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Artificial Neural Networks for Obtaining New Medical Knowledge: Diagnostics and Prediction of Cardiovascular Disease Progression

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Abstract

Objectives: Development of a mathematical model and its implementation as a computer program for diagnostics and prediction of progression of the most widespread cardiovascular diseases; the program is to model different variants of disease progression for an observed patient, and to select individual recommendations for correction of his or her lifestyle, regimen and diet. **Methods:** Combination of technologies of neural networks and expert systems with a resulting synergistic effect. **Results and Conclusion:** Investigations of the developed mathematical model showed that it is able to reveal new knowledge which is yet unknown to medical science. In the course of software experiments performed by means of a diagnostics-and-prediction system, we revealed the facts showing that modern medical practice patterns of giving one and the same recommendations to all the cardiac patients without exception (including keeping to a hypocholesteric diet, giving up pernicious habits, limiting coffee and alcoholic drinks, losing weight and limiting intellectual and physical activity) are not always correct. Our investigations showed that some of these recommendations are not just unhealthy, but harmful for a number of patients. The neuro-expert diagnostics-and-prediction system presented in this paper allows doctors to reveal such non-typical patients and to develop individual recommendations especially for them.

Keywords

Diagnostics; Modeling; Prediction; Forecast; Prognostic; Neural networks; Medical systems; Cardiovascular disease; Cardiac disease; Heart disease

Introduction

Currently, scientific literature says a lot about successful experience in the development and use of medical diagnostics systems based on artificial neural networks [1-9]. Artificial neural networks (ANNs) are known [10,11] to be one of the most effective strategies of artificial intelligence. ANNs presented by McCulloch and Pitts [12] and Rosenblatt [13] are realized on the principles of structure and functioning of human brain. From its prototype – brain – ANN inherits its useful properties: ability to extract information out of statistic data; ability to generalize this data in the form of rules and regularities of subject areas; intuition as the ability to make correct conclusions and to make forecasts and predictions in case regular logic is powerless.

However, the analysis of the papers devoted to the application of ANNs to medical practice shows that, as a rule, most of them touch upon only the issue of diagnostics. But the range of ANN abilities is much wider and is definitely not limited by just making a correct diagnosis. In addition, the experience of the Perm branch of the Russian Academy of Sciences (www.PermAi.ru) which applied ANNs in many poorly formalized subject areas, such as industry, economy and business, political science and sociology, criminalistics and ecology, testifies that, besides solving the diagnostics problems, ANNs can be used in investigations of modeled subject areas. ANN is a powerful tool for obtaining new scientific knowledge unknown before, for revealing rules and regularities of the subject areas under study. Besides, ANNs are suitable for long-term forecasts or predictions of the modeled phenomena development. But medical literature does not describe any experience in this kind of ANN application.

In this regard, the objective of the present paper is an attempt to use the ANN not only for diagnostics, but also for prediction of the disease progression for different periods of time, as well as an attempt to use the ANN for finding new, yet undiscovered medical knowledge.

Principle of ANN

As mentioned before, ANNs are implemented on the principles of brain structure and functioning. Just like our brain, ANNs consist of a number of elementary cells – mathematical neurons imitating biological neurons of the human brain. These mathematical neurons exchange signals according to the rules similar to the rules of human brain. Knowledge in neural networks is encoded by means of electrical conduction between the connecting conductors – just the way it occurs in our brain. These electrical conductions are called forces of synaptic connections. Knowledge is not fed into them initially but is acquired automatically by their training, which is based on examples, characterizing the subject area.

The story of ANN invention, its principle of work and examples of application are described in detail by many authors [10,11]. In the following section of the paper, we present the structure of our ANN and formulas according to which signals transform in ANNs. Also,

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we focus on questions of comparison of the neural network modeling methodology and the standard statistical methodologies, such as regression, which is widely used in medical science.

ANN and Regression

ANNs appeared in the middle of the twentieth century as a brand new strategy of artificial intelligence, as an alternative to expert systems [11]. Before ANNs were invented, the 'artificial brain' represented a 'black box' (i.e. it was not important what was inside as long as it was solving intellectual problems), but the creation of ANNs marked the beginning of a new era – the era of software and computers 'in the image and likeness' of the human brain.

However, if we turn away from intriguing words about brain modeling, and look at ANNs from the viewpoint of pure mathematics, we will be able to see ANNs as a simple mathematical apparatus focused on the solving of the traditional mathematical problem of data approximation (data fitting problem). In fact, from the mathematical standpoint, the 'trained' neural network is a nonlinear vector function approximating statistical data. This function connects input and output variates (i.e. controlling and controlled variates). In mathematics, such functional dependences are called the nonlinear multidimensional regression equations; therefore, ANN technologies (at least, some of them) can be considered as one of new methods of forming regression equations.

What is the difference between this new method and classical methods of regression analysis?

Before answering this question, let us note that the classical methods of regression analysis [14] assume the regression model construction as any linear or nonlinear function of any form. And, besides, mathematical formulas are not connected with any physical or other kind of interpretations.

Contrary to classical methods of regression analysis, neural network technologies have a profound physical, psychological and all-philosophical meaning [10,11]. They model the brain both at functional and structural levels.

Classical methods of regression analysis pursue the goal of statistical data fitting (approximation) by any mathematical functions, in most cases – by linear ones. Neural networks also make approximations, but these approximations are based only on those mathematical functions according to which (as many hypotheses say) brain neurons work. And data transformations by means of these mathematical functions are performed in the sequence discovered by biologists in the course of natural neural experiments.

The methods of classical regression analysis realize ideas of ingenious mathematicians, but the ANN technologies realize the 'invention' of Nature herself – the principles of brain structure and functioning. The consequences of these fundamental differences are the differences between neural network and regression modeling capabilities.

Comparing the traditional methods of regression analysis and the ANN technologies, we can see the following advantages of the latter:

- The classical methods of regression analysis require introduction of hypotheses about a character of cause–effect relations between input and output variables, whereas the ANN technologies do not need that at all.
- The classical methods of regression analysis exclude the existence of linear correlation between the input parameters, whereas ANN technologies do not require this condition to be fulfilled.
- The classical methods of regression analysis often require observations (which are usually not numerous) to be clustered, whereas the ANN technologies in most cases cope without any preliminary data clustering.
- Qualitative ANN modeling usually requires significantly smaller amounts of statistical data.
- The ANN technologies imply a possibility of multi-sequencing (parallelization) of computing processes between individual neurons, thus saving a considerable amount of time.
- There are some cases where the application of ANN technologies yields positive results, while the classical methods of regression analysis are just powerless.

A drawback of the ANN modeling method in comparison with the classical methods of regression analysis is insufficient development of its theoretical base and, consequently, a lack of accurate instructions on development of optimal ANN models taking into account features of specific subject areas. This is the reason why some researchers are inclined to classify the process of ANN modeling as an art, rather than a science.

And finally, we should note that the choice of technology is often a subject of endless discussions leading to nothing. Researchers and specialists, who have become experts in one of the technologies, begin to criticize the other technologies. The authors of the present paper believe that these two technologies should not be in opposition. Our experience shows that for achieving the goals successfully, it is useful to apply all available technologies and scientific methods, irrespective of their philosophical base.

ANN and Expert Systems

Modern medical practice widely uses diagnostic software based on the technology of expert systems [11]. Knowledge (data) is replenished into such systems by skilled medical experts and is registered in the form of rules formalizing the regularities of medical science. The users (doctors) feed symptoms and parameters of their patients into the expert systems, so that the systems make diagnoses by matching the necessary rules and building logical chains.

Unlike ANNs, the expert systems use only the knowledge which the experts managed to formalize and feed into the expert systems' memory. Contrary to this, ANNs draw knowledge from real-world experiences, which are richer than theoretical ones. Therefore, ANNs are able to obtain and apply the essentially new knowledge, which is yet unknown to modern medical science.

In certain cases, expert systems can also form logical chains unknown to medical specialists and, thus, generate new knowledge. But this knowledge is formed on the basis of the rules taken from the database of expert systems, and therefore, according to the Gödel theorem terminology, it 'does not enhance the axiomatic system', so the process of obtaining that knowledge is not the act of creativity. In other words, knowledge generated by expert systems cannot be essentially new. It is not beyond the knowledge of experts, the authors of such expert systems. This is the shortcoming of expert diagnostic systems in comparison with diagnostic systems based on ANNs.

The ANN Model for Diagnostics of Cardiovascular System Diseases

As shown by Yasnitsky *et al.* [15], a suitable type of ANN structure intended for problems of medical diagnostics, is represented by a

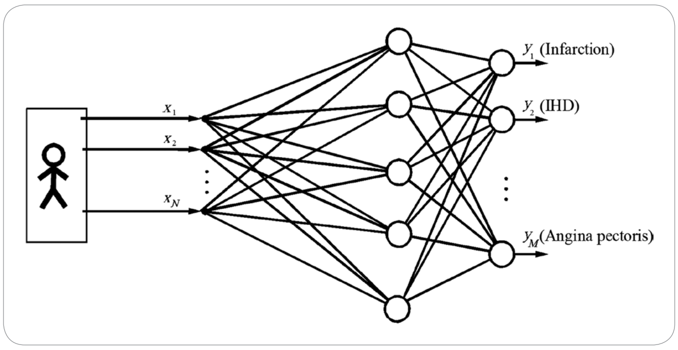

Figure 1: Schematic diagram of the neural network system for medical diagnostics

perceptron with sigmoid activation functions [10,11], where the input data is the information about a patient, and the output data is the disease diagnosis (see Figure 1). The input parameters $x_1, x_2,..., x_N$ characterize patient's passport data and complaints, anamnesis of his or her disease and life, and objective examination data. These are different values, for example, body temperature, blood pressure and pulse rate. These are the numbers encoding the patient's characteristics, for example, 1 (if the patient is male) or 2 (if female).

The output parameters $y_1, y_2,..., y_M$ encode the diagnoses of diseases, namely, a doctor's degree of confidence on a 100-mark grading scale. For example, if the output parameters are $y_1 = 0$, $y_2 = 100$, and $y_M = 75$, it means the doctor is sure that the patient has no myocardial infarction, but has an IHD (ischaemic heart disease also known as coronary heart disease), and angina pectoris; however, as to the latter diagnosis, the doctor is not 100% sure, but only 75%.

A number of examples in the subject area are formed by filling in the questionnaires containing information about 800 cardiac patients. Seven hundred forty patients were diagnosed with ischemic heart disease in its various manifestations (myocardial infarction, stable and unstable angina pectoris and its aftereffects in the form of acute left ventricular failure and chronic heart failure). Sixty patients were diagnosed with high blood pressure (hypertension). The questionnaires contained 67 parameters including passport data, complaints, case history and clinical picture, results of laboratory and instrumental analyses, including coronary angiography. Based on interviews and examination of patients, along with laboratory and instrumental analyses, medical experts graded the level of their diagnostic confidence using the 100-mark scale.

This set of examples was completed with 300 more questionnaires of patients with the diagnosis of cardiovascular disease ***excluded***. This was made for the purpose of training the ANNs so that after training they would be able not only to diagnose diseases, but also to state their ***absence***.

According to the ANN design technology [11,12], the entire set of those examples was split into three: training L, testing T, and confirming P as 70% : 20% : 10%. In the initial version of ANNs, the perceptron-type network contained $N = 67$ input neurons and $M = 6$ output neurons, corresponding to six cardiovascular diagnoses mentioned in Table 1. The initial quantity of neurons of the hidden layer was calculated according to the Arnold–Kolmogorov–Hekht-Nilsen formula [10] and then specified in the course of the neural network subsequent optimization.

Diagnosis	Error [epsilon]$_P$, %
Cardiac infarction	0.9
Ischemic heart disease	1.3
Chronic heart failure	1.7
Unstable angina pectoris	13.4
Acute left ventricular failure	28.6
Stable angina pectoris	31.2

Table 1: Errors of diagnoses

We used sigmoid functions as activation functions for the neurons of the hidden layer and for the output neuron, so that these neurons were computed using the following formulas:

$$S_i = \sum_{j=1}^{J} w_{ij} x_j \qquad (1)$$

$$y_i = \frac{1}{1+e^{-S_i}} \qquad (2)$$

where J is the number of inputs to a neuron, x_j is the input signals received by a neuron, y_i is its output signal and w_{ij} is the weight coefficients (the strength of synaptic connections), which are determined as a result of ANN training with the training set.

The goal of ANN training is the following: each set of input parameters $(x_1, x_2,..., x_N)_q$ (where $q = 1, 2,..., Q$ and Q is the quantity (number) of training examples (in our case – questionnaires)) is to be responded with a set of values of output parameters $(y_1, y_2,..., y_M)_q$, minimally different from the corresponding values of the output parameters preset by the training set of examples. In other words, the purpose of neural network training is to minimize the training error ε_L defined as a mean square difference between the values of output parameters (diagnoses) $(y_1, y_2,..., y_M)_q$ given in the questionnaires and those output values which are calculated by the ANN. This goal is reached by selection of synaptic weights w_{ij} by means of ANN training algorithms based on the iterative formula:

$$w_{ij}(t + 1) = w_{ij}(t) + \Delta w_{ij} \qquad (3)$$

where $w_{ij}(t + 1)$ is the synaptic weight of the connection between i-th and j-th neurons in the new epoch (iteration) $(t + 1)$; $w_{ij}(t)$ is the similar synaptic weight calculated in the old training epoch t; and Δw_{ij} is the synaptic weight increment calculated by means of formulas, preset by a training algorithm.

As a rule, these algorithms make the iterative process move towards an anti-gradient of the hypersurface representing the dependence of the training error [epsilon]$_L$ on w_{ij}. The ANN was trained by methods of back propagation of error (BPE) and elastic back propagation, Levenberg–Marquardt method, etc. [10]. For each variant of ANN, we selected the most effective method of training.

After the ANN had been trained, we tested its diagnostic properties using the test set (T), that is, by applying the examples (questionnaires) which were not used during ANN training. We call the mean square error calculated by means of testing examples as the testing error and designate it as [epsilon]$_T$.

Developing the neural network diagnostic system in this paper, we introduced and applied one special method when we used M neural networks with N inputs and one output with a mutual interface instead of the classical scheme of perceptron ANNs with N inputs and M outputs. The structure of each ANN was optimized to minimize the testing error [epsilon]$_T$.

Computing experiments showed that the replacement of ANNs with several outputs by the set of ANNs with one output allows us to reduce diagnostic errors by 3-6%.

Results and Discussion

Testing

As noted above, the entire set of examples was split into three non-overlapping sets: training L, testing T and confirming P. The training set of examples was used for training ANNs; the testing set was used for selecting their optimal structures (number of hidden neurons and types of activation functions). The training set L was used for calculation of the training error [epsilon]$_L$, and the testing set T was used for calculation of the testing error[epsilon]$_T$. For final testing of diagnostic properties of the network, we used the confirming set P which was not used either in training or in optimization of the ANN. As a result, we obtained the error [epsilon]$_P$ which we call an ANN error.

The values of the mean square error [epsilon]$_P$ computed in the course of diagnostics of each disease with the use of the confirming set P are given in Table 1.

As can be seen from the table, the diagnoses made by the doctor and ANN differ from one another by a quantity of [epsilon]$_P$ from 0.9% (myocardial infarction) to 31.2% (stable angina pectoris). Thus, we can conclude that the presented diagnostic system is suitable for preliminary diagnostics of six cardiovascular diseases given in Table 1.

Besides, it can be used as a mathematical model of the subject area under study. It means that by carrying out virtual computing experiments with the model, varying the input parameters, and observing the behaviour of output signals, we can study the subject area, educe and investigate medical regularities revealed by the ANNs during training. And as the ANNs did not get their knowledge from books, but were trained by real examples of medical practice, we can expect that they acquired some regularities which are probably unknown to modern medical science.

Prediction of Disease Progression

As we can see from Table 1, the neural network diagnostic system provides a diagnostic error acceptable for medical practice. So, we can conclude that the mathematical model which we developed is adequate to the subject area within the framework specified in the table of errors (Table 1), and therefore, it is suitable for investigation of regularities of this subject area. Moreover, the model can be used both for diagnosing diseases and for predicting their progression. But this begs the question of how to interpret the results of ANN calculations, that is, the output values $y_1, y_2,..., y_M$. Earlier they implied the sense of the doctor's degree of diagnostic confidence, and while filling out the questionnaires the doctors set them within the range from 0 to 100 points. Later, when new patients arrived, ANNs began to deliver results not only within that range, but also beyond it. Thus, when making predictions for 10 or 15 years ahead, ANNs could estimate their diagnostic confidence as 150 points or even 200 points. It is clear that such predictions are not absolutely correct from the medical viewpoint, but we should remember that the computing experiments are performed in virtual conditions, not in real ones.

It is obvious that the higher the degree of ANN's confidence when the ANN decides a diagnosis, the more patient parameters $x_1, x_2,..., x_N$ are indicative of that diagnosis, and the faster the disease progression. Therefore, we take the results $y_1, y_2,..., y_M$ of ANN calculations as the level or the degree of disease progression (development) with *points* as measuring units.

Now let us discuss how it is possible (after making a diagnosis by means of our mathematical model) to carry out the prediction of disease progression for future periods of time. It is logical to do this by increasing the input parameter which is responsible for the patient's age and observing the ANN output values. However, the predictions obtained by this method usually turn out to be excessively optimistic due to the fact that, in this case, the only parameter to be varied is the patient's age, but the possibility of other symptoms' occurrence and onset of other diseases with age is not taken into account.

In this regard, we made an attempt to add the expert knowledge to the neural network knowledge. As a source of expert knowledge, we used the European guidelines on cardiovascular disease prevention in clinical practice, known as 'SCORE', recommended by the Fourth Joint Task Force of the European Society of Cardiology and other societies on cardiovascular disease prevention in clinical practice in 2007, intended for calculation of risk of death from cardiovascular diseases.

The analysis of averaged data of these guidelines showed that according to 'SCORE', for each 5-year period from 50 to 65 years of age, the risk for the average patient increases [alfa]≈1,6 times, as it is represented in Figure 2. We suggest this expert knowledge to be used for parametric identification of the neural network mathematical model. At that, we introduce a hypothesis that the 'SCORE' risks are in direct proportion to the disease progression degree calculated by means of our mathematical model.

Assume that the neural network mathematical model estimated the degree of cardiovascular disease progression of a certain patient as y_0. Suppose we have to project a forecast for the next 5 years and investigate how this predicted value would vary with a change of lifestyle and living conditions of the patient.

Having increased the input 'age' parameter of the neural network model x_0 by 5 years and performed calculations with the ANN, we obtain a new predicted value of the disease progression degree which we denote by y. Then, [beta] $= y/y_0$ is the coefficient showing how many times the degree of cardiovascular disease progression increased in the forecast period of 5 years.

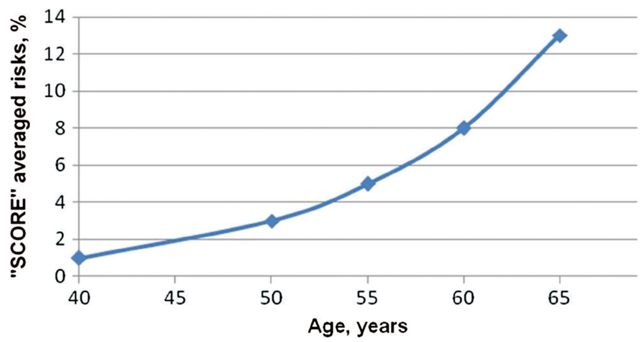

Figure 2: Dependence of averaged 'SCORE' risks on the patient's age.

Let us note that this prediction is carried out by means of the neural network model with only one parameter (the patient's age) to be varied, while the rest of the parameters remain the same. Therefore, such prediction does not take into account the possibility of other symptoms' occurrence and onset of other diseases with age.

In order to take into account the specified age-related changes, we suggest correcting the predicted value y by the formula:

$$z = y\left[\frac{\text{alfa}}{\text{beta}}\right] \qquad (4)$$

where z is the corrected predicted value of the disease progression degree of the patient under study.

Then, the influence of patient's lifestyle and living conditions changes on his or her disease progression degree predicted for 5 years (i.e. for the value z) is to be studied. We vary one of the input parameters of the model x_1, for example, the 'patient's weight' parameter, and by means of the neural network model, we obtain the disease progression degree value y_1 corresponding to this variation which then is corrected by the same formula as given by Equation (4): $z_1 = y_1\dfrac{[\text{alfa}]}{[\text{beta}]}$.

After that, some other input parameter (e.g. smoking) of the neural network model x_2 is varied, and the corresponding value y_2 of the disease progression degree is calculated; then it is corrected by Equation (4). And so on.

As a result, we obtain the following health evaluation for the patient:

y_0 – for the current day;

z – for 5 years ahead in case the patient's lifestyle and living conditions remain unchanged;

z_1 – for 5 years ahead with the input parameter x_1 varied;

z_2 – for 5 years ahead with the input parameter x_2 varied;

and so on.

Providing the trained ANN with this kind of interface, which automatically follows the steps of the algorithm for parametrical identification of the neural network model given above, we obtain a hybrid diagnostics-and-prediction neural expert system.

Let us notice that this system operates on the basis of both neural network knowledge from our medical practice, and expert knowledge from 'SCORE'. The system is created by two technologies: technology of neural networks and technology of expert systems [11], which is why it is called 'hybrid'.

Finally, we give the improved values of the coefficient α, calculated by 'SCORE', which are to be used when calculating the predictions:

– for 5 years: [alfa] = 1,6;

– for 10 years: [alfa] = 2,7;

– for 15 years: [alfa] = 4,3.

Figures 3-5 present the examples of results of diagnoses and prediction of IHD progression degree of three patients (P_1, P_2, and P_3) for the next 5, 10, and 15 years, calculated by considering changes of their regimen, lifestyle and drugs intake. The results of modeling given in Figure 3 belong to the patient P_1 (who was a 47-year-old woman, 172 cm (5.6 ft) tall, weighting 64 kg (141 lb), keeping to a hypocholesteric,

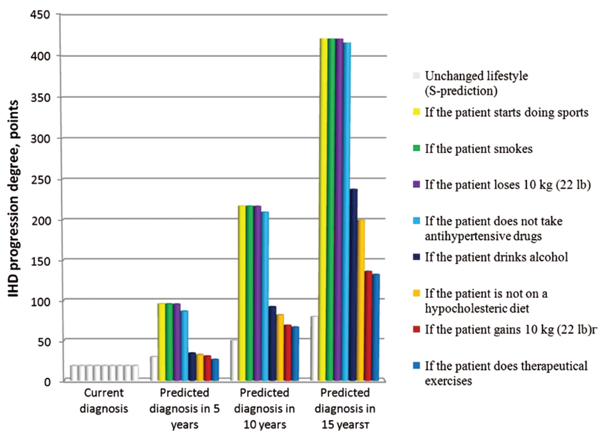

Figure 3: Results of diagnostics and prediction of IHD progression degree for the patient P_1 for 5, 10, and 15 years considering changes in her lifestyle, diet and living conditions.

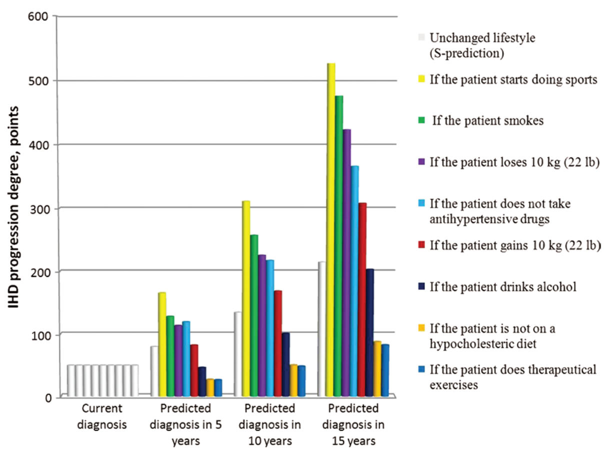

Figure 4: Results of diagnostics and prediction of IHD progression degree of the patient P_2 for 5, 10, and 15 years considering changes in her lifestyle, diet and living conditions.

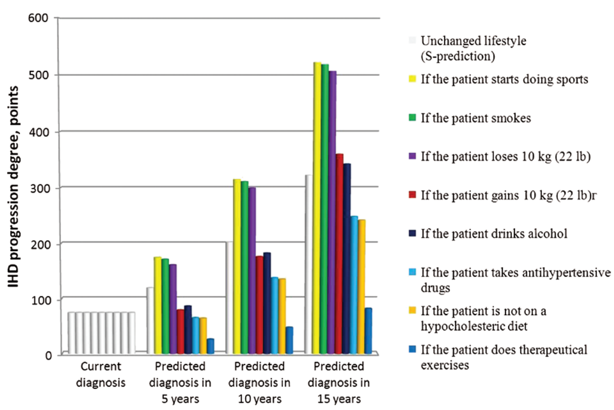

Figure 5: Results of diagnostics and prediction of IHD progression degree of the patient P_3 for 5, 10, and 15 years considering changes in his lifestyle, diet and living conditions.

alcohol-free diet, non-smoking, regularly taking antihypertensive drugs, and not doing sports or therapeutic exercises). The patient P_1 was diagnosed with IHD by the doctors with the 20-point confidence degree of disease progression (see the set of bars marked 'Current diagnosis' at the histogram in Figure 3). There are three groups of bars representing the expected (predicted) values of IHD progression degree for 5, 10, and 15 years. In each set of bars, the leftmost bar corresponds to the IHD expected (predicted) progression degree provided that the patient's lifestyle, diet and regimen remain unchanged during the period of prediction. Hereinafter, we call this kind of prediction as 'S-prediction'. It coincides with the prediction made by 'SCORE'.

The second bar from the left in each set corresponds to the case if the patient starts playing sports professionally; the third bar – if the patient starts smoking; the fourth bar – if the patient loses 10 kg (22 lb); the fifth bar – if the patient quits taking her antihypertensive drugs; the sixth bar – if the patient starts drinking alcohol regularly; the seventh bar – if the patient quits keeping a hypocholesteric diet; the eighth bar – if the patient gains 10 kg; the ninth bar – if the patient starts doing therapeutic exercises regularly.

As we can see from the histogram in Figure 3, if this patient does not change her diet and lifestyle (this case is called the S-prediction), then in 5 years, IHD may progress from 20 to 30 points, in 10 years – to 50 points, and in 15 years – up to 80 points.

From this figure, we can see that if this patient starts doing sports, or starts smoking, or loses 10 kg in weight, or quits taking antihypertensive drugs, then in 5 years, her IHD progression degree will reach a 100-point mark, and in 10 and 15 years will go beyond 200 and 400 points, which can be interpreted as a life-threatening condition.

If the patient starts drinking alcohol regularly, or gives up a hypocholesteric diet, or gains 10 kg, or starts doing therapeutic exercises regularly, then in 5 years, it will not cause any relevant change in her IHD progression degree in comparison with the S-prediction. However, in 10 years of regular alcohol intake, this patient's IHD progression degree can come up to a 92-point mark, non-compliance with hypocholesteric dietary instructions – up to a 82-point mark, gaining 10 kg – up to 70 points, and regular therapeutic exercises – up to 67 points. According to our prediction, in 15 years of regular alcohol intake, this patient's IHD progression degree can come up to a 237-point mark, non-compliance with a hypocholesteric diet – up to 200 points, and gaining 10 kg or regular therapeutic exercises – up to 135 points.

Thus, from all the considered options, the S-prediction appeared to be the best for this patient. So, on the basis of the modeling results, we can also advise the patient P_1 not to do any sports at all (neither any hard physical activity nor work), not to smoke, to continue taking antihypertensive medicines, and also to maintain her body weight. Besides, in the next 10 and 15 years, this patient can be recommended to keep strictly to a hypocholesteric diet and never drink alcoholic beverages, and also to avoid even easy physical activity and exercise stress including therapeutic exercises.

Analyzing the performed researches, we can see that the results of predictions of the patient's health condition do not contradict the traditional medical opinion that IHD progression depends on excess cholesterol, high blood pressure, doing sports professionally, regular smoking and alcohol intake. However, the results of our further researches showed that there can be patients with a bit different regularities coming to light when modeling their health condition. One of such non-typical examples is given in Figure 4, which shows the results of predictive calculations for the patient P_2, a 73-year-old woman, 150 cm (5 ft) tall, weighing 60 kg (132.3 lb), non-drinking, non-smoking, keeping to the hypocholesteric diet, regularly taking antihypertensive drugs, never doing sports and/or therapeutic exercises. Her current diagnosis is IHD with the 50-point progression degree.

As we can see from Figure 4, unlike the previous case, the S-prediction is definitely not the best variant: if the patient does not change her lifestyle and diet, then in 5 years, her IHD will progress from 50 to 80 points, in 10 years it will go beyond 100 points, and in 15 years may reach 200 points, which is critically dangerous to life. Doing sports, smoking, losing or gaining weight and ignoring antihypertensive drugs can cause even faster progression of this disease.

Nevertheless, the results of computer modeling show that predictions of a health condition for the considered patient can become better due to regular therapeutic exercises and also in case the patient gives up the hypocholesteric diet or starts drinking alcohol regularly. Moreover, alcohol can help this patient to slow down the disease progression only during the first 5 and 10 years, but giving up the hypocholesteric diet or regular therapeutic exercises will make her diagnosis twice as good as the initial one in the first 5 years, and in the next 10 and 15 years, these activities will significantly slow down the disease progression so that it will not be able to reach the 100-point mark.

Figure 5 shows the results of modeling for the patient P_3, a 57-year-old man, 158 cm (5.2 ft) tall, weighing 95 kg (209.4 lb), non-drinking, non-smoking, keeping to the hypocholesteric diet and not taking antihypertensive drugs. He is diagnosed with IHD (by doctors) with the 75-point confidence degree of disease progression.

As can be seen from the figure, if this patient does not change his lifestyle, regimen and diet, in 5 years, his IHD can increase from 75 to 120 points, in 10 years – to 200 points, in 15 years – may exceed a 300-point mark. The situation can be aggravated by doing sports, smoking and losing weight, which is the same as in the cases considered above.

His disease progression during the first 5 years will be slowed down if he gains 10 kg, or starts drinking alcohol or antihypertensive drugs, or quits his hypocholesteric diet, or starts doing therapeutic exercises regularly. The latter is the most effective. Further predictions for 10 and 15 years show that doing therapeutic exercises regularly is the most suitable recommendation for this patient, as keeping to this recommendation will allow him to keep IHD progression below the 80-point mark during the whole predicted period.

Let us remind ourselves that the obtained predictions are the results of mathematical modeling, and therefore they are true within the error of the mathematical model. As for the traditions of medical science, they require further investigations with thorough practical testing.

Discussing the Predicted Results

In an attempt to explain the results presented in Figures 3-5, we faced the following questions:

1. Why, according to the obtained predictions, is the hypocholesteric diet good for the patient P_1, but detrimental for P_2 and P_3?
2. Why are sports or other regular physical activity detrimental for the patient P_1, but good for P_2 and P_3?
3. Why does regular drinking for the first 10 years increase the IHD progression degree of P_1, but reduces the progression degree of P_2 and P_3?

Besides, there is one very natural question – how reliable are such unusual results?

Before we start discussing these questions, let us remind ourselves that the history of science (especially physics, chemistry and astronomy) has a lot of cases where the application of mathematical modeling allowed researchers to make important discoveries. As it has already been noted, examples of new regularities in economy, business, industry, political science, criminalistics and ecology, discovered by the method of neural network mathematical modeling are reflected in papers of the Perm branch of the Russian Academy of Sciences. Besides, there have been cases (which are quite common in our practice) when neural network predictions could not be explained or reasoned logically, or were explained but only after some time (www.PermAi.ru).

In our opinion, medical science is not an exception.

From the results of neural network mathematical modeling presented in Figures 3-5, it follows that the common medical practice of giving the same recommendations to all the cardiologic patients without any special exception (keep to a hypocholesteric diet, not to gain weight, to take antihypertensive drugs, not to drink alcohol, not to smoke, etc.) definitely is not absolutely correct. Our computer experiments showed that these recommendations really reduce IHD progression for the majority of patients. However, there are cases where some of these traditional recommendations can be harmful. For example, 569 real patients participated in our virtual computer experiments, and the results showed that:

– losing weight is detrimental to 30% of them;

– hypocholesteric diet is detrimental to 24%;

– not drinking alcohol is detrimental to 15%;

– giving up smoking is detrimental to 0%;

– taking antihypertensive drugs regularly is detrimental to 0%.

Let us note once again that the quantitative data presented here are true only within the error of the used mathematical model. Therefore, the authors of this paper suggest that these data should be considered only as qualitative and only for discussions and further researches, corrections and improvements.

We still have not succeeded in revealing the exact input parameters (out of 67 ones) of the neural network mathematical model responsible for the fact that some recommendation is good or bad to the patient's health. Still, it is clear that any recommendation depends on a combination of many factors, the most significant of them are:

– pulmonary congestion according to the index of thoracic fluid volume;

– presence of diastolic dysfunction according to polyrheocardiographic criteria;

– depression of cardiac contractile function according to polyrheocardiographic and echocardiographic criteria;

– increase of general cholesterol level;

– akinesis, hypokinesis zones in left ventricle myocardium;

– ejection fraction less than 50%;

– presence of pathologic Q waves on an ECG;

– cyanosis of the skin and visible mucosa;

– an expressed crease or fold in the earlobe;

– cardiovascular interventions;

– peripheral oedema.

Probably, after performing a series of purposive investigations, we will be able to present the medical knowledge (found by neural network mathematical modeling) in a visual form, allowing doctors to reveal non-typical patients without extra assistance. But currently, we can recommend using our diagnostics-and-prediction system for solving this problem.

Conclusions

The present paper presents and realizes the method of ideological combination of two alternative artificial intelligence strategies – neural networks and expert systems. This resulted in a synergistic effect: the hybrid neuro-expert system created as a result of this combination is able not only to make diagnoses of diseases, but also to predict their progress for certain periods of time.

In our opinion, our idea to unite and combine two strategies of artificial intelligence corresponds to psychological ideas of how a person makes decisions. First, his or her decisions get 'formed' under the influence of intuition, emotions and experience. According to the main hypotheses of neuroinformatics [10,11], those preliminary emotional and intuitive decisions are developed as a result of computing activity of neurons of a person's biological neural network. However, then those preliminary decisions (including diagnoses, forecasts and predictions) are corrected, and the final decisions are made by the person after discussion, that is, with use of expert knowledge including rules and regulations of his or her environment or subject area.

According to the computing experiments performed by means of our diagnostics-and-prediction system, the ANNs which this system in based on received knowledge about the subject area, including the knowledge which is yet unknown to medical science. The system was used for investigation of the subject area for the purpose of revealing and studying the medical regularities acquired by the ANN during training. As a result, we revealed the facts contradicting the common medical tradition of making the same recommendations to all cardiac patients without exception (namely, keep to a hypocholesteric diet, give up pernicious habits, limit caffeine and alcohol intake, lose weight and limit intellectual and physical activity). A series of computer experiments performed by means of diagnostics-and-prediction system showed that these recommendations are very useful for the majority of people, but not for all the patients. Our studies showed that the mentioned standard recommendations are not suitable for some patients and can be dangerous for their health. Our system of diagnostics and prediction allows doctors to reveal such non-typical patients.

In conclusion, it should be noted that the opened possibility to predict a course and progression of diseases allows a doctor to control these processes. Now, for each patient, it is possible to model different versions of his or her disease progression, and, consequently, to choose the most suitable recommendations concerning the patient's lifestyle, diet and medicines, etc.

So, in this paper, we develop the methodological base of artificial intelligence, and create a useful tool for medical practice to obtain new medical knowledge; all these help to make steps towards providing a solution for a vital problem of personalized medical service.

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