Scandinavian Journal of Gastroenterology, 2006; 41: 257–263

ORIGINAL ARTICLE

Evaluation of artificial neural networks in the classification of primary oesophageal dysmotility

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Abstract

Objective. Artificial neural networks (ANNs) can rapidly analyse large data sets and exploit complex mathematical relationships between variables. We investigated the feasibility of utilizing ANNs in the recognition and objective classification of primary oesophageal motor disorders, based on stationary oesophageal manometry recordings. ***Material and methods***. One hundred swallow sequences, including 80 that were representative of various oesophageal motor disorders and 20 of normal motility, were identified from 54 patients (34 F; median age 59 years). Two different ANN techniques were trained to recognize normal and abnormal swallow sequences using mathematical features of pressure wave patterns both with (ANN+) and without (ANN−) the inclusion of standard manometric criteria. The ANNs were cross-validated and their performances were compared to the diagnoses obtained by standard visual evaluation of the manometric data. ***Results***. Interestingly, ANN−, rather than ANN+, programs gave the best overall performance, correctly classifying >80% of swallow sequences (achalasia 100%, nutcracker oesophagus 100%, ineffective oesophageal motility 80%, diffuse oesophageal spasm 60%, normal motility 80%). The standard deviation of the distal oesophageal pressure and propagated pressure wave activity were the most influential variables in the ANN− and ANN+ programs, respectively. ***Conclusions***. ANNs represent a potentially important tool that can be used to improve the classification and diagnosis of primary oesophageal motility disorders.

Key Words: *Achalasia, artificial neural networks, diagnosis, diffuse oesophageal spasm, oesophageal manometry, oesophageal motor disorders, peristalsis*

Introduction

Oesophageal manometry is commonly performed in clinical practice to quantitatively assess oesophageal motor function. Although primary oesophageal motility disorders such as achalasia and diffuse oesophageal spasm (DOS) are well-described clinical entities, several aspects regarding their manometric diagnosis remain controversial; the entities of nutcracker oesophagus and ineffective oesophageal motility (IOM) are even less well defined [1–6]. Moreover, while recent advances in both practice guidelines [1,2] and technology [7–9] have been beneficial, the clinical classification of oesophageal motility disorders based on conventional stationary manometry continues to demand a visual interpretation of the recordings. The inherent inter- and intra-observer bias in this approach hinders the reproducible characterization of oesophageal manometric studies [1,2].

Haylett et al. [10] used non-linear chaos theory to assess and quantify oesophageal motor dysfunction; it was concluded that for the classification of oesophageal motor disorders, especially DOS and non-specific oesophageal motility disorders, such non-linear techniques may be superior to conventional techniques. Artificial neural networks (ANNs) are mathematical models that use non-linear statistical analysis to elucidate previously unrecognized relationships between given input variables and an output variable [11,12]. The basic principle of ANNs, which are based on a set of multilayered

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(Received 17 March 2005; accepted 29 June 2005)

ISSN 0036-5521 print/ISSN 1502-7708 online
DOI: 10.1080/00365520500234030

interconnected processing elements tied together with weighted connections, is "learning" through examples; their accuracy and reliability in terms of diagnosis and outcome prediction have been reported in a number of diverse clinical settings [13–15]. Kruse-Andersen et al. [16] trained an ANN with a sample of oesophageal pressure events and non-events derived from ambulatory recordings of normal subjects. A subsequent comparison of the trained ANN with an analysis program (Multigram) developed by an expert panel revealed the ANN to be more sensitive than the program in recognizing true contractions. We are not aware, however, of any data on the use of ANNs as a tool to aid the diagnosis of oesophageal motor disorders.

The overall aim of the current study was therefore to evaluate the feasibility of utilizing ANNs in the recognition and objective classification of primary oesophageal motor disorders, based on stationary oesophageal manometry recordings. The specific aims were 1) to compare the diagnostic performance of two different ANN validation techniques against the manometric diagnosis provided by experienced observers on the basis of a visual and semi-quantitative analysis, and 2) for each of these ANN techniques, to compare the performance with and without the input of standard diagnostic manometric criteria.

Material and methods

Oesophageal manometry

Manometric data were obtained from 54 patients (34 F, median age 59 years) referred for oesophageal manometry to the Gastrointestinal Investigation Unit of the Royal North Shore Hospital. Usage of these data was approved by the hospital's Human Research Ethics Committee. Oesophageal manometry was performed in a method similar to that published previously [17]. In brief, an 8-channel sleeve catheter (Dentsleeve, Belair, Australia) was introduced transnasally, and positioned such that the sleeve was located across the lower oesophageal sphincter (LOS). The catheter, perfused with water by a low-compliance capillary infusion system, was connected via external transducers to an Apple Computer-based data acquisition system (Neomedix Gastromac, Software Version 3.3.5, Sydney, Australia), with the sample frequency set at 20 per second for each channel. A minimum of 10 water swallows, each of 5 ml water at room temperature, with at least 30 s between swallows, was administered in a supine position to evaluate primary peristalsis.

The final manometric diagnosis in each patient was determined by visual and semiquantitative analysis, based on the consensus of three experienced observers according to published criteria [1,2] for evaluation of the manometric tracings: 22 studies were categorized as normal, 15 as IOM, 9 as achalasia, 6 as nutcracker oesophagus and 2 as DOS.

Artificial neural networks

(i) Design. A multilayered back-propagation ANN that runs in conjunction with Microsoft Excel (BioActivNet BAN98, AiMaze, Sydney, Australia) was used. The essential features of such an ANN are as follows: (i) during the learning (training) process, signals feed forward through an input processing layer, then through a single hidden layer of processing elements, then finally through an output layer; (ii) error signals propagate backwards to adjust the weights of the connections between processing elements until the discrepancy or mean squared error (MSE) between the true output and the network-predicted output is minimized; (iii) various constraints, such as the number of elements in the hidden layer, can be manually imposed on the ANN; and (iv) the connection weightings define the strength of the interconnections between processing elements, and are comparable to regression coefficients in linear models.

(ii) Input data preprocessing. Based on the consensus of the three experienced observers, a total of 100 swallow sequences, 20 representative of the characteristic dysmotility present in each of the five diagnostic categories, were selected from the 54 patient studies as the source data for the ANN training. Approximately equal numbers of swallow sequences were selected from each patient. For each swallow sequence, the pressure values recorded from specific oesophageal body locations (catheter channels 3, 4 and 5), the LOS (channel 7), and channel 8 (intragastric pressure, taken as baseline pressure) were exported from the Neomedix program in Excel format. These data were preprocessed to reduce cough and respiratory artefacts, by using the moving average of 10 consecutive pressure values to smooth the pressure curves.

The individual pressure events (phasic contractions) in each channel were characterized on the basis of six mathematical features or classifiers (Table I), while eight additional features encoded the relationships between pressure events in one channel with pressure events in other channels (Table II; Figure 1). It should be noted that the input variables summarized in Tables I and II do not represent major criteria currently used to discriminate between primary oesophageal motility disorders. Standard, current manometric criteria [1,2],

Table I. Specific artificial neural network (ANN) input features for characterization of pressure events within an individual catheter channel.

Feature	Description
AUC	Area under pressure curve, calculated by integration
SD	Standard deviation of all pressure values in channel
Onset	Point of initial upstroke of phasic contraction
Duration	Time from onset to end of phasic contraction, where end is taken as the point at which pressure returns to baseline value
Tmax	Elapsed time from initiation of swallow to peak amplitude of phasic contraction in the individual channels
Median time	Time which divides the AUC into two equal values

which were applied by the observers, were also encoded into numerical inputs. These criteria were as follows: presence of "nutcracker" oesophagus (peak amplitude in channel 5, i.e. distal oesophagus, $\geq$180 mmHg); propagated pressure wave activity (Tmax at channel 5 > Tmax at channel 4 > Tmax at channel 3; with Tmax as defined in Table I); and incomplete LOS relaxation (based on the pressure difference between channels 7 and 8). The above features provided for a maximum of 55 possible ANN inputs: the features summarized in Table I yielded 24 inputs, the features summarized in Table II yielded 28 inputs, and there were three inputs based on standard manometric criteria. The outputs were encoded by assigning an arbitrary number (0–4) to each diagnostic category (normal, nutcracker oesophagus, IOM, DOS, achalasia).

(iii) Training. Each ANN training run involved two sets of momentum and learning rates [18]. A high learning rate produces faster learning, but increases the risk of the ANN overshooting the generalized solution. A high momentum reduces the risk of the ANN becoming trapped into a particular solution, but also increases the risk of overshooting [18]. Optimal rates for a particular set of inputs and outputs were determined empirically during training. After each training run, the optimal set of input variables was selected by pruning redundant variables, identified by cross-correlation of the data. Variables that were highly correlated with other variables or were assigned a low weighting during training were systematically removed. Overtraining or memorization of the data was avoided by using a standard training-stopping criterion and by minimizing the number of elements in the hidden layer. Thus, training was continued for as long as the test MSE decreased appreciably, ceasing before the MSE reached zero [11,18].

(iv) Cross-validation techniques. Two established cross-validation techniques, namely "leave-one-out" and "leave-25-out" were used to evaluate the performance of each ANN [18]. The leave-one-out method automatically trained on all swallow sequences except one and then tested the omitted case; this process was repeated until every sequence had served once as a cross-validation example. The leave-25-out method was performed manually on two data sets produced by random division of the database: a training set of 75 swallow sequences (15 from each diagnostic category) and an independent set of 25 sequences (5 from each category). The ANN was trained on the first set and tested on the second set, to which it had not been previously exposed.

Table II. Specific ANN input features for characterization of the relationships between pressure events in individual catheter channels.

Feature	Description
Correlation	Correlation between the pressure values in two different channels
Weighted mean	Mean of all pressure values in channels 3, 4 and 5 combined
LOS Pr	Mean LOS pressure from start of swallow to end of contraction of channel 5
Angle	The position in space of the peak amplitude of one channel in relation to another, calculated in degrees (0 to 360) or quadrants (1–4), using vectors (see Figure 1)
Resultant vector	The vector between the above two points of peak amplitude (see Figure 1)
Pressure moments	The moment of the integrated pressure values: the mean deviations of the integrated pressure curves around the integrated mean raised to different powers (e.g. 1, 2, 3, 4, 5)
Skewness	The degree of asymmetry of the pressure curves around Tmax, calculated by moments to the 2nd power
Kurtosis	Calculated similarly to skewness, but with moments to the 4th power

Abbreviations: ANN = artificial neural network; LOS = lower oesophageal sphincter.

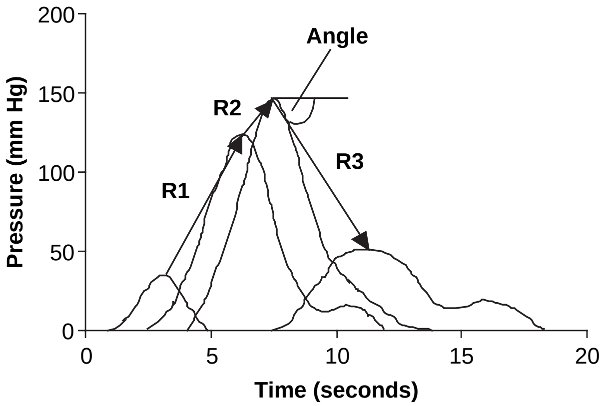

Figure 1. Superimposed pressure curves from four adjacent channels, illustrating angle and resultant vectors (R1, R2, R3) (see Table II).

Statistical analyses

The performance of each ANN was assessed by determining the percentage of correctly classified cases for each validation technique, both with and without the manometry criteria inputs, when compared to the manometric diagnosis determined by the observers. The connection weightings of each input parameter, both with and without the standard manometric criteria, were examined with the number of elements in the hidden layer kept constant, and were expressed as a percentage. The Kolmogorov-Smirnov goodness-of-fit test (K-S) was used to check the pooled connection weightings of each ANN for normality of distribution. Chi-squared and Fisher's exact tests were used to compare the performance of the ANNs. These analyses were conducted with SPSS for Windows (release 11.5; SPSS Inc., Chicago, Ill., USA), with the level of significance set at $p < 0.05$.

Results

Leave-one-out technique

For this technique, when the standard manometry criteria inputs were withheld from the ANN training set, the ANN with the highest performance level (23 inputs, 4 elements in the hidden layer and 5 in the output layer) correctly classified 82% of the swallow sequences: all achalasia, 19 nutcracker oesophagus, 16 IOM, 15 normal and 12 DOS sequences (Figure 2). When the standard manometry criteria inputs were utilized in the ANN training set, the ANN with the highest performance level (16 inputs, 4 elements in the hidden layer and 5 in the output layer) correctly classified 80% of the swallow sequences (Figure 2). There was no significant difference between the performances of these two ANN programs ($\chi^2 = 0.13$, $p = 0.72$).

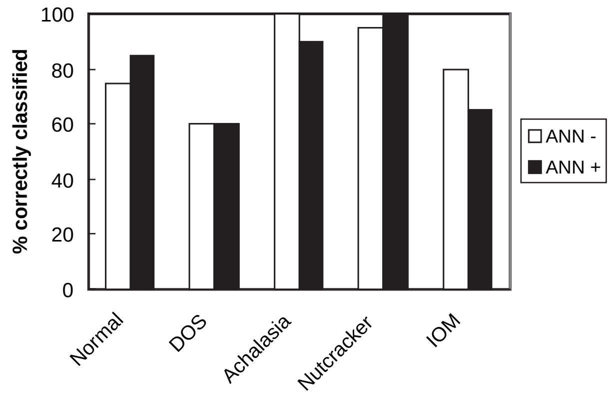

Figure 2. Performance (% of swallow sequences correctly classified) of the leave-one out cross-validation, for the ANN trained without (ANN−, unshaded bars) and the ANN trained with (ANN+, shaded bars) standard manometric criteria. The overall performance of the ANN− program (82% correctly classified) was not significantly different from that of the ANN+ program (80% correctly classified). Abbreviations: ANN = artificial neural network; DOS = diffuse oesophageal spasm; IOM = ineffective oesophageal motility.

Leave-25-out technique

For this technique, the ANN with the highest performance level (35 inputs, 3 elements in the hidden layer and 5 in the output layer) was again observed when the ANN was trained *without* the manometry criteria inputs (Figure 3). Eighteen of the 25 swallow sequences (72%) were correctly classified, including all achalasia and nutcracker oesophagus, and 80% of normal and IOM sequences. However, this ANN failed correctly to classify any DOS sequences. In contrast, when the standard manometry criteria inputs were utilized,

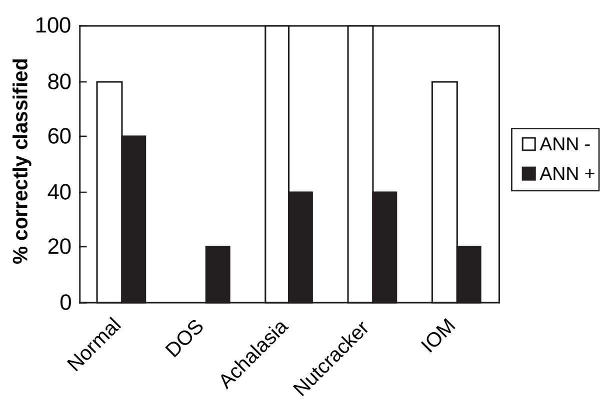

Figure 3. Performance (% of swallow sequences correctly classified) of the leave-25-out cross-validation, for the ANN trained without (ANN−, unshaded bars) and the ANN trained with (ANN+, shaded bars) standard manometric criteria. The overall performance of the ANN− program (72% correctly classified) was superior to that of the ANN+ program (36% correctly classified; $p = 0.01$). Abbreviations: ANN = artificial neural network; DOS = diffuse oesophageal spasm; IOM = ineffective oesophageal motility.

there was a markedly poorer performance for all categories with the exception of DOS, such that overall only 36% of swallow sequences were correctly classified (Figure 3; $\chi^2 = 6.52$, $p = 0.01$ versus performance of ANN trained without manometry criteria).

Comparison of cross-validation techniques

When the overall results of the leave-one-out cross-validations were compared with those of the leave-25-out technique, there was no difference in the performance of the two ANNs trained *without* the manometry criteria inputs (82% versus 72%, $\chi^2 = 1.25$, $p = 0.26$). However, for the ANNs trained *with* the standard manometric criteria, the leave-one-out performance was superior to that of the leave-25-out technique (80% versus 36%, $\chi^2 = 18.88$, $p < 0.001$).

Connection weightings

For ANNs trained *without* the manometry criteria, analysis of connection weightings for the two optimally-performing ANNs showed that the standard deviation of the distal oesophageal contractile amplitude was the most highly weighted classifier (weighting = 10%). For ANNs trained *with* the manometry criteria inputs, propagated pressure wave activity was the most highly weighted classifier (weighting = 42%). The connection weightings for ANNs trained *without* the manometry criteria were normally distributed (K-S Z score = 0.91, $p = 0.38$), whereas the weightings for the ANNs trained *with* the manometry criteria were not normally distributed (K-S Z score = 1.76, $p = 0.004$).

Discussion

To our knowledge, this study is the first to investigate the feasibility of utilizing ANNs in the diagnosis of oesophageal motility disorders. An important finding is that the diagnostic accuracy of ANNs remained high in the absence of standard clinical manometric criteria as input variables. This suggests that, with additional refinements, ANNs are likely to be able to characterize oesophageal contraction disorders on the basis of their intrinsic mathematical capabilities alone. The ANNs we developed were able correctly to diagnose all achalasia and nutcracker oesophagus swallow sequences, and a majority of the ineffective and normal sequences. The accuracy for DOS was suboptimal for the leave-25-out technique; it is likely that the reduced size of the training data set, together with the lack of more sensitive classifiers for this motility disorder, contributed to the weaker performance of this ANN in correctly classifying DOS contractile sequences. With respect to IOM, the lack of more distinctive wave pattern characteristics, when compared to achalasia and nutcracker oesophagus, likely contributed to a lower degree of accuracy.

ANNs have been increasingly used in medical decision-making over the past few years. Several studies have demonstrated the accuracy and reliability of the ANN technique in diagnostic decisions [13,19,20], tumour staging [21], prediction of disease outcome [14,15,22,23] and medical imaging [24]. The value of ANNs is that learning occurs through exposure to a training data set consisting of pairs of input–output data. ANNs learn to link input data with output data, modifying the weights of the connections between their processing elements. The knowledge acquired through the learning process enables ANNs efficiently to assign a diagnosis (output) to new data sets. In our study, the superior performance of the ANN in the leave-one-out cross-validation compared to the leave-25-out cross-validation demonstrates a trade-off between the training sample size and the ANN's predictive accuracy. An increase in the training sample size from 75 to 100, and training the ANN with all DOS swallow sequences, led to an increase in the diagnostic accuracy of the ANN.

In the present study considerable effort was made to determine the best network architecture. Encoding the features of oesophageal motility was an important initial task. Although ANNs can be used non-parametrically, training the network with excessive input data (potentially over 4000 data points per manometry trace) and using a small number of training examples would have led to paralysis of the network [19]. Extensive pre-processing of input data was therefore undertaken, using Microsoft Excel, to extract the essential features from the oesophageal motility traces and transform them into numerical values. The ANN was then used to select those features that were the most important in performing the discrimination task. The advantage of encoding features mathematically is that it represents a more logical approach to quantifying features of the motility data and hence identifying novel aspects of oesophageal dysfunction.

In regard to the connection weightings of the input variables, propagated pressure wave activity was determined by the ANN to be the most important diagnostic feature when manometric criteria were included as inputs. This corresponds with standard clinical practice where the presence of propagating sequences is the most important characteristic used to distinguish normal patterns from abnormal motility. Using the input model based on mathematical relationships of the data only, the standard deviation of the contractile amplitude in the distal oesophagus was determined by the ANN to be the most important classifier. This suggests that abnormalities in the swallow sequences were predominantly associated with distal oesophageal contractions, a finding consistent with recent concepts [3–5]. Also of considerable interest is the finding that the percentage weightings of the classifiers were more evenly distributed in the ANN model without the manometry criteria, compared to the ANN model with the manometry criteria. This suggests that ANNs are capable of learning higher-order relationships within the motility data by taking several different factors into account, rather than relying heavily on one classifier (such as peristalsis) for their decision-making process. Therefore, unlike current manometric analysis where the diagnosis may be biased towards certain visual factors, ANNs are able to exploit many different mathematical relationships of the oesophageal motility data to support their classification.

We acknowledge that our results have several limitations. First, the number of training patterns used for this feasibility study was relatively small. As five patterns per input variable have been proposed as an adequate number [25], a set of 100 to 150 representative pressure wave patterns for each motor disorder and for normal subjects would be ideal, assuming 20 to 30 inputs were utilized. Secondly, our manometric data were collected retrospectively, and we used ANNs to classify discrete swallow sequences rather than a series of patient swallows. Thirdly, a single output node was used to encode each of the five different manometric categories, and this may have created relationships between one output class and its neighbouring classes, which may have affected the optimum performance of the ANN. The use of multi-output ANNs would be more desirable, since multiple output nodes improve the separation of different classes and have been shown to be superior for multiclassification tasks [19]. These factors may well have reduced the performance of the ANNs, and if addressed could substantially improve the ANN accuracy.

In further studies more advanced approaches to signal processing and computer programming could be applied; for example automated pre-processing packages [26,27], cubic B-splines [28] or largest Lyapunov exponents [10]. In addition, "unsupervised" ANNs, i.e. those that can group similar patterns into clusters or categories, could be explored as pre-processing tools. An example of this type of ANN is the Learning Vector Quantizer (LVQ), which does not need to be trained with the correct diagnosis, although follow-up data must still be gathered to make sense of predictions. The network is thus not biased to train in a particular way. By presenting a large number of input patterns to the LVQs, the network adjusts its weights so that patterns that are similar to each other are classified into a particular group [18,19]. If the raw manometry data are directly entered and the connection weights of each cluster are examined, patterns such as IOM could, in theory, be more accurately classified by this LVQ technique.

In conclusion, with varying degrees of accuracy, we used non-linear ANN techniques to classify oesophageal motor disorders on the basis of discrete oesophageal manometric recordings. The ANNs were trained to merge basic mathematical measurements of oesophageal motor data with strict manometric criteria in an attempt to classify oesophageal motility disorders accurately in comparison with a standard visual classification. However, ANNs that were trained without encoding strict manometric criteria performed remarkably well, proving that the ANN was able to exploit higher-order relationships within the data and to characterize complex abnormalities in oesophageal contractions. The non-linear ANN technique therefore represents a potentially important diagnostic tool to improve the classification and diagnosis of primary oesophageal motor disorders, and further studies are warranted.

Acknowledgements

Financial support from the Bowel Cancer and Digestive Research Institute, Australia and advice regarding study design from Dr. Ross Smith and Mr. Graeme Snowdon are gratefully acknowledged.

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