



A Novel Analysis of Diabetes Mellitus by Using Expert System Based on Brain Derived Neurotrophic Factor (BDNF) Levels

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Abstract:

In this paper a novel concept of designing and building intelligent expert system for the detection and diagnosis of Diabetes Mellitus is introduced. The expert system classification is based on critical diabetic parameters like Brain-Derived Neurotrophic Factor (BDNF) levels, and Fasting Blood Glucose (FBG). The proposed rule-based expert system constructs large-scale knowledge-base based on the behavior of the BDNF related diabetic data. The system will give an expert decision taking into consideration all the valid ranges of diabetic parameters. The proposed expert system can work effectively even for large sets of patient data.

Keywords:

BDNF, FBG, Type2 diabetes mellitus, expert system, and rule based system.

Introduction:

Expert or knowledge-based systems are the commonest type of AI systems in routine clinical use. They contain medical knowledge, usually about a very specifically defined task, and are able to reason with data from individual patients to come up with reasoned conclusions. Although there are many variations, the knowledge within an expert system is typically represented in the form of a set of rules ^[1]. Rule based system can be used to develop the knowledge base used by expert systems. Given a set of clinical cases that acts as examples, rule-based system can produce a systematic description of those clinical features that uniquely characterize the clinical condition. This knowledge can be expressed in the form of simple rules or often as decision tree. Figure 1 shows the concept of a knowledge based expert system. The expert system receives facts from the user and provides expertise in return. The two main components of an expert system (invisible from outside) are the knowledge base and inference engine. ^[2]

Knowledge Base: It contains the domain knowledge coded in the form of knowledge. It stores all relevant information, data, rules, cases and relationships used by the expert system. The knowledge base can combine the

knowledge of multiple human experts. A knowledge base is the nucleus of an expert system. A knowledge base is not a data base. The knowledge base is created by the knowledge engineers who translate the knowledge of real human experts into rules. In a rule based expert system a knowledge base is usually stored in terms of if-then rules. The knowledge base of expert systems contains both factual and heuristic knowledge. *Factual knowledge* is that knowledge of the task domain that is widely shared, typically found in textbooks or journals, and commonly agreed upon by those knowledgeable in the particular field. *Heuristic knowledge* is the less rigorous, more experiential, more judgmental knowledge of performance. In contrast to factual knowledge, heuristic knowledge is rarely discussed, and is largely individualistic. It is the knowledge of good practice, good judgment, and plausible reasoning in the field. For the difficult problems with which expert system are concerned it uses heuristics: Strategies that often lead to correct solution, but that also sometime fail.

Inference Engine: The Inference engine may infer solutions or conclusions from the knowledge base, based on the facts supplied by the user. The inference engine acts as an interpreter or scheduler that interprets which rules matches with the facts. The word inference or reasoning is very important in expert system; because reasoning is the standard technique by which expert system solve problems. It makes inferences by deciding which rules are satisfied by facts, prioritizes the satisfied rules, and execute the rule with the highest priority. These conclusions are the expert system's response to the user queries, as the user supplies facts or other information to the expert system for getting the expertise or expert advice. So the purpose of inference engine to seek information and relationship from the knowledge base and to provide answers, predictions and suggestions in the way a human expert would. The inference engine must find the right facts, interpretations and rules and assemble them correctly. Two types of inference methods are commonly used.

Forward Chaining and backward chaining

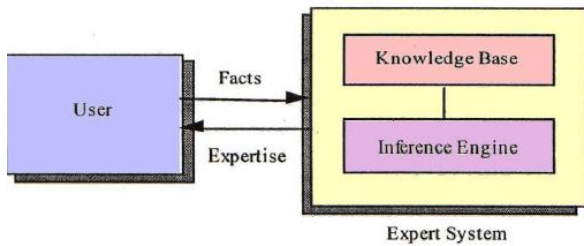


Fig.1: Main components of an expert system

The other components are:

User interface: The mechanism by which the user and the expert system communicate. There is specialized user interface software available, that can be used to designing, updating and using expert system. The purpose of user interface is to ease use of expert system for developers, users and administrators.

Explanation facility: The explanation facility allows the user to understand how the expert system arrived at certain results. It explains the reasoning of the system to the user.

Working memory: It is a global database of facts used by the rules. This data is supplied by the end user.

Agenda: A prioritized list of rules created by the inference engine, whose patterns are satisfied by facts in working memory.

Knowledge acquisition facility: The overall purpose of knowledge acquisition facility is to provide a convenient and efficient means for capturing and storing all components of a knowledge base. It also provides an automatic way for the user to enter knowledge in the system instead of having the knowledge engineer explicitly code the knowledge. The knowledge acquisition facility is an optional feature on many systems. Some expert system tools like KEE (Knowledge Engineering Expert) can learn by rule induction through examples and can automatically generate rules. The examples are generally from tabular or spreadsheet type data better suited to decision trees. General rules constructed by knowledge engineer can be much more complex than the simple rules from rule induction. Figure 2 shows the structure of an expert system.

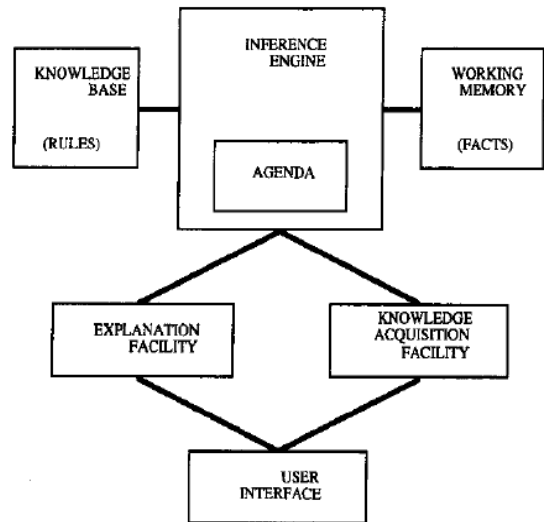


Fig. 2: Structure of a rule based expert system

Definition of disease Diabetes Mellitus:

Diabetes Mellitus is a clinical syndrome characterized by hyperglycemia due to absolute or relative deficiency of insulin. The lack of insulin affects the metabolism of the body. It causes increased blood sugar levels. That is there is not enough insulin to reduce the percentage of glucose to its normal level. All the people with diabetes have one thing common. They have too much sugar or glucose in their blood. This is because a diabetic patient's body is unable to remove excess glucose from the blood and deliver it to the cells as a source of energy.

Material and Methods:

Diabetes Diagnosis:

Some diabetic patients will not get any warning sign or symptoms. The only way to be sure is to have blood test for glucose. The diabetic's diagnosis tests include-

BDNF (brain-derived Neurotrophic factor): It is majorly expressed and regulatory Neurotrophic in the brain. Multiple trophic effects of BDNF are enhanced by binding to its high affinity receptor, TrKB (receptor tropomyosin-related kinase B) and subsequent involvement in many cellular signaling pathways. These BDNF/ TrKB complex are attractive therapeutic agents in the pathophysiology of many neurodegenerative disorders and also low levels of BDNF are associated with obesity and type 2 diabetes mellitus characterized by impaired glucose tolerance and insulin resistance. [3]

Fasting Blood Glucose: The fasting blood glucose (FBG) test is the standard test for diabetes. It is a simple blood test taken after 8 hours of fasting. Results

indicate: FBG levels are considered normal up to 70-99 mg/dL. Levels between 100 and 125 mg/dL are referred to as impaired fasting glucose or pre-diabetes. These levels are considered to be risk factors for type 2 diabetes and its complications. Diabetes is diagnosed when FPG levels are 126 mg/dL or higher on two or more tests on different days.

High-Density Lipoprotein (HDL):

Each bit of HDL cholesterol is a microscopic blob that consists of a rim of lipoprotein surrounding a cholesterol center. The HDL cholesterol particle is dense compared to other types of cholesterol particles, so it is called high-density. HDL cholesterol is the well-behaved "good cholesterol." This friendly scavenger cruises the bloodstream. In the process it removes harmful bad cholesterol. High HDL levels reduce the risk for heart disease but low levels increase the risk. A cholesterol test or lipid panel tells the level of HDL cholesterol. HDL cholesterol levels greater than 60 milligrams per deciliter (mg/dL) are high and good. HDL cholesterol levels less than 40 mg/dL are low indicates causes diabetes and cardio vascular diseases. In general, people with high HDL are at lower risk for heart disease. People with low HDL are at higher risk.

Low-Density Lipoprotein(LDL):

Studies have shown that higher levels of type-B LDL particles (as opposed to type-A LDL particles) promote health problems and cardiovascular disease, they are often informally called the *bad cholesterol* particles, (as opposed to HDL particles, which are frequently referred to as *good cholesterol* or *healthy cholesterol* particles).

Normal ranges

In the USA, the American Heart Association, NIH, and NCEP provide a set of guidelines for fasting LDL-Cholesterol levels, estimated or measured, and risk for heart disease. As of about 2005, these guidelines were:^{[9][10][11]}

Level mg/dL	Level mmol/L	Interpretation
25 to <50	<1.3	Optimal LDL cholesterol, levels in healthy young children before onset of atherosclerotic plaque in heart artery walls
<70	<1.8	Optimal LDL cholesterol, corresponding to lower rates of progression, promoted as a target option for those known to clearly have advanced symptomatic cardiovascular disease

<100	<2.6	Optimal LDL cholesterol, corresponding to lower, but not zero, rates for symptomatic cardiovascular disease events
100 to 129	2.6 to 3.3	Near optimal LDL level, corresponding to higher rates for developing symptomatic cardiovascular disease events
130 to 159	3.3 to 4.1	Borderline high LDL level, corresponding to even higher rates for developing symptomatic cardiovascular disease events
160 to 199	4.1 to 4.9	High LDL level, corresponding to much higher rates for developing symptomatic cardiovascular disease events
>200	>4.9	Very high LDL level, corresponding to highest increased rates of symptomatic cardiovascular disease events ^[4]

C-reactive protein (CRP): C-reactive protein (CRP) is protein found in the blood, the levels of which rise in response to inflammation (i.e. C-reactive protein is an acute-phase protein). Its physiological role is to bind to phosphocholine expressed on the surface of dead or dying cells (and some types of bacteria) in order to activate the complement system via the C1Q complex.^[8] CRP is synthesized by the liver^[5] in response to factors released by macrophages and fat cells (adipocytes).^[6] It is a member of the pentraxin family of proteins ^[5] it is not related to C-peptide or protein C. C-reactive protein was the first pattern recognition receptor (PRR) to be identified.^[7]

Body Mass Index (BMI):

The BMI is one way to determine whether or not an adult is overweight. BMI assesses height and weight; muscle mass is not a part of the equation. BMI is calculated by dividing a person's weight (in kilograms) by his or her height (in meters, squared). BMI can also be calculated by multiplying weight (in pounds) by 705, then Indian Body Mass Index Example (Formula And Table Chart) Body Mass Index for Indian men and women (except pregnant women) can be calculated by using Kg and metros dividing by height (in inches) twice. A person with a BMI of 18.5 to 24.9 is considered to be at a healthy weight. A person with a BMI of 25-29.9 is considered to be overweight. A BMI

over 30 is considered obese. A BMI of 40 or above indicates that a person is morbidly obese. The Body Mass Index is a measure of the body weight relative to height which can be used to determine if you are underweight, at a normal weight, overweight or obese. BMI indicates you are Underweight for BMI less than 18.5, Normal for BMI 18.5 - 22.9, Overweight for BMI 23.0 - 24.9, Obese for BMI 25.0 and above.

However, in humans with type 2 diabetes, levels of BDNF were decreased independent of obesity, suggesting that BDNF may regulate obesity and insulin resistance via different mechanisms, particularly through the insulin-stimulated phosphoinositide 3-kinase(PI3K) pathway important not only to neuronal survival and synaptic plasticity but also to insulin receptor signalling and insulin resistance.^[14]

The following Table 1 shows all parameter combinations.^[12]

Table 1 : Diabetic parameters, valid ranges clinical diagnosis

Parameter Name		Range	Notations	Meaning	
AGE		50-60 Years	D11(AGEa)	Old	
GENDER		Male	D21(GENm)	Male	
		Female	D22(GENf)	Female	
Weight		50-80 Kgs	D31(Weightw)	Mass	
Height	Male	1.524 - 1.8288 mts	D41(Heightm)	Height males	
	Female	1.4224- 1.6460 mts	D42(Heightf)	Height Females	
B M I	M E N	Low	0-18.5 Kg/mt ²	D511(BMIml)	Underweight Very Low Normal
		Medium	18.6-24.9 Kg/mt ²	D512(BMIImm)	Normal Healthy
		High	25-29.9 Kg/mt ²	D513(BMImh)	Overweight Pre Diabetic
		Very High	30 and above Kg/mt ²	D514(BMIvvh)	Obesity and Diabetic
	W O M E N	Low	0-18.5 Kg/mt ²	D521(BMIfl)	Underweight Very Low
		Medium	18.6-22.9 Kg/mt ²	D522(BMIfm)	Normal Healthy
		High	23-24.9 Kg/mt ²	D523(BMIfh)	Overweight Pre Diabetic
		Very High	25 and above Kg/mt ²	D524(BMIfvh)	Obesity and Diabetic

BDNF	Low	0-950 pg/mL	D61(BDNFI)	Diabetic	
	Medium	951-1599 pg/mL	D62(BDNFm)	Pre Diabetic	
	High	1600-2400 pg/mL	D63(BDNFh)	Healthy	
FBG	Low	70-99 mg/dL	D71(FBGI)	Healthy	
	Medium	100-125 mg/dL	D72(FBGm)	Pre Diabetic	
	High	126 and above	D73(FBGh)	Diabetic	
CRP	Low	0-0.9 mg/dL	D81(CRPI)	Healthy	
	Medium	1.0-2.9 mg/dL	D82(CRPM)	Pre Diabetic	
	High	3 and above mg/dL	D83(CRPh)	Diabetic	
HDL	L o w	Men	0-40mg/dL	D911(HDLI)	Diabetic
		W o m e n	0-50 mg/dL	D912(HDLm)	Diabetic
	Medium	50-59 mg/dL	D92(LDLh)	Pre Diabetic	
High	60 and above	D93(HDLh)	Healthy		
LDL	Low	2.6-3.3 mg/dL	D101(LDLI)	Healthy	
	Medium	3.4-4.0 Mg/dL	D102(LDLm)	Pre Diabetic	
	High	4.1-4.9 mg/dL	D103(LDLh)	Diabetic	
DM	Very Low	O1(DMvl)	Healthy		
	Low	O2(DMI)	Healthy		
	Medium	O3(DMm)	Pre-Diabetic		
	High	O4(DMh)	Diabetic		
	Very High	O5(DMvh)	Diabetic		

Results and Discussions:

Based on the values given in Table 1, the expert system rules are framed as part of the knowledge base . The inference engine part of the expert system will apply these rules in order to reach a decision on the clinical condition of the patient.^[13]

The diabetic parameters like BDNF, FBG, CRP, etc. are classified into several ranges as shown below:

AGE{old}, GENDER { male,female}, WEIGHT {mass},HEIGHT {males height,Females height}, BMIMEN {low,medium,high,Very high}

BMIWOMEN{low,medium,high,Very high},
 BDNF{low,medum,high} FBG{low,medium,high}
 ,CRP{low,medium,high} HDL{low,medium,high}
 ,LDL{low,medium,high},DM{verylow, low, medium,
 high, very high}.

For example, for BDNF and HDL parameter, low indicates Diabetic condition, Medium indicates the Pre Diabetic, and high indicates healthy clinical condition. For FBG, LDL, CRP-parameters, low indicates Healthy condition, Medium indicates the Pre Diabetic, and high indicates Diabetic clinical condition. For BMI parameter, Very low and low indicates Healthy condition, Medium indicates the Pre Diabetic, high and very high indicates Diabetic clinical condition. Based on the above classification, we can frame the expert system rules. Three rules correspond to healthy, prediabetic and diabetic clinical conditions s discussed below.

Rule 1: Diabetic Condition for Males:

If (AGE between 50-60) and (GENDER is male) and (WEIGHT between 50-80) and (HEIGHT is 1.524-1.8288) and (BMI is very high) or (BDNF is low) or (FBG is high) or (CRP is high) or (HDL is low) or (LDL is high) or or then Diabetic Mellitus (DM) is very high.

Based on the table 1, this rule can be written in the notation form as shown below:

if (D11and D21 and D31and D41or D514 or D61 or D73 or D83 or D911 or D103) then O is O4 or O5.

Rule 2: Diabetic Condition for Females:

If (AGE between 50-60) and (GENDER is female) and (WEIGHT between 50-80) and (HEIGHT is 1.4224-1.6460) and (BMI is very high) or (BDNF is low) or (FBG is high) or (CRP is high) or (HDL is low) or (LDL is high) or or then Diabetic Mellitus (DM) is very high.

Based on the table 1, this rule can be written in the notation form as shown below:

if (D11and D21 and D31and D41or D514 or D61 or D73 or D83 or D911 or D103) then O is O4 or O5.

Rule 3: Pre Diabetic Condition for Males:

If (AGE between 50-60) and (GENDER is male) and (WEIGHT between 50-80) and (HEIGHT is 1.524-1.8288) and (BMI is very high) or (BDNF is medium) or (FBG is medium) or (CRP is medium) or (HDL is medium) or (LDL is medium) then Diabetic Mellitus (DM) is medium

Based on the table 1, this rule can be written in the notation form as shown below:

if (D11and D21 and D31and D41or D513 or D62 or D72 or D82 or D92 or D102) then O is O3.

Rule 4: Pre Diabetic Condition for Females

If(AGE between 50-60) and (GENDER is female) and (WEIGHT between 50-80) and (HEIGHT is 1.4224-1.6460) and (BMI is high) or (BDNF is medium) or (FBG is medium) or (CRP is medium) or (HDL is medium) or (LDL is medium) or then Diabetic Mellitus (DM) is medium.

Based on the table 1, this rule can be written in the notation form as shown below:

if (D11and D22 and D31and D42or D523 or D62 or D72 or D82 or D92 or D102) then O is O3.

Rule 5: Diabetic-Free, Healthy Condition for Males

If(AGE between 50-60) and (GENDER is male) and (WEIGHT between 50-80) and (HEIGHT is 1.5240-1.8288) and (BMI is low or Medium) or (BDNF is high) or (FBG is low) or (CRP is low) or (HDL is high) or (LDL is low) or then Diabetic Mellitus (DM) is very low or low.

Based on the table 1, this rule can be written in the notation form as shown below:

if (D11and D21 and D31and D41or D512 or D63 or D71 or D81 or D93 or D101) then O is O1 or O2.

Rule 6: Diabetic-Free, Healthy Condition for Females

If(AGE between 50-60) and (GENDER is female) and (WEIGHT between 50-80) and (HEIGHT is 1.4224-1.6460) and (BMI is low or Medium) or (BDNF is high) or (FBG is low) or (CRP is low) or (HDL is high) or (LDL is low) or then Diabetic Mellitus (DM) is very low or low.

Based on the table 1, this rule can be written in the notation form as shown below:

if (D11and D22 and D31and D42or D522 or D63 or D71 or D81 or D93 or D101) then O is O1 or O2.

In this way the diabetic mellitus clinical diagnosis expertise has been captured from the diabetic consultant in the form of several rules.

By using the BDNF related data of patients, we checked around 260 patients of whom 128 are male patients and 132 are female patients. It was found that the system consistently gave accurate clinical diagnosis whether the patient was diabetic or nearly diabetic or healthy and diabetic-free.

Conclusion:

The proposed expert system based on critical diabetic parameters like BDNF (brain-derived Neurotrophic factor) levels, and FBG (Fasting Blood glucose) is found to be effective in diagnosis of diabetic mellitus clinical condition. Patient data of south Indian states was considered for experimental validation of the proposed system. The rule based expert system determines the diabetic condition based on the high or

low values of BDNF levels along with other relevant clinical parameters for diabetic mellitus condition.

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