To what extent can artificial neural network support nuclear medicine?

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Abstract

Artificial Neural Networks (ANN) are computer programs that emulate the operation of a large number of processing units that mimic the fundamental mechanisms of the biological activity of nervous cells as well as their connections and interactions. As a human brain, an ANN has the ability to learn from the experience of general relations between variables and thus ANN are particularly suitable to capture the natural complexity of medical data. Today ANN are widely used as a tool for computer aided diagnosis. This editorial discusses to what extent ANN can support Nuclear Medicine.

Introduction

The physician's request for accurate and fast analysis of medical imaging data motivated the employment of artificial intelligence (AI) technologies [1]. Artificial neural network (ANN) is one of the powerful AI techniques and emulate the activity of biological neural networks in the human brain. Basically, an ANN is a mathematical model implemented through a computer program that reproduces the connection of a large number of processing units that mimics the fundamental mechanism of the biological activity of nervous cells as well as their connections and interactions.

The techniques of ANN have the ability to learn from a data set and to build weight matrices to represent the learning patterns [1]. A schematic representation of an ANN is shown in Figure 1. ANN have been successfully applied in Medicine and in other disciplines including pattern classification, decision making, adaptive control, parameter estimation and fault diagnosis [2-4]. The most attractive property of ANN in the medical field is the ability to identify strongly nonlinear multidimensional relationships in clinical data not apparent to other forms of analyses thus improving the diagnostic accuracy. Differently from classical standard statistical techniques (e.g. multiple regression) that allow the separation of diagnostic classes only in case the data are linearly separable, ANN are suited to solve a wide class of linearly non-separable problems that may be present in medical data [5]. The ANN techniques are today applied in many areas as shall be described below.

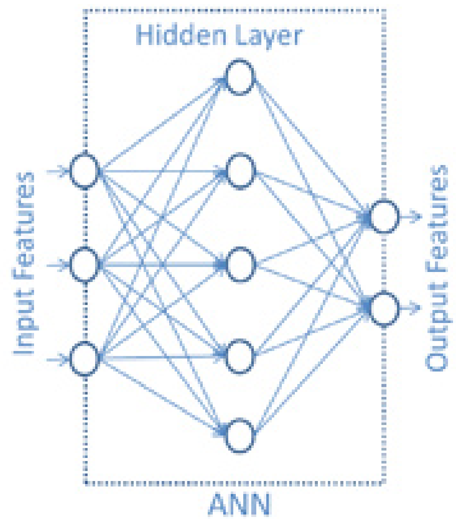

Figure 1. Block diagram of an ANN. The circles (neurons) represent the computation units, the connection lines represent the inter neurons connections (synapses).

The techniques of ANN are today employed in many areas dealing with nuclear medicine such as for medical image preprocessing, image segmentation and image object detection and recognition [6, 7] and are also used for image restoration, and for noise and tremor removal using an advanced data fusion technique based on Kalman filters [8-9].

Another very important use of ANN is as a tool for computer aided diagnosis (CAID) that is becoming one of the major research subjects in medical imaging [10]. In this context the salient features, to be used for diagnosis, are extracted from the images either by human assistance or automatically from raw data using features extraction algorithms originally developed for robotic applications [11]. Despite the intrinsic complexity of the mathematical structure, the success of ANN in CAID is a result of its uncomplicated usage as a conventional tool. The user has to simply select representative data and start a training algorithm. This technique automatically produces an adequate structure of data upon which it generates the final result and today many simple ANN based softwares are available for the physician for CAID purposes [12, 13].

Artificial neural networks in Nuclear Medicine

Some representative papers on the application of ANN in Nuclear Medicine will follow to highlight the benefits of ANN for CAID.

According to a recent paper [14] CAID has already become a part of the routine clinical work-up for the diagnosis of breast cancer with mammograms. The computer output is used as a "second opinion" in helping radiologists' image interpretations. The computer algorithm generally includes image processing, image feature extraction, analysis and data classification procedures exploiting advanced data processing tools such as ANN.

The techniques of ANN were first used in 1990 for CAID of interstitial lung diseases and since then, this method has been widely used to support the diagnosis of various diseases with different imaging modalities, in particular for the differential diagnosis of lung nodules and interstitial lung diseases by chest radiography, CT and PET/CT [14]. For example, other researchers [15] investigated the role of ANN to differentiate benign and malignant pulmonary nodes using features obtained by CT, ^{18}F-FDG PET, and both CT and ^{18}F-FDG PET.

Three ANN schemes were implemented using as inputs imaging features extracted from CT alone, PET alone and both CT and PET with the addition of clinical features (patient age, sex, smoking status, and history of previous malignancy) and the output predicted by ANN classifiers was evaluated using receiver-operating-characteristic (ROC) analysis. The results showed that the ANN based on both PET and CT had a better statistical prediction ability to differentiate benign from malignant pulmonary nodules than the ANN based on PET alone and CT alone. The clinical value of this paper to characterize SPN depended on the above analytical evaluation of PET, CT and PET/CT by comparing many clinical parameters.

Other researchers [16] used a back-propagation ANN trained on ^{18}F-FDG PET-and CT-derived data on a cohort of 133 patients with surgically proven non-small cell lung cancers to investigate if ANN accuracy was better to that of a trained ^{18}F-FDG PET reader in predicting the true surgicopathologic nodal stage. The ANN was able to correctly identify the N stage in 87.3% of the testing (validation) cases comparing with 73.5% for the ^{18}F-FDG PET expert reader. The authors concluded that a back-propagation ANN was more accurate to predict hilar and mediastinal nodal involvement than an expert ^{18}F-FDG PET reader. The clinical relevance of these findings consisted of the possibility to use such a tool to enhance the accuracy of clinical interpretations and to help to train residents and fellows in reading PET scans.

Other researchers [17] investigated the performance of an ANN to evaluate ^{18}F-FDG uptake in the liver as investigated by PET/ CT scan, compared with the results of expert interpretation of abdominal liver magnetic resonance images (MRI). Interpretations of the scans from PET/CT examinations by trained neural networks were cross-classified with expert interpretations of the findings obtained by MRI for the differential diagnosis between intrahepatic benign or malignant lesions. The significance of the difference between neural network receiver operator characteristics (ROC) curves and the ROC curves obtained by the performance of two expert readers in the interpretation of liver ^{18}F-FDG uptake was calculated showing that ANN trained on PET/CT scan data resulted sensitive and specific to evaluate the presence of intrahepatic malignancy, being comparable with interpretation by expert observers. Therefore the authors concluded that ANN can improve the accuracy of the human interpreter, if used in conjunction with human expertise.

It is worth of notice that many papers have investigated the role of an ANN based analysis in the diagnosis of different brain diseases. An interesting study [18] showed the usefulness of an ANN in the differential diagnosis between patients with Alzheimer's disease (AD) and age-matched control subjects undergoing ^{99m}Tc-HMPAO brain SPET using cortical circumferential profiling. The performance of an ANN classifier, trained using the obtained data, was compared with that of more traditional statistical techniques (discriminant function line and discriminant analysis classifier) and that of two expert observers, demonstrating that the ANN classifier had a better performance than that of the other statistical techniques and the expert observers.

A similar study by other researchers [19] evaluated the diagnostic performance of artificial ANN in discriminating patients with probable AD, mild or mild cognitive impairment and normal controls by means of perfusion brain SPET data. The results were compared with those obtained by discriminant analysis, showing that the feed-forward ANN analysis classified patients better than discriminant analysis in both parts of the study.

The ability of ANN to discriminate AD patients and normal subjects identifying subgroups of patients sharing similar perfusion deficits (as evaluated by xenon-133 brain SPET) was further confirmed by a more recent study [20]. A cluster analysis of the group of AD patients identified 3/4 subgroups with different combinations of blood flow pathology, but in all subgroups a significant bilateral temporoparietal perfusion impairment was present. Therefore the authors concluded that ANN analysis represented a valid method to discriminate AD patients from normal controls basing on perfusion pattern.

Another application of ANN in Neurology is represented by the use of CAID to investigate the ability of brain SPET with the dopaminergic tracer ^{123}I-FP-CIT (^{123}I-N-omega-fluoropropyl-2beta-carbomethoxy-3beta-(4-iodophenyl)nortropane, DaTSCAN) with semiquantitative analysis in the investigation of movement disorders. Two papers, the first in 2006 [21] and the second in 2010 by our group [22] evaluated the ability of ANN to contribute to the differential diagnosis between Parkinson's disease (PD) and essential tremor (ET).

The first paper as above [21] investigated if a two-stage analysis was able to differentiate between parkinsonian syndromes of various stages and ET and if such a two-stage analysis can be performed in a single step using ANN. In the first stage they assessed the striatum-to-occipital cortex ratio to evaluate non-early parkinsonian syndromes (and patients with a low ratio would be stopped at this step) and in the second stage they measured the putamen-to-caudate nucleus ratio. Finally, the two-stage analysis was performed and repeated, in a single step, using an ANN, showing that the two-stage analysis was less effective than the single step process using the ANN, that was clearly able to discriminate between parkinsonian syndromes and ET in all subjects. The authors concluded that results of the single stage ANN analysis were very definite and it may be considered to have potential in the quantification of DaTSCAN images for clinical use. The limitation of this study consisted of the reduced

Table 1. *Results of a research using the PubMed database (http://www.ncbi.nlm.nih.gov/pubmed) on the number of papers published in the period 1980-2012 using the keyword listed in the first column, to show the increasing role of ANN in Nuclear Medicine and Radiology.*

Keywords		1980-2000	2001-2006	2007-2012
Neural Network		3824	4057	5846
»	» + PET	27	34	32
»	» + SPET/SPET	16	5	12
»	» +MRI	22	44	113
»	» + CT	17	24	51
»	» + Radiology	12	5	3
»	» + Nuclear Medicine	4	3	2

number of subjects studied (n. 18) and the fact that the "gold standard" outcome was the judgement of a single experienced observer. However the paper is original and interesting from a clinical point of view.

Our paper [22] evaluated data from 216 patients, 89 with ET, 64 with early PD and 63 with advanced PD undergoing brain SPET with ^{123}I-FP-CIT with semiquantitative analysis. We compared two different artificial neural network classifiers using ^{123}I-FP-CIT SPET data, a probabilistic neural network (PNN) and a classification tree (ClT). Our results confirmed that PNN allowed to obtain valid classification results (higher than 90%), while ClT was able to provide a reliable classification (higher than 80%) producing cut-off values (if the caudate nucleus value was higher than 6.97 patients were classified as having early PD, and if the value was <6.97 patients were classified as having advanced PD) useful to differentiate ET and PD of different severity.

Finally, we would like to underline that the above cited papers are only a selection of the most representative using ANN in Nuclear Medicine, because many other papers on this topic are available in the international literature and the trend is increasing in the recent years, as documented in Table 1, showing the results of a research using the PubMed database on the number of papers published in the period 1980-2012 using the keyword listed in the first column, to evidence the increasing role of ANN in Nuclear Medicine and Radiology.

In conclusion, this editorial demonstrated the wide flexibility of the ANN to obtain promising results with significant diagnostic accuracy in many CAID problems in Nuclear Medicine. However more work is necessary before these networks can be widely applied.

The authors declare that they have no conflicts of interest.

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