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Clinical Data Analysis with the Use of Artificial Neural Networks of Treatment Evaluation in Adolescent Idiopathic Scoliosis

Analiza danych klinicznych za pomocą sztucznych sieci neuronowych podczas oceny leczenia skoliozy idiopatycznej

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Abstract

Background. An advanced multivariate data processing method, artificial neural network (ANN) analysis, was demonstrated to provide an objective evaluation of medical strategy by making use of large collections of routine clinical parameters of patients with adolescent idiopathic scoliosis. The ANN method allowed for detection of complex systematic relationships between diverse patient, disease and treatment variables.

Material and Methods. Two hundred ninety-three patients with adolescent idiopathic scoliosis were the subjects of the study for whose fifteen disease and treatment variables were determined.

Results. It was revealed by ANN that it is possible to perform the correct classification of patients regarding deterioration, stabilization or improvement of their health observed after four years of treatment.

Conclusions. ANN has been recommended as a new promising alternative to classical regression analysis of multivariable clinical data. By means of ANN practically useful systematic information may be extracted from large sets of data otherwise hardly interpretable in comprehensive physical terms. That information can be valuable for general prognosis and appropriate adjustment of the treatment (*Adv Clin Exp Med* 2004, 13, 4, 623–629).

Key words: artificial neural networks, adolescent idiopathic scoliosis.

Streszczenie

Wprowadzenie. Sztuczne sieci neuronowe (SNN) zostały wykorzystane do oceny strategii terapeutycznej leczenia skoliozy idiopatycznej. Analiza SNN została przeprowadzona na dużym zbiorze rutynowo uzyskiwanych danych klinicznych. Metoda pozwoliła na ocenę złożonych zależności między zmiennymi charakteryzującymi pacjenta, chorobę i strategię terapeutyczną.

Materiał i metody. Studia przeprowadzono na grupie 293 pacjentów ze skoliozą idiopatyczną, których charakteryzowało 15 zmiennych.

Wyniki. Z wykorzystaniem sztucznych sieci neuronowych wykazano możliwość przeprowadzenia prawidłowej klasyfikacji pacjentów w zależności od tego, czy ich stan zdrowia się pogorszył, nie zmienił lub poprawił po czterech latach leczenia.

Wnioski. Sztuczne sieci neuronowe są polecane jako nowe, obiecujące, alternatywne w stosunku do klasycznej analizy regresyjnej, narzędzie do analizy danych klinicznych. Za pomocą SNN możliwe jest wyekstrahowanie praktycznie użytecznej informacji z dużego zbioru danych klinicznych, w inny sposób trudnych do interpretacji. Informacja ta może być wartościowym wskaźnikiem prognostycznym oraz pomocna podczas ustalania strategii terapeutycznej (*Adv Clin Exp Med* 2004, 13, 4, 623–629).

Słowa kluczowe: sztuczne sieci neuronowe, skolioza idiopatyczna.

Actual trends in therapy of scoliosis occur to be a causal treatment because of the increased knowledge regards etiopathogenesis of the disease. Appearance of atrophic and degenerative changes in muscular and connective tissues, which stabilize the spine, seems to be a secondary change with respect to the damage of sensory part of reflex arc in spinal cord, disturbances in nervous-muscular connections and dysfunction of central nervous system [1, 2]. Therefore, proper rehabilitation aimed at both the controlling nervous system and the static-dynamic system of spine may lead to positive results of conservative therapy. The incidence of adolescent idiopathic scoliosis in Poland concerns from 2% to 14% of population, depending on the region of the country and the appropriate definition of scoliosis. On the other hand, in Western Europe the frequency of scoliosis varies from 2% to 3%. Of all kinds of scoliosis 80-90% is idiopathic scoliosis.

Along with several other non-operative methods, the techniques of surface electrical stimulation were introduced to the therapy of scoliosis at the beginning of 1970s [3]. The results were controversial. Initially, even 70-75% stabilization was reported [4]. Now, the opinion seems to prevail that this form of treatment does not alter the natural course of the disease [5]. The standard method of limiting of the progression of minor curves is still spinal bracing. The efficacy of bracing in preventing further progression of scoliosis has now also been found controversial, however. Some studies confirm the claims that the braces diminish progression [6] but other data suggested that such a treatment did not influence the natural history of scoliosis [7].

Scoliosis has recently been also studied employing the tools of advanced statistics. Haheer et al. constructed an outcome questionnaire to evaluate patient satisfaction and performance and to discriminate among the scoliosis patients those affected with the adolescent idiopathic scoliosis [8]. 24 questions were divided into the following seven equally weighted domains as determined by factor analysis: pain, general self-image, postoperative self-image, general function, and overall level of activity, postoperative function and satisfaction. In another study, Climent et al. approached the problem of measuring quality of life in adolescents with spine deformities [9]. They used factor analysis to reduce the number of variables. Validity of the construct was assessed using principal component analysis followed by a procedure called varimax rotation.

In various diseases the prognostic and treatment evaluation indexes have been proposed which are derived by multiple regression analysis of a number of patient, disease and treatment parameters [10, 11]. The fundamental problem with multiple regression analysis is that the parameters (independent

variables) considered simultaneously cannot be mutually related, i.e. they should be orthogonal [12]. To find a representative (and sufficiently large for statistical reasons) set of treatment parameters which would be orthogonal, is difficult. Therefore, prognostic indexes derived by means of multiple regression analysis are of rather limited reliability.

The artificial neural network (ANN) analysis is a new method of data analysis, which is to emulate the brain's way of working. Neural networks exhibit the way in which arrays of neurons probably function in biological learning and memory. ANNs differ from classical computer programs in that they "learn" from a set of examples rather than are programmed to get the right answer. The information is encoded in the strength of the network's "synaptic" connections [13, 14].

In chemistry and related fields of research interest in neural-network computing has been noted since 1986 [15, 16]. ANNs found application to classification of chemical compounds, modeling of structure-activity relationships, identification of potential drug targets and the localization of structural and functional features of biopolymers [17]. Also, the suitability of neural networks to describe the strong correlation between the carcinogenicity of polycyclic aromatic hydrocarbons and their structural parameters from ^{13}C -NMR was reported [18]. A good performance of ANN in predicting bioactivity classes based on physicochemical parameters of agents was demonstrated for dihydrofolate reductase inhibitors [19, 20]. Antitumor activity predicting potency of ANNs was also illustrated [13]. In that work the patterns of activity against a panel of 60 malignant cell lines was analyzed. Given six possible classes of drug mechanism, the ANNs missed the correct category for only 12 of 141 agents studied (8.5 percent). ANNs were proposed as decision support systems in dentistry [21], urology [22-24], and to assess HIV/AIDS-related health performance [25].

Previously, an advanced multivariate data processing method, principal component analysis (PCA), was demonstrated to provide an objective evaluation of treatment strategy by making use of large collections of routine clinical parameters of adolescent idiopathic scoliosis patients [26]. That method allowed for detection of complex systematic relationships between diverse patient, disease and treatment variables. Nowadays, the goal of the study was to check the prognosis of recovery for individual patients with adolescent idiopathic scoliosis with the use of artificial neural network (ANN) analysis. That way an attempt was undertaken to objectively check whether treatment used provided deterioration, stabilization or improvement regards patient's health.

Materials and Methods

Patients

Data for 293 patients with adolescent idiopathic scoliosis were collected. A total number of 15 variables was identified and subjected to ANN for all the patients (Tab. 1). Individual quantity

ranges were arbitrary determined before computer processing, e.g. angle of scoliosis varying from 0 to 49 degrees was divided in subclasses differing in 5 degrees. Exemplary data for selected twenty patients are presented in Table 2.

The angle of scoliosis, length of scoliosis, upper and lower limit of scoliosis and atlantal were measured by the Cobb method. The prognostic fac-

Table 1. Variables considered in artificial neural network (ANN) analysis.

Tabela 1. Zmienne rozważane w analizie metodą sztucznych sieci neuronowych

Variable no. (Numer zmiennej)	Variable name (Nazwa zmiennej)
I	Years since examination 1–14 years, 2–13 years, 3–12 years, 4–11 years, 5–10 years, 6–9 years, 7–8 years, 8–7 years
II	Sex 1 – female, 2 – male
III	Age at the time of scoliosis detection 1–4 years, 2–5 years, 3–6 years, 4–7 years, 5–8 years, 6–9 years, 7–10 years, 8–11 years, 9–12 years, 10–13 years, 11–14 years, 12–15 years
IV	Period of lateral electrical surface stimulation (LESS) treatment 1–0 years, 2–1 year, 3–2 years, 4–3 years, 5–4 years, 6–5 years, 7–6 years
V	Age at the start of the treatment 1–4 years, 2–5 years, 3–6 years, 4–7 years, 5–8 years, 6–9 years, 7–10 years, 8–11 years, 9–12 years, 10–13 years, 11–14 years, 12–15 years, 13–16 years, 14–17 years, 15–18 years, 16–19 years, 17–20 years, 18–23 years
VI	Upper limit of scoliosis 1 – vertebra 1, 2 – vertebra 2, 3 – vertebra 3, 4 – vertebra 4, 5 – vertebra 5, 6 – vertebra 6, 7 – vertebra 7, 8 – vertebra 8, 9 – vertebra 9, 10 – vertebra 10, 11 – vertebra 11, 12 – vertebra 12, 13 – vertebra 13
VII	Lower limit of scoliosis 1 – vertebra 6, 2 – vertebra 7, 3 – vertebra 9, 4 – vertebra 10, 5 – vertebra 11, 6 – vertebra 12, 7 – vertebra 13, 8 – vertebra 14, 9 – vertebra 15, 10 – vertebra 16, 11 – vertebra 17
VIII	Atlantal 1 – vertebra no. 4, 2 – vertebra no. 6, 3 – vertebra no. 7, 4 – vertebra no. 8, 5 – vertebra no. 9, 6 – vertebra no. 10, 7 – vertebra no. 11, 8 – vertebra no. 12, 9 – vertebra no. 13, 10 – vertebra no. 14, 11 – vertebra no. 15
IX	Length of scoliosis 1 – number of vertebrae 4, 2 – number of vertebrae 5, 3 – number of vertebrae 6, 4 – number of vertebrae 7, 5 – number of vertebrae 8, 6 – number of vertebrae 9, 7 – number of vertebrae 10, 8 – number of vertebrae 11, 9 – number of vertebrae 12, 10 – number of vertebrae 13, 11 – number of vertebrae 14
X	Type of scoliosis 1 – dex, 2 – sin;
XI	Time of treatment II with electrostimulation 1–1 year, 2–2 years, 3–3 years;
XII	Angle of scoliosis in degrees, examination I before treatment 1–(0–10), 2–(11–19), 3–(20–29), 4–(30–39), 5–(40–49)
XIII	F-factor, examination I before treatment 1–(0–3), 2–(3.01–5), 3–(5.01–)
XIV	Rotation, examination before treatment 1–0, 2–1, 3–2, 4–3, 5–4
XV	Risser test before treatment 1–0, 2–1, 3–2, 4–3
Class	Prognosis of recovery 1 – deterioration, 2 – stabilization or improvement

Table 2. Variables considered in artificial neural network (ANN) analysis and their values for twenty patients**Tabela 2.** Zmienne rozważane w analizie metodą sztucznych sieci neuronowych i ich wartości dla 20 pacjentów

No	I	II	III	IV	V	VI	VII	VIII	IX	X	XI	XII	XIII	XIV	XV	Class
1	7	1	3	5	7	5	5	4	4	1	1	2	1	2	1	1
2	6	1	7	1	7	6	6	5	4	1	1	1	1	2	1	2
3	7	1	11	2	12	3	9	5	10	1	2	2	1	2	4	1
4	8	2	3	1	3	4	9	6	9	1	1	1	1	2	1	1
5	6	1	8	1	8	5	6	5	5	1	1	1	1	2	1	2
6	8	2	11	1	11	5	9	6	8	1	1	1	1	2	3	1
7	8	1	9	1	9	6	6	5	4	2	1	1	1	2	1	1
8	6	1	9	2	10	5	6	5	5	1	2	4	2	3	1	2
9	6	1	8	2	9	5	4	6	7	1	2	1	1	2	1	1
10	8	1	8	1	8	6	6	5	4	1	1	1	1	2	1	2
11	8	1	11	2	12	12	11	11	3	2	1	1	1	2	1	2
12	6	1	1	2	2	8	10	8	6	1	2	2	1	2	1	1
13	8	1	7	1	7	5	8	6	7	2	1	1	1	2	3	2
14	7	1	12	1	12	6	6	5	4	1	1	1	1	2	4	2
15	8	1	4	2	5	5	6	5	5	1	1	2	1	2	1	1
16	6	2	7	1	7	8	8	7	4	2	1	1	1	2	1	2
17	8	1	12	2	13	5	4	4	3	1	1	3	2	2	3	2
18	4	1	7	2	8	5	8	6	7	1	1	1	1	2	3	1
19	7	1	10	1	10	4	5	4	5	1	1	2	1	2	4	2
20	3	1	6	2	7	5	8	6	7	1	1	1	1	2	1	1

tor F was determined according to Harrington method. Rotation degree of the spinous appendix of vertebra was evaluated by the Nash and Moe method in 0–4 scale. Risser's test was performed to test bone maturity. The final evaluation of the treatment results was based on the following criteria: angle of scoliosis in degrees after treatment, F-factor after treatment, rotation after treatment, Risser-test after treatment, upper limit of scoliosis after treatment, lower limit of scoliosis after treatment, atlantal after treatment, length of scoliosis after treatment and type scoliosis after treatment.

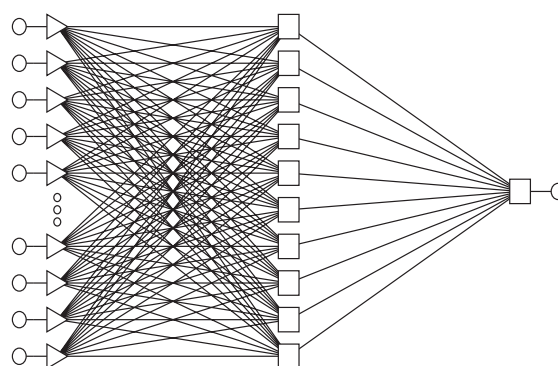
ANN Analysis

Artificial neural networks (ANN) analysis was run on a personal computer using a Statistica Neural Networks software (StatSoft, Tulsa, OK, USA).

Artificial neural network based on multilayer perceptron consisting of 15 artificial neurons in input layer, 10 in hidden layer and 1 neuron in output layer was used. The architecture of the model utilized is depicted in Figure 1. Supervised method of learning with back-propagation strategy was used. Variables for patients analyzed were divided into three sets: learning set with 173 patients, validating set with 60 patients and testing set with 60 patients. The learning of the ANN with back-propagation strategy [27–32] was executed during

100 epochs, learning coefficient was 0.1 and momentum equaled 0.3. Then ANNs learned with the use of conjugate gradient algorithm [33, 34] up to 500 epochs. Data from learning set were presented in randomized manner during the learning process.

A straightforward method for evaluation of the quality of the predictions made by the ANN is to compare the classifications assigned by the ANN to the classifications assigned *a priori*. Prediction quality can be measured more precisely using the receiver operating characteristic (ROC) curve [35, 36]. Rather than depending upon a particular classification threshold, the ROC curve integrates infor-

**Fig. 1.** Architecture of artificial neural network used

Ryc. 1. Architektura sztucznej sieci neuronowej użytej w badaniach

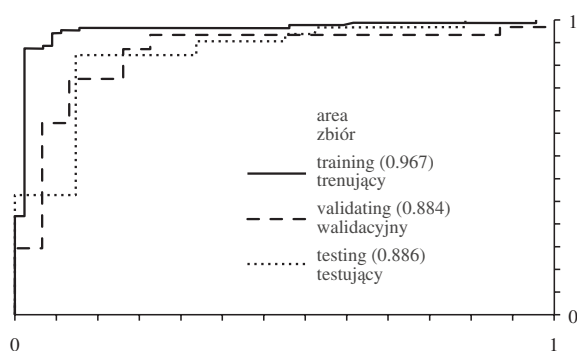


Fig. 2. Receiver Operating Characteristic curves (ROC curves) for training, validating and testing set of data

Ryc. 2. Krzywa ROC dla zbiorów trenującego, walidacyjnego i testującego

mation about the complete ranking of examples created by the ANN. The ROC curve plots, for varying classification thresholds, the number of true positives (sensitivity) as a function of false positives (specificity). The area under this curve, normalized to range from 0 to 1, is called the ROC score. A perfect classifier will rank all of the positive examples above negative examples, yielding a score close to 1. A random classifier will produce an appropriate diagonal curve, yielding a score close to 0.5. ROC for learning, validating and testing set of data is presented in Figure 2. It is seen that in all cases area under the curve exceed the value 0.88 and models based on the chosen ANN can be treated as the sensitive and accurate classifiers.

Results and Discussion

In Table 3 ANN classification statistics are collected for training, validating and testing sets. The most interesting are variables directly con-

nected to the prognosis of recovery. With the use of the proposed method it was possible to differentiate the patients with deterioration and stabilization or improvement of the health after four years of treatment with very limited error. The prognostic potency of ANN regards the training set of patients is excellent and proves good choice of the network proposed. 53 patients in the testing set of total number of 59 have been correctly classified in the group of patients with deterioration of their health, what means that one is able to predict the survival of the patients with adolescent idiopathic scoliosis utilizing the variables used with very high probability. Reasonably low percent (10%) of classifications in that set of data was wrong. However, even better predictions were obtained for testing set of patients with observed stabilization or improvement. Here only 3.5% of classifications were wrong.

Very similar results were obtained also in validating set of data. Here among 20 patients with deterioration of their health, 80% were classified correctly and among 40 patients with observed stabilization or improvement 10% of them ANN classified as wrong. Learning set of data is important for ANN to recognize the relationships between input and output data. The goodness of that recognition is checked with the use of validating set of data. That set of data does not change the weights values in the network but is able to tell about the realistic predictive properties of the designed ANN. On that basis decision about the continuation or finalization of the learning process is performed and it is done on the independent set of data (validating set) without using testing set of data, which is used only to final revision of the ANN designed. And in the case of testing set of

Table 3. Classification statistics for ANN used

Tabela 3. Statystyki klasyfikacyjne dla użytej sztucznej sieci neuronowej

	Training set (Zbiór trenujący)		Validating set (Zbiór walidacyjny)		Testing set (Zbiór testujący)	
	deterioration (pogorszenie)	stabilization or improvement (stabilizacja lub poprawa)	deterioration (pogorszenie)	stabilization or improvement (stabilizacja lub poprawa)	deterioration (pogorszenie)	stabilization or improvement (stabilizacja lub poprawa)
Total (Razem)	59	114	20	40	18	42
Right (Poprawnie)	53	110	16	36	16	37
Wrong (Błędnie)	6	4	4	4	2	5
Right % (Poprawnie %)	89.8	96.5	80.0	90.0	88.9	88.1
Wrong % (Błędnie %)	10.2	3.5	20.0	10.0	11.1	11.9

data only 2 among 18 patients with deterioration of their health were classified incorrectly. 5 patients with observed stabilization or improvement were classified incorrectly in that set of data among 42 patients with adolescent idiopathic scoliosis considered.

Finally, it can be emphasized that ANN offers an opportunity to test a practically unlimited number of either mutually related or unrelated factors. Therefore, the approach can be applied in an objective, quantitative analysis of a multitude of presently available patient and disease factors of sociological, morphological, genetic and therapeutic nature.

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