates had made the first observations on Epilepsy). This system is intended to be used by neurologists specialized on epilepsy domain. The reasoning mechanisms of the system simulate the reasoning process of top neurologists. The system’s inference engine applies uncertain reasoning by using weights and certainty factors, suggested by expert physicians. Meta-knowledge guides the reasoning process of the HIPPOCRAT-EES. The interface of the system is window-based and user-friendly. The working environment is proportional to the real clinical environment of neurologist. In addition, the interface for updating the knowledge base (KB) takes into consideration the computing capabilities of end users, i.e. neurologists.

A decision support system (DSS) for epilepsy classification in childhood is presented in [2]. This DSS divides knowledge base into a set of independent sections. The system accepts as input the symptoms of the epileptic seizure and classifies this seizure based on the international classification of epileptic seizures [3]. Then, the user inputs clinical and laboratory data in order to build a decision tree which represents the possible diagnoses. The system further questions the physician in order to discriminate the final diagnosis among the possible ones. The methodology in [2] decomposes diagnosis into a set of smaller size sub-diagnoses. Thus, diagnosis complexity is reduced. Design emphasis is given on features that direct the system to reach a correct diagnosis on its own, rather than allowing the user to choose between alternative diagnoses. The system’s diagnosis follows the “international classification of epilepsies and epileptic syndromes” [1].

Another diagnostic epilepsy system called “Epilepsy Expert” is presented in [4]. This system is designed to diagnose epilepsy for both children and adults. It combines techniques from decision trees, if-then rules and hypertext. The user can select one of its four subsystems for the diagnosis task. Each subsystem uses a different methodology for diagnosis. This system derives several alternative diagnoses. These diagnoses consist mainly of hypertext information which could be used as advice by the physician.

The above systems do not consider uncertainty. Our expert system supports the following operations. First, the physician fills in the symptoms and the lab findings of the patient. HIPPOCRAT-EES responses with a list of possible epilepsy types (differential diagnosis) sorted in increasing order based on
certainty factors. Second, the doctor specialist can update the knowledge base from a window-based, pop-up menu driven interface. Finally, the physician can have graphical display of the rules of the system. This feature helps the user to understand the decision process of the system and eventually update the rules.

The remainder of this paper is organized as follows: Section 2 focuses on the methodology that has been followed for the development of HIPPOCRAT-EES. Section 3 presents the evaluation results of our system. Finally, Section 4 discusses conclusions and future work.

2. Methodology
2.1 Knowledge Representation
According to our conceptual design each epilepsy type corresponds to one rule of the knowledge base. ILAE classification suggests more than 50 epilepsy types [1]. Each epilepsy type, in our system, is expressed in terms of 28 diagnostic criteria, according to the expert neurologist. These criteria are the following [2], [5]:

Seizure type, seizure focus, seizure severity, electroencephalogram (EEG) type, patient age, pregnancy status, delivery status, family inheritance, school performance, lab findings existence, lab finding focus, behavior estimation, neurological estimation, psychomotor development, vocalization during seizure, fever, number of seizures per day, seizure during/after sleep, metabolic symptoms, toxic poisoning, head injury, existence of disease that affects the nervous system, existence of disease that does not affect the nervous system, acquired aphasia symptoms, primary visual ictal seizure, speech problems during seizure, behavioural problems during seizures.

There are 19 different seizure types [3] and about 41 different EEG types [2], [5]. The general form of the if-then rules is as follows:

\[
\text{If } (\text{Seizure_{type} \in ST_{set}}) \land \\
(\text{Seizure_{focus} \in SF_{set}}) \land \\
(\text{Seizure_{severity} \in SS_{set}}) \land \\
(\text{EEG \in EEG_{set}}) \land \\
(\text{Age \in Age_{set}}) \land \\
(\text{Pregnancy\_status \in PS_{set}}) \land \\
(\text{Delivery\_status \in DS_{set}}) \land \\
(\text{Family\_inheritance \in FI_{set}}) \land \\
(\text{School\_performance \in SP_{set}}) \land \\
(\text{Lab\_findings \in LF_{set}}) \land \\
(\text{Behavior \in Be\_set}) \land \\
(\text{Neurological\_estimation \in NE_{set}}) \land \\
(\text{Psychomotor\_development \in PD_{set}}) \land \\
(\text{Lab\_focal \in LFoc\_set}) \land \\
(\text{Vocalization \in yes\_no\_set}) \land \\
(\text{Seizures\_Per\_Day \in SPD\_data\_set}) \land \\
(\text{Seizure\_During\_Sleep \in yes\_no\_set}) \land \\
(\text{Seizure\_After\_Sleep \in yes\_no\_set}) \land \\
(\text{Seizure\_Fever \in yes\_no\_set}) \land \\
(\text{Metavolic\_Symptoms \in yes\_no\_set}) \land \\
(\text{Toxic\_Poisoning \in yes\_no\_set}) \land \\
(\text{Head\_Injury \in yes\_no\_set}) \land \\
(\text{Neurous\_System\_Disease \in yes\_no\_set}) \land \\
(\text{NOT\_Neurous\_System\_Disease \in yes\_no\_set}) \land \\
(\text{Acquired\_Aphasia \in yes\_no\_set}) \land \\
(\text{Primary\_Visual\_Ictal\_Seizure \in yes\_no\_set}) \land \\
(\text{Speech\_Problems \in yes\_no\_set}) \land \\
(\text{Behavior\_Problems\_During\_Seizure \in yes\_no\_set})
\]

then Epilepsy_{type} = ET

where, \( \land \) stands for and. All the elements of the sets ST_{set}, SF_{set}, ..., LF_{set} are pairs of the form (value, weight). The elements of the yes_no_set are pairs of the forms (yes, weight) and (no, weight). The elements of the set SPD_{data_set} have the form ((minimum_value, maximum_value), weight). ET has the form (epilepsy type, certainty factor). The certainty factor is derived from the weights of the diagnostic criteria.

The rules of our system have been implemented in SICStus Prolog [6]. Each rule of HIPPOCRAT-EES has been implemented as a Prolog fact and as a Prolog rule. This implementation allows the dynamic update of the knowledge base of the system by using the meta-programming features of Prolog.

2.2 Reasoning under uncertainty
The term uncertainty means non-availability of accurate information in decision making. The main sources of uncertainty in problem solving are due to imprecise data, incomplete data, and subjective description of knowledge. The existence of uncertain knowledge requires the development of reasoning mechanisms which will handle this type of knowledge. Several techniques have been proposed to handle uncertain knowledge like certainty factors, fuzzy logic and others. Experts use inexact reasoning methods because exact methods either may not be known or may be impractical. Inexact methods of reasoning are important in many expert systems applications. Correct medical diagnosis is possible to be derived from ambiguous symptoms.
Certainty Factors (CF) in our system are arithmetic values in the interval [0, 1]. They express the expert’s belief for the truth of the derived epilepsy type. Each value represents the degree of truth of the derived epilepsy type. For example, the values 1, 0.5 and 0 stand for absolute certainty, 50% certainty and 0% certainty, i.e. absolute uncertainty, for the truth of the derived epilepsy type. Certainty factors appear only in the conclusions of the rules of HIPOCRAT-EES.

Weights are assigned to each sub expression in the premise of each rule. That is, each of the 28 diagnostic criteria is assigned a weight. The weights are values in the interval [0, 1]. Each weight represents a percentage of the certainty factor of the derived epilepsy type. The weight of each of the 28 diagnostic criteria contributes to the certainty factor, truth, of the conclusion of the rule. Let’s assume that a diagnostic criterion has weight w. This means that the weight of this criterion for the truth of the epilepsy type is w. For example, weight 1 or 0.5 or 0.03 etc in the value of a diagnostic criterion in the premise of a rule means contribution to the certainty factor of the epilepsy type in the conclusion of the rule by 1 or by 0.5 or by 0.03 etc respectively. Weight 0 in a value of a diagnostic criterion in the premise of a rule has one of the following meanings:

1) The specific value of this criterion does not contribute to the certainty factor of the epilepsy type in the conclusion of the rule.
2) I don’t know the weight of the specific value of this criterion.
3) I don’t care about the weight of the specific value of this criterion for the conclusion of this rule.

The certainty factor CF of the conclusion of each rule is the summation of weights of sub expressions in rule hypothesis. The summation of weights expresses the expert’s belief for the truth of the derived epilepsy type. If we see a rule as a tree then the certainty factor of the rule corresponds to the total weight of the tree [7]. The summation of the weights in the premise of each rule must be ≤ 1. This is verified by the system during construction of the rule.

Instances of rules of the following general form are derived for each patient case.

\[
\text{School\_performance} = \text{Value\_SP} \wedge \\
\text{Lab\_findings} = \text{Value\_LF} \wedge \\
\text{Behavior} = \text{Value\_B} \wedge \\
\text{Neurological\_estimation} = \text{Value\_NE} \wedge \\
\text{Phychomoto\_development} = \text{Value\_PD} \wedge \\
\text{Lab\_focal} = \text{Value\_LFOc} \wedge \\
\text{Vocalization} = \text{Value\_Voc} \wedge \\
\text{Seizures\_per\_day} = \text{Value\_SPD} \wedge \\
\text{Seizure\_during\_sleep} = \text{Value\_SDS} \wedge \\
\text{Seizure\_after\_sleep} = \text{Value\_SAS} \wedge \\
\text{Fever\_in\_seizure} = \text{Value\_FIS} \wedge \\
\text{Metabolic\_symptoms} = \text{Value\_MS} \wedge \\
\text{Toxic\_poisoning} = \text{Value\_TP} \wedge \\
\text{Head\_injury} = \text{Value\_HI} \wedge \\
\text{Nervous\_system\_disease} = \text{Value\_NSD} \wedge \\
\text{NOT\_Nervous\_system\_disease} = \text{Value\_NNSD} \wedge \\
\text{Acquired\_aphasia} = \text{Value\_AA} \wedge \\
\text{Primary\_visual\_ictal\_seizure} = \text{Value\_PVIS} \wedge \\
\text{Speech\_problems} = \text{Value\_SP} \wedge \\
\text{Behavior\_problems\_during\_seizure} = \text{Value\_BPDS} \wedge \\
\text{Epilepsy\_type} = \text{Value\_ET}\]

For this rule instance we have,

\[
CF = W1 + W2 + W3 + \ldots + W28 \leq 1.
\]

and \(W1 + W2 + \ldots + W28 \leq 1\). The calculated certainty factor CF of the conclusion is the expert’s belief of the truth of the derived epilepsy type that is based on the weights of 28 diagnostic criteria.

The values of certainty factors are estimations of the experts. This is one advantage over statistical methods which require collection of complete sets of data. In addition, certainty factors have simple computations. This is another advantage over methods like Bayesian inference and fuzzy logic.

This method of weights and certainty factors to uncertainty is the most suitable for this problem domain because expert neurologists follow this approach during diagnosis. That is, we have simulated the diagnosis reasoning mechanism of experts. The certainty factors in our system are quite different from the conventional one in [8],[9]. The main different features in HIPOCRAT-EES are the following:

1) Certainty factors take values in interval [0,1]. That is, disbelief is not measured.
2) Certainty factors are not combined because rules are not combined.
3) Rule premises have weights and rule conclusions have certainty factors. In addition, certainty factors are derived from weights in rule premises.

2.3 An Example

The rule for the epilepsy type named “localization-related, idiopathic, benign frontal epilepsy” (coded as 1.1.E) is as follows:

\[
\text{If } \begin{align*}
\text{Seizure_type} &\in \{\text{ia1, 0.2}, \text{ic, 0.2}, \text{ib1b, 0.2} \} \\
\text{Seizure_focus} &\in \{\text{frontal, 0.05}, \text{anything, 0.0} \} \\
\text{Seizure_severity} &\in \{\text{slight, 0.05}, \text{intermediary, 0.05}, \text{anything, 0.0} \} \\
\text{EEG} &\in \{\text{c33, 0.3}, \text{c34, 0.3}, \text{b1-f, 0.3}, \text{anything, 0.0} \} \\
\text{Age} &\in \{\text{3, 0.03}, \text{4, 0.05}, \text{5, 0.05}, \text{6, 0.05}, \text{7, 0.05}, \text{8, 0.05}, \text{9, 0.03} \} \\
\text{Lab_findings} &\in \{\text{normal, 0.05}, \text{anything, 0.0} \} \\
\text{Vocalization} &\in \{\text{yes, 0.3} \}
\end{align*}
\wedge
\text{then } \text{Epilepsy_type} = (1.1.E, \text{CF})
\]

Where:

- “ia1”, “ic”, and “ib1b” are the coded types of the seizures “simple partial with motor symptoms”, “partial secondary generalized”, and “complex partial - begins simple partial and ends up to impairment of consciousness” respectively.
- “c33”, “c34”, “b1-f” are the coded types of the EEGs, “frontal paroxysms”, “frontal paroxysms - in sleep only”, “spikes (single, random or many) with frontal focus” respectively.

Let’s assume that the clinical and laboratory data values of a patient case are as in Table 1. Based on this clinical and laboratory data of patient the system fires among others the rule for epilepsy type “localization-related, idiopathic, benign frontal epilepsy” (1.1.E).

<table>
<thead>
<tr>
<th>Findings-symptoms</th>
<th>Values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Seizure Type</td>
<td>ia1</td>
</tr>
<tr>
<td>Seizure Focus</td>
<td>frontal</td>
</tr>
<tr>
<td>Seizure Severity</td>
<td>don’t know</td>
</tr>
<tr>
<td>EEG Type</td>
<td>b1-f</td>
</tr>
<tr>
<td>Age</td>
<td>7</td>
</tr>
<tr>
<td>Family Inheritance</td>
<td>suspicious</td>
</tr>
<tr>
<td>Lab Findings</td>
<td>suspicious</td>
</tr>
<tr>
<td>Vocalization</td>
<td>yes</td>
</tr>
</tbody>
</table>

Table 1: Sample of clinical and laboratory data.

The instance of this rule that is evaluated is the following.

\[
\begin{align*}
\text{(Seizure_type = ia1)}^{W_1=0.2} \wedge \\
\text{(Seizure_focus = frontal)}^{W_2=0.05} \wedge \\
\text{(Seizure_severity = anything)}^{W_3=0.0} \\
\text{then } \text{Epilepsy_type} = \text{1.1.E, CF}
\end{align*}
\]

The final certainty factor is the summation of the weights of the diagnostic criteria of the hypothesis. That is,

\[
\text{CF} = 0.2+0.05+0.0+0.3+0.0+0.3 = 0.9
\]

The diagnostic category named localization-related, idiopathic, benign frontal epilepsy (1.1.E) will be in the list of epilepsy types suggested by the system with CF 0.9.

2.4 Meta-rules and the Diagnosis Process

The clinical and laboratory values for a specific patient are inserted into the system. The system fires rules in order to derive possible epilepsy types and the corresponding certainty factors. There are four meta-rules which guide the rule selection. These meta-rules drive the diagnosis process by following different diagnostic paths. The design of these meta-rules depends on four classes of important clinical and laboratory data which direct the diagnosis towards specific classes of epilepsy types.

Seizure Type Meta-rule.

The seizure type is an important clinical criterion. This criterion results in the selection and firing of the rules that have in their premises a sub expression with same seizure type as the one of the patient case.

The EEG Type and the Seizure Focus Meta-rules.

Sometimes EEG focus is not same as the seizure focus. The estimation of seizure focus is derived subjectively by the physician. On the other hand, EEG focus is derived mechanically. When a neurologist has observed a seizure focus, he assumes it as important factor for the diagnosis. If he doesn’t observe any focus, then he assumes seizure as generalized. In this case, EEG results are critical for the diagnosis especially if they show focus acceptable by the physician. Therefore, EEG data and the seizure’s focus are combined to formulate the following meta-rule.

\[
\text{if the EEG’s focus is not same as seizure’s focus then}
\]

the reasoning process is directed by the seizure’s focus;

\[
\text{if the seizure type is generalized (no focus) then}
\]

the reasoning process is directed by the EEG’s potential focus;
This meta-rule specifies the important diagnosis criterion for certain cases of patients. Then, rules are selected and fired based on this criterion.

**Important Electroencephalograph (EEG) Types Meta-rule.**

There are some specific EEG types which affect very much the final conclusion, i.e. the derived epilepsy type. For example, the observation of “rolantic spikes” in EEG directs diagnosis towards “localization-related, idiopathic, benign childhood epilepsy, with centrotemporal spikes”. In most such cases no other data are required in the diagnosis process. Let’s assume that $S$ is the set of specific EEG types. This meta-rule is formulated as follows:

If the lab data have shown an EEG type $g$ and $g \in S$ then the derivation of the diagnosis is based on the EEG data

**Secondary Symptoms Meta-rule.**

This meta-rule uses the following list of secondary symptoms in order to select appropriate rules. One or more of these symptoms may have occurred in a patient case.

- Vocalization during seizure
- Seizures per day
- Seizure during sleep
- Seizure after sleep
- Fever before and during Seizure
- Metabolic symptoms
- Toxic poisoning
- Head injury
- Nervous system disease
- NOT a nervous system disease
- Acquired aphasia
- Primary visual ictal seizure
- Speech problems
- Behavior problems during seizure

2.5 Illustration of HIPPOCRAT-EES through Screen Snapshots

The screen snapshots in figures 1, 2, 3, and 4 illustrate some features of HIPPOCRAT-EES. Note that the interface of the system has been implemented in Visual Basic. The first and second screen snapshots illustrate the forms that have to be filled in by a neurologist for a patient and the system’s response from the processing of these data. The third and the fourth screen snapshots illustrate the list of available rules in the KB and their graphical presentation. The weight of each data value is shown by touching the value with the mouse.

3. Results

HIPPOCRAT-EES has been tested in 42 cases of children with seizures. The evaluation of our system has shown the following preliminary results.

- HIPPOCRAT-EES has correctly diagnosed 35 cases out of 42, i.e., 83.3% successful diagnosis.
- In addition, 3 correctly diagnosed patient cases out of 42, i.e. 7.1%, were in the lists of possible ones.

Note that the correct diagnosed cases had the highest certainty factors in the suggested list of the possible ones. The total successful diagnosis of HIPPOCRAT-EES is 90.4%.
4. Conclusions

HIPPOCRAT-EES preliminary results are satisfactory compared with the results of the systems in [2] and [4].

The results from the evaluation of the decision support system in [2] are as follows. The system has derived correct diagnosis in 85.2% of patient cases, partial successful diagnosis in 8.2% of patient cases and absolute incorrect diagnosis in 6.6% of patient cases. The diagnosis of the DSS in [2] is more accurate than the one of HIPPOCRAT-EES. On the other hand, the DSS in [2] does not derive alternative diagnoses as HIPPOCRAT-EES does. In addition, the KB of the DSS in [2] can not be updated by physicians like HIPPOCRAT-EES.

The diagnosis of the system in [4] has been compared with the diagnosis of three experts. The evaluation results are 72% correct diagnoses, 8% partially correct diagnoses and 20% incorrect diagnoses. The evaluation of the subsystem that uses electroencephalographs for the diagnosis has given 48% correct diagnoses, 28% partially correct diagnoses and 24% incorrect diagnoses. The subsystem which is based on hypertext has given the best results, i.e. 80% correct diagnoses [10]. The performance of HIPPOCRAT-EES is better than the system in [4]. In addition, the system in [4] can be characterized more as an advisory system that the user could consult, rather than as a diagnostic tool like HIPPOCRATES-EES.

We expect the performance of HIPPOCRAT-EES to be further increased by adjusting the weights in the rule premises. Neurologists can enrich the KB of the system and refine the rules which do not derive accurate diagnosis. The methodology of HIPPOCRAT-EES could be applied to any rule-based expert system, whose significance of terms in hypotheses of rules has to be specified.

The use of weights to express the significance of terms in hypotheses of rules specified by expert physicians and to derive the certainty factors of rules is a novel one. It is not used in any rule-based expert system, whose significance of terms in hypotheses of rules has to be specified.

The use of weights to express the significance of terms in hypotheses of rules specified by expert physicians and to derive the certainty factors of rules is a novel one. It is not used in any rule-based expert system, whose significance of terms in hypotheses of rules has to be specified.

1) The use of uncertain reasoning.
2) The graphical presentation of the rule base.
3) The adaptability of the system to new knowledge. That is, the rule base of the system can be updated directly by the doctor specialist without intervention from the knowledge engineer.
4) The use of meta-rules to direct the reasoning of the system.

The strengths of our system are: a) the efficient way of representing expert’s beliefs about the significance of terms in the hypotheses of rules and b) the adaptability of the method to other application domains. On the other hand, the limitation of this method is that significance of terms specified by experts may be inaccurate.

The features of our system that can be further improved and the directions for future research are as follows.
1) The uncertainty reasoning mechanism can be improved by adjusting the weights in some rules. Fuzzy logic can be considered as an alternative technique for uncertainty.
2) A machine learning subsystem can be added into our system. Such a component can derive rules from diagnosed cases of patients.
3) An explanation reasoning subsystem is required as well.

This expert system is intended to be used as a consultation system by neurologists in order to reach a decision and for differential diagnosis of epilepsy cases.

Acknowledgements

This study is partially supported by:
- BIOPATTERN: Computational Intelligence for biopattern analysis in Support of eHealthcare (EU - 6th FP/IST).
- Archimedes II: Funding of research groups at Technological Educational Institute of Crete (EU-ESF, Operational Programme for Education and Initial Vocational Training).

References


