Assessment of respiratory system mechanics by artificial neural networks: an exploratory study

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1Department of Emergency and Transplantation, Bari University Hospital, 70124 Bari, Italy; 2Department of Clinical Physiology, Öppslaga University Hospital, S-75185 Uppsala, Sweden; and 3Department of Anaesthesia, Sahlgrenska University Hospital, S-41345 Göteborg, Sweden

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Perchiazzi, Gaetano, Marieann Högman, Christian Rylander, Rocco Giuliani, Tommaso Fiore, and Göran Hedenstierna. Assessment of respiratory system mechanics by artificial neural networks: an exploratory study. J Appl Physiol 90: 1817–1824, 2001.—We evaluated 1) the performance of an artificial neural network (ANN)-based technology in assessing the respiratory system resistance (Rrs) and compliance (Crs) in a porcine model of acute lung injury and 2) the possibility of using, for ANN training, signals coming from an electrical analog (EA) of the lung. Two differently experienced ANNs were compared. One ANN (ANN_BIO) was trained on tracings recorded at different time points after the administration of oleic acid in 10 anesthetized and paralyzed pigs during constant-flow mechanical ventilation. A second ANN (ANN_MOD) was trained on EA simulations. Both ANNs were evaluated prospectively on data coming from four different pigs. Linear regression between ANN output and compliance by ANNs may require different approaches.

MATERIALS AND METHODS

Experimental design. The study was divided into three parts. The first phase intended to train an ANN to extract Rrs and Crs from the tracing of Pao, Vt, and V˙I, using data from an animal model of acute lung injury (ANN_BIO). The progressive worsening of the lung after the induction of

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damage yields different “snapshots” of the respiratory mechanics as reflected by Rrs and Crs changing over the time (see Fig. 1). These snapshots were the examples necessary to train the ANN. Ten pigs were used to provide this pool of data (the reference group). An expert made a manual calculation of Rrs and Crs directly on all curves. This was then used as a reference to which the performance of the ANN was compared.

During the second phase, an electrical analog of the lung was used to produce another pool of data. With the use of the same ranges of Rrs, Crs, and time constants (τ; τrs = Rrs·Crs) as found in the reference group, different sessions of mechanical ventilation were simulated. Then, the Pao, Vt, and Vi collected from the model were used to feed an ANN (ANNMOD) having the same architecture as the one applied previously. After premedication with azaperone (0.04 mg/kg), atropine (0.04 mg/kg), Dormitor Vet., and fentanyl (5 μg/kg) with glucose 25 mg/ml was given at the average rate of 5 mg/kg, Dormitor Vet., Orion Pharma, Sollentuna, Sweden) was fractionally injected directly into the central venous catheter in repeated doses of 0.5 ml. Before entering the circulation, it was mixed in a three-way stopcock with the turbulent flow of a high-pressure washing line opened during the injection. This procedure allowed as complete as possible dispersion of the OA into the infusate, avoiding large droplets. Administration of OA was suspended if SaO2 fell to 80%. Any fall in systemic arterial pressure during OA injection was countered using epinephrine, in boluses of 0.01 mg.

Respiratory variables recording. A D-Lite connector (Datex Ohmeda) was mounted to the endotracheal tube. The two sampling ports of the D-Lite were connected to a differential pressure transducer (Sensys, SensorTechnics, Puchheim, Germany). The transducer was calibrated at the beginning of each experimental session, using a water column for static pressures. Calibration of flow measurement was performed with a source of constant flow, the transducer to be calibrated and a precision flowmeter (calibration analyzer TS4121/P, Timeter Instrument, St. Louis, MO) connected in series. Moreover, by using a pneumatic short-circuit system (20) driven by a magnetic valve, it was possible to check the transducer for the zero point value at the beginning and repeatedly during the experimental sessions. Data from the transducer were collected by the Carina 2.4.0 acquisition program (C-O Sjöberg Engineering, Upplands-Väsby, Sweden), purposely written for the LabView acquisition system (LabView 4.0.1, National Instruments, Austin, TX). The traces of flow and pressure, collected in real time at 200 Hz, were stored on the hard disk of a personal computer. Pressure and flow tracings were recorded after a stabilization period of 60 min following instrumentation and 5, 20, 35, 50, 65, 95, and 125 min after the first administration of OA. Each recording comprised duplicate e-IHMs separated by 10 or more normal breaths. By this means, 16 curves per animal were recorded. In the period between 65 and 95 min after the first administration of OA, the PEEPs of 5 cmH2O was randomly changed to 0 or 10 cmH2O. After that, PEEPs was returned to 5 cmH2O. This intervention was introduced to provide a further source of variability during the processes of training and testing the ANNs.

Measurement of Rrs and Crs. From the recorded curves, it was necessary to obtain Rrs and Crs independently from the ANNs to have a standard of comparison. Crs was calculated.
as the ratio between \( V_T \) and \( \Delta p_{\text{st}} \), where \( \Delta p_{\text{st}} = P_2 - \text{PEEP} \), where \( P_2 \) is the pressure recorded after 2 s of end-inspiratory hold (4). Calculation of \( V_T \) was performed by integration of the inspiratory flow. \( \text{Rrs} \) was defined by the drop in pressure (\( \Delta p_{\text{dyn}} \)) divided by \( V_{\text{I}} \), where \( \Delta p_{\text{dyn}} = P_{\text{peak}} - P_1 \) (4). \( P_{\text{peak}} \) is the maximum pressure that is reached just before the e-IHM and \( P_1 \) is the level of pressure as soon as flow is stopped by the e-IHM. The measurements were corrected for the closing time of the ventilator valves according to Kochi et al. (17).

Preprocessing of raw data. The recording of \( \text{Pao} \) during e-IHM, from the PEEP preceding the breath to 2 s after the e-IHM (comprising 3.2 s of recording), was submitted to the ANN. The traces were resampled at 50 Hz to avoid redundancy of information among neighbor points (passing from 640 to 160 points per curve). Each pattern to be analyzed by the ANN comprised the 160 points described, \( V_T \) and \( V_{\text{I}} \), arriving to a final input vector of 162 points (see Fig. 2). Both input and output vectors were rescaled to obtain values that ranged between 0 and 1. When the ANN yielded its computation of \( \text{Rrs} \) and \( \text{Crs} \), it was remultiplied by the scale factor to get the measure in centimeters of \( \text{H}_2\text{O} \) times seconds per liter and milliliters per centimeters of \( \text{H}_2\text{O} \), respectively.

Neural networks. A series of feed-forward ANNs were implemented via software on a computer (Neural Networks Toolbox ver. 3.0 for MatLab ver. 5, The MathWorks, Natick, MA). The learning algorithm was resilient backpropagation, using as increment change (\( \delta \)) a value of 1.2 and as decrement \( \delta \) a value of 0.5. They consisted of three layers, whose activating functions were log-sigmoid for the input and intermediate layer and linear for the output layer. The numbers of neurons in the input and output layers were conditioned by the dimensions of the input pattern and by the number of expected variables from the net. In this way, the input layer was composed of 162 neurons and the output layer of 2 neurons, one yielding \( \text{Rrs} \) and the other one \( \text{Crs} \).

Choice of the best architecture. To choose the best architecture of the ANN, i.e., the number of intermediate neurons that provided the best performance for the required task (see below), a series of tests was performed. These included training several ANNs differing from each other by the number of intermediate neurons. Architectures having all the possible finite numbers of intermediate neurons between 2 and 30 were studied, reaching a total of 29 different architectures. The technique used was a multifold cross-validation method with early stopping (for details, see Haykin, Ref. 11). The pool of curves obtained by the reference group was composed of 160 traces in random order and was divided into eight groups. Each ANN was trained on seven groups and validated on the last one. This procedure was done eight times for each net, leaving out a different group for the validation. Each training process had to stop if the error on the validation set rose. The performance of each ANN was computed eight times, once per training/validation session. It was assessed by calculating the mean squared error (MSE) of the ANN on \( \text{Rrs} \) and \( \text{Crs} \). Moreover, it was possible to use the average MSE of the best network as our target MSE for ANN_{BIO} final training.

Training of ANN_{BIO}. After the choice of architecture and target MSE to aim at, it was necessary to train the ANN to assess respiratory system mechanics. The pool of data coming from the reference group (160 curves) was randomly divided in two new subsets. One made up the final training pool composed of 128 curves (80% of the reference group data), and the other formed the final test pool (Te_{BIO-P}) with 32 curves (20% of reference group data). The training stopped if the performance goal (lowest MSE, produced by the best architecture, in the previous experimental phase) was met, if the number of presentations of the training set exceeded 1,000 iterations, or if the MSE on Te_{BIO-P} started to rise.

Fig. 2. Recorded curves, after the sampling, are sent to the artificial neural network (ANN). The first 160 neurons receive pressure data, and the last 2 neurons receive data for tidal volume (\( V_T \) and flow at peak pressure (\( V_{\text{I}} \). After processing by the intermediate layer (27 neurons), information arrives to the output layer, which yields respiratory system resistance (\( \text{Rrs} \)) and compliance (\( \text{Crs} \)). See text for details.
(early stopping). Fifty different ANNs, having the same architecture but different node weights, were trained. The one having the lowest MSE on TeBIO-P was eligible for the prospective test. Assessment of training was performed by measuring the final MSE on TeBIO-P and by computing linear regression between results from ANN output and those manually calculated.

**Electrical analog of the lung.** An electrical analog of the lung was implemented on a computer via software (Pater program, University of Bari, Italy). It reproduced the model proposed by Otis et al. (22) in 1956 and was composed of two parallel limbs connected to the equivalent of airway opening by a common resistance. Each limb consisted of a resistor and a capacitor, connected in series. This circuit is a bicompartamental model of the lung. By changing the values of resistance and compliance, different conditions were simulated. “Ventilation” of the model is obtained by simulating the application of forcing currents, whose variation in time is equal to the ventilatory pattern. Resistance and compliance were kept constant and invariable over the time during each ventilatory session. Each session consisted of six respiratory cycles to ensure that the last cycle was performed under steady-state condition. The values assigned to each resistance and compliance were chosen to reproduce the same steady-state condition. The values assigned to each resistance and compliance, different conditions were simulated. Resistance and compliance, different conditions were simulated.

Manually computed mechanics. Crs dropped from 28.5 ± 7.4 to 16.5 ± 4.3 ml/cmH2O and Rrs rose from 13.8 ± 2.8 to 19.7 ± 8.8 cmH2O·s·l−1 over a 125-min period after first OA injection (means ± SD). In particular, pigs belonging to reference group showed Crs decreasing from 30.2 ± 6.4 to 16.9 ± 3.7 ml/cmH2O and Rrs increasing from 14.4 ± 3.0 to 23.1 ± 9.0 cmH2O·s·l−1. Pigs in the prospective group had a Crs that changed from 24.0 ± 8.2 to 15.6 ± 5.5 ml/cmH2O and a Rrs from 12.1 ± 1.2 to 12.9 ± 1.5 cmH2O·s·l−1 (see Fig. 4).

**Choice of ANN architecture.** The architecture having the lowest average MSE over the eight sessions of cross-validation test was the one with 27 intermediate neurons. It reached an average MSE of 0.0006. ANN training. After training was completed, the performance of the ANN BIO on TeBIO-P was expressed by a MSE of 0.00081. The linear regression between neural network output and manually computed values had a regression coefficient (R) of 0.97 for Rrs; for Crs it was R = 0.99. ANN MOD, after training, showed a MSE of 0.00056 on TeMOD-P. Linear regression between ANN MOD output and manually calculated values had R = 0.99 on Rrs and R = 1.00 on Crs (see Table 1).

**Prospective test.** Linear regression between measured respiratory mechanics by ANN BIO and manually computed values was expressed by R = 0.40 on Rrs and R = 0.98 on Crs with MSE = 0.0037. For ANN MOD, regression was expressed by R = 0.61 on Rrs and R = 0.98 on Crs with MSE = 0.0038.

The measurement errors, expressed as means ± SD, were −2.11 ± 4.61 cmH2O·s·l−1 on Rrs and 0.17 ± 1.14 ml/cmH2O on Crs for ANN BIO. Values for ANN MOD
Neural networks trained on biological and electrical analog data, respectively; TrBIO-P, pool of curves from reference group of pigs, for training pigs. See text for explanation.

ANNBIO; TrMOD-P, pool of curves from electrical analog, for training ANNMOD; TeBIO-P, pool of curves from reference group, for testing.

Results

In both ANNs, the performance in assessing lung mechanics was separately assessed. In both ANNs, the performance on the lowest error on electrical analog tracings were picked error on biological tracings and the ANN with the lowest error on biological tracings and the ANN with the same architecture (i.e., the same number and the same disposition of nodes) the ANN with the lowest error on electrical analog tracings were picked out. Finally, these two ANN faced data coming from different individuals (the prospective group), and their performance in assessing lung mechanics was separately assessed. In both ANNs, the performance on the prospective group was very good for the assessment of Crs and not as good for the assessment of Rrs.

About the methods. The decision to avoid corrections for temperature, humidity, intrinsic PEEP, and endotracheal tube resistance is a consequence of the aims of this study. We wanted to evaluate whether the ANNs “saw what we could see” in the traces. All the information that was not directly transferable to the ANN was not used in the computation.

Scaling the input and the output vectors of an ANN is a transparent procedure. In fact, the values that the ANNs yielded were multiplied again for the scale factor. Scaling all the input vectors to obtain “small numbers” (namely, having mean values of the input close to zero) is claimed to hasten the learning process.

We introduced an electrical analog of the lung, mathematically implemented on a computer, to evaluate its usefulness in training an ANN. It is a noise-free source of data that can simulate infinite combinations of Rrs and Crs. By this means, it is possible to obtain tracings created by combinations of Rrs and Crs that, although possible, are unlikely to be found in the spectrum of natural variability.

In studies of these new methods, models have great importance. ANNs learn by experience. However, in the field of experimental biology, it is not so easy to obtain the large number of examples that are required to train ANNs. Models can provide the number of examples necessary for training both in the normal range of variability and in extreme conditions.

The process of choosing the best “physical” structure of an ANN (i.e., the architecture) is different from the process of training it. After we chose the architecture of the ANN, the only information we used in the successive phases of the experiments was the number and disposition of nodes plus the MSE that was reached. This value of MSE was used as the performance goal at which we could aim during the effective training phase.

Dimensioning the architecture of the ANNs was accomplished on biological tracings. The reason for this choice lies in the fact that any ANN has to be dimensioned on the most complicated task that is foreseeable during its use. In fact, real recordings contain different forms of biological noise, which makes the task of

DISCUSSION

The best ANN architecture for the assessment of respiratory system mechanics was chosen by first using a pool of data (from the reference group of pigs). Then, the ANNs’ training started. Fifty ANNs were trained and tested using biological data from the reference group, and another fifty were trained and tested using biological data from the prospective group. ANNs yielded were multiplied again for the scale factor. Scaling all the input vectors to obtain “small numbers” (namely, having mean values of the input close to zero) is claimed to hasten the learning process (12).

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Table 1. Results

<table>
<thead>
<tr>
<th>Artificial Neural Network</th>
<th>Trained On</th>
<th>Tested On</th>
<th>Linear Regression for Rrs</th>
<th>Linear Regression for Crs</th>
<th>MSE</th>
</tr>
</thead>
<tbody>
<tr>
<td>ANN_BIO</td>
<td>TrBIO-P</td>
<td>TeBIO-P</td>
<td>y = 0.93x + 1.26</td>
<td>y = 0.99x + 0.13</td>
<td>0.00081</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>R = 0.97</td>
<td>R = 0.99</td>
<td></td>
</tr>
<tr>
<td></td>
<td>PR-P</td>
<td></td>
<td>y = 0.84x + 4.16</td>
<td>y = 0.97x + 0.44</td>
<td>0.0037</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>R = 0.40</td>
<td>R = 0.98</td>
<td></td>
</tr>
<tr>
<td></td>
<td>TrMOD-P</td>
<td>TeMOD-P</td>
<td>y = 0.96x + 1.02</td>
<td>y = 1.00x + 0.00</td>
<td>0.00056</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>R = 0.99</td>
<td>R = 1.00</td>
<td></td>
</tr>
<tr>
<td></td>
<td>PR-P</td>
<td></td>
<td>y = 1.52x − 6.95</td>
<td>y = 0.97x − 1.00</td>
<td>0.0038</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>R = 0.61</td>
<td>R = 0.98</td>
<td></td>
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</tbody>
</table>

Rrs and Crs, resistance and compliance, respectively, of the respiratory system; MSE, mean squared error; ANN_BIO and ANN_MOD, artificial neural networks trained on biological and electrical analog data, respectively; TrBIO-P, pool of curves from reference group of pigs, for training ANN_BIO; TrMOD-P, pool of curves from electrical analog, for training ANN_MOD; TeBIO-P, pool of curves from reference group of pigs, for testing ANN_BIO; TeMOD-P, pool of curves from electrical analog, for testing ANN_MOD; PR-P, prospective pool of curves from the prospective group of pigs. See text for explanation.
extracting lung mechanics variables more complex compared with the same task performed on simulated tracings.

After we decided their architecture in the previous part of the study, 50 ANNs were trained on biological data and 50 on model tracings. Each ANN started with random weights assigned to its connections, and the process of learning consisted of adjusting them. Although two networks having the same architecture can show similar performance on the same task, in reality they start the process of learning from different “backgrounds.” This background is the random assignment of weights to the ANN when it is initialized. This means that, to observe similar performance by two physically similar ANNs, it is necessary to push the number of iterations to a high number. To optimize our computational resources, we preferred to stop the training after a discrete number of iterations and evaluate the performance. The ANNs with the lower MSE were the ones in which the convergence to a minimum error was also driven by a favorable random matrix of weights assigned at the beginning.

About the results. ANN_BIO and ANN_MOD were able to learn the relation between the input pattern and the corresponding Rrs and Crs. This fact is demonstrated by the performance showed on their respective test groups (TeMOD-P and TeBIO-P), expressed by $R$ of no lower than 0.97. However, we did not consider these results sufficient to get any conclusion about their possible use. Hence, the decision for a prospective study was made. As a result, in these prospective tests, the performance on Crs remained very good, both by ANN_BIO and ANN_MOD. However, this was not true for Rrs. In fact, the regression coefficient of ANN performance vs. manually computed results was 0.98 for Crs (in both networks) but only 0.40 (in ANN_BIO) and 0.61 (in ANN_MOD) for Rrs.

The values of Rrs and Crs expressed by the reference and the prospective group of animals may belong to different statistical populations (Fig. 3). However, the problem of statistical difference between the groups has not been addressed in this paper because it was not required by the study.

ANNs perform better when they face data that are internal to the range of variation of the data used for training. Whether the two groups are statistically different has no importance. In fact, each tracing of the prospective group is a single entity that is given alone to the network and to which the network answers with an output based on its previously acquired knowledge. This means that the sequence of curves or their characteristics do not affect the performance of an ANN on a successive one.

As can be seen in Fig. 3, the measures of Rrs and Crs in the prospective group are reported to be near the lower limits of the variability spectrum. Moreover, ANN_BIO was also tested on a few values (equal to 3% of the 64 measurement composing the prospective group) that were outside the range of its training. But this fact cannot explain the poor regression between Rrs measurements.

More probably, the reason for poorer performance on Rrs lies in the architecture of the net. In fact, the strength of ANNs and, in general, of processing systems distributed in parallel is attributed to the capability of extracting information from numerous data. Thus, if a part of these vectors differs from the prototype used for training, the overall performance should not be much affected.

To extract Crs, ANNs can use all the points from P₁ to P₂ (2 s, for a total of 100 points at 50 Hz sampling). We can consider also information present in the slope of Pao during inspiration (~1 s, another 50 points) because flow is constant and the ratio of volume to Pao,
although in dynamic conditions, is a measure of Crs. Information regarding resistance is only in two small groups of points. These are the drop between $P_{\text{peak}}$ and $P_1$ and also the very first rise in pressure, at the beginning of the flow (the so-called resistive rise). It comprises only 20–30 points.

If the signal presents any source of error, because each point contributes only for a fraction to the final calculation, calculations based on more points have higher probabilities of compensating for an error. Considering that resistance in this particular setting is calculated only on a few points (in comparison to compliance), the possibilities of being affected by whatever kind of noise are greater than for compliance.

For future development of ANN in the evaluation of respiratory mechanics, the use of two different ANNs may be considered: one for Crs and another for Rrs. In fact, we must consider that global error function such as MSE computes the error on both Rrs and Crs. And so, for a given target MSE, if Crs is perfectly assessed by the ANN, the results on Rrs could also be less good, on condition that overall MSE is within the imposed limit.

This consideration brings another important point into the discussion. It is the idea that different ANN architectures (and indirectly the way they are fed by information) could have different performance on the same task. We wanted to explore the practical problems of their use in our field of research. To perform this particular task, it was necessary to reduce to the minimum the preprocessing of curves (hence the decision of giving to the ANNs the complete Pao curve) and to train the ANNs to calculate Rrs and Crs at the same time and in the same way. Moreover, we reduced all the operations requiring choices by human “experts” (i.e., cutting parts of the trace, or picking only significant points). They could have shown better performances if, instead of complete traces, we gave only some characteristics of the curves. However, in this case, we would not have had the possibility of evaluating the robustness of ANNs to noise and perturbation of signals. In fact, adding the step of human choice in picking what is important and what is not, we would have also added another source of error.

Another important message arrives from the comparison between ANN_BIO and ANN_MOD. Electrical analogs of the lung can be used in the training phase of ANNs. The two differently experienced ANNs have largely similar performances in the assessment of Crs. This suggests that training the ANNs can also be done by the use of models, hence the possibility of cutting the time required for training them.

**Perspectives.** The most important achievement of this study is that an ANN able to extract Crs from Pao and Vi signals has been built up. Now the question is whether we should use these methods or whether there is any case for using ANNs instead of usual techniques. It must be clear that, when we have the equation to solve a problem and good data to assign to equation parameters, ANNs are not the best choice. Their limit is that they may have less precision (although well trained) if they compete against a defined equation and pure data. So, for research purposes, manual calculation of respiratory variables may still remain as the reference method. This means that we may not have the need of using ANNs as an “instrument of comprehension” in research. In fact, a trained ANN is a black box: able to reproduce the mechanics of a system but unable to give plain explanation in what way it does it. This is also the key point when comparing ANNs to methods of function fitting. In fact, curve fitting is an analytical method, requiring a preconceived idea about the number of variables and the complexity of the equation to be applied for solving a particular problem.

An ANN does not require any insight into the mechanics of the system by the researchers. But it has an advantage over other methods: a property known as robustness. It is the property for which degradation of its performance is slow and smooth in case of bad inputs (noise, malfunctioning of sensors) that makes it a suitable choice for controlling machines. In the world of mechanical ventilation in intensive care units, the need is arising for a tool to interface information from sensors to guide ventilators in closed loop (24). Our opinion is that, for their characteristics, as shown in neighboring fields of research (15), ANNs may play a key role in this development.

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