

## ANALYSIS OF DYNAMIC POSITRON EMISSION TOMOGRAPHY IMAGES USING A NEURAL NETWORK

The imaging of neurotransmitter receptors by positron emission tomography (PET) scanning is useful for assessing drug potency. We obtained two time series of PET images forming a time history of brain activity. In one time series, the subject was given a histamine blocker; no blocker was administered in the other. In both cases a radioligand was used for imaging. The images were input to an adaptive resonance theory (ART) neural network, which categorized the blocked and unblocked PET scan time series differently. Differences corresponded to areas of high histamine receptor density. Although the sample size was small, the disparity in the blocked and unblocked results agreed with locations of histamine receptors, indicating that the ART neural network has promise as a means of determining the effectiveness of histamine blockers.

### INTRODUCTION

Many diseases and syndromes are caused by abnormalities in the behavior of receptors. Positron emission tomography (PET) is used to quantitatively image neuroreceptor systems of the human brain *in vivo*. Such imaging involves the injection of a radioligand (a neurotransmitter-like substance tagged with a positron-emitting isotope) or tracer, which is imaged by a PET scanner. Receptor-rich areas will bind the ligand more strongly than receptor-poor areas. The goals of pattern recognition are to identify and separate those regions of interest for further quantitative analysis of the data.

In this study, we analyzed PET image sequences by using an adaptive resonance theory (ART) neural network. The goals were to show that the ART network could separate image pixels into receptor-rich and receptor-poor regions and that receptor blockage would reduce the number of image pixels in receptor-rich regions.

Dynamic PET studies involving a series of PET images taken to obtain a time history of brain activity have previously been analyzed by factor analysis.<sup>1</sup> In this method, a time series for each pixel of a dynamic PET study is created and is represented by a linear combination of several independent factors. However, the kinetics of the injected tracer are not always linear, so representing the activity of the tracer using a linear equation may not be accurate. Also, the results of factor analysis depend on the method applied for factor extraction and rotation, and thus may not be reproducible.

### DESCRIPTION OF THE DATA

The data for this study were obtained from a normal volunteer who was injected twice with [<sup>11</sup>C]pyrilamine as the radioligand.<sup>2</sup> The first injection was given with no pretreatment ("unblocked"). The second injection was given after administration of an H<sub>1</sub> receptor antagonist

("blocked"). For the dynamic PET studies, 13 scans were taken over 90 min. The scans were not evenly spaced in time. Scanning duration increased with time following injection to compensate for data degradation due to physical decay of the isotope.

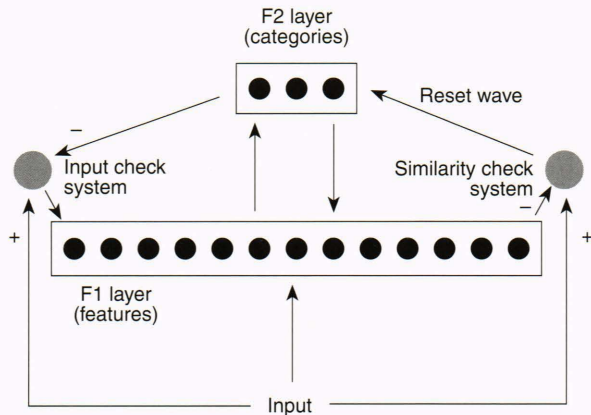
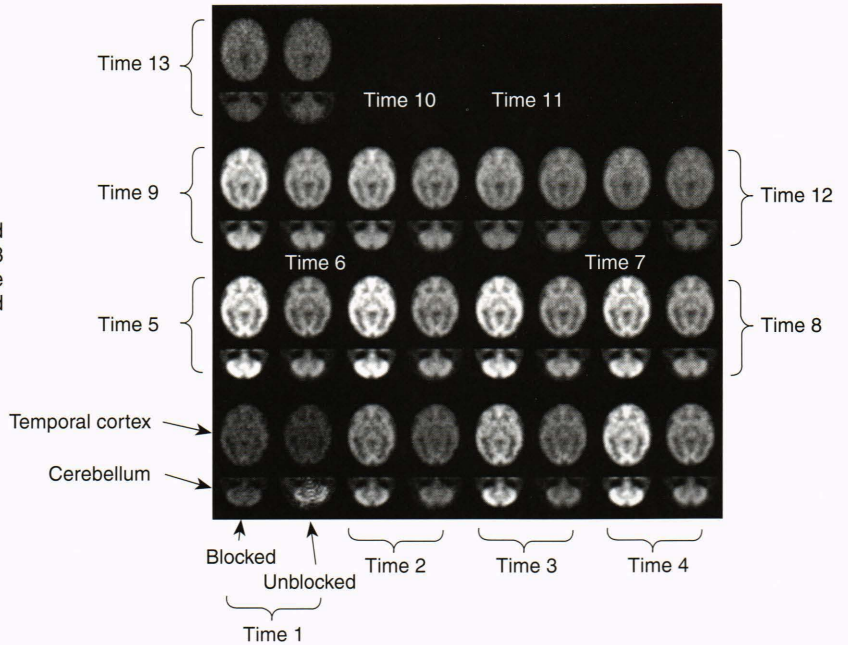
Figure 1 shows the PET scans obtained. The two brain slices are at the level of the temporal cortex and the cerebellum. Images of the two slices for both the unblocked and blocked study are displayed as 64 × 64 pixel matrices; thus both the unblocked and blocked images are displayed by 32 × 64 pixels. For our study, a time series of 13 points was created for each pixel, that is, 32 × 64 = 2048 time series were obtained for the blocked and unblocked states.

### ADAPTIVE RESONANCE THEORY NEURAL NETWORK

The time series were input to an ART neural network,<sup>3</sup> which is self-organizing. The desired output need not be known to train the network. Figure 2 shows the basic operation of an ART neural network. The network classifies similar pixel time histories into categories.

The input is fed to the F1 layer and leads to activity in the feature detector neurons in F1. Each neuron in the F1 layer represents a feature (i.e., pixel intensity at 1 of 13 times). The activity passes through weighted connections to the neurons in the F2 layer. This is the bottom-up pathway. Each F2 neuron represents a category. It adds together its input from the F1 neurons and responds by sending information back to the F1 layer. This is the top-down pathway. The top-down pathway is a template of critical features for a category. Each neuron in F1 is connected to every neuron in F2 by a bottom-up connection, and each neuron in F2 is connected to every neuron in F1 by a top-down connection. When the bottom-up and

**Figure 1.** Two brain slices each for blocked and unblocked studies for PET scans at 13 different times, forming a time history. The time history for each pixel in blocked and unblocked scans was input to a neural network.



**Figure 2.** ART neural network. Features are input to the F1 layer, and the ART neural network indicates the category of the input in the F2 layer. The input check system ensures there is input. The similarity check system controls how similar sets of input must be to be put into the same category.

top-down activities are very similar, resonance occurs and a category is chosen.

The neural network learns categories by adjusting the top-down and bottom-up connection weights. These weights are changed in response to the presentation of input patterns. Thus, during learning, the template for a particular category is adjusted every time a new input is added to that category. During learning, only one F2 neuron (category) is active at a time. Thus, while the template for one category is being learned, the templates for other categories are unaffected.

The input check unit shown in Fig. 2 prevents purely top-down signals from leading to F1 activity. If an F2 neuron were active without any input, the top-down pathway would lead to activity in the F1 layer, and the bottom-up pathway would lead to reinforcement in the F2

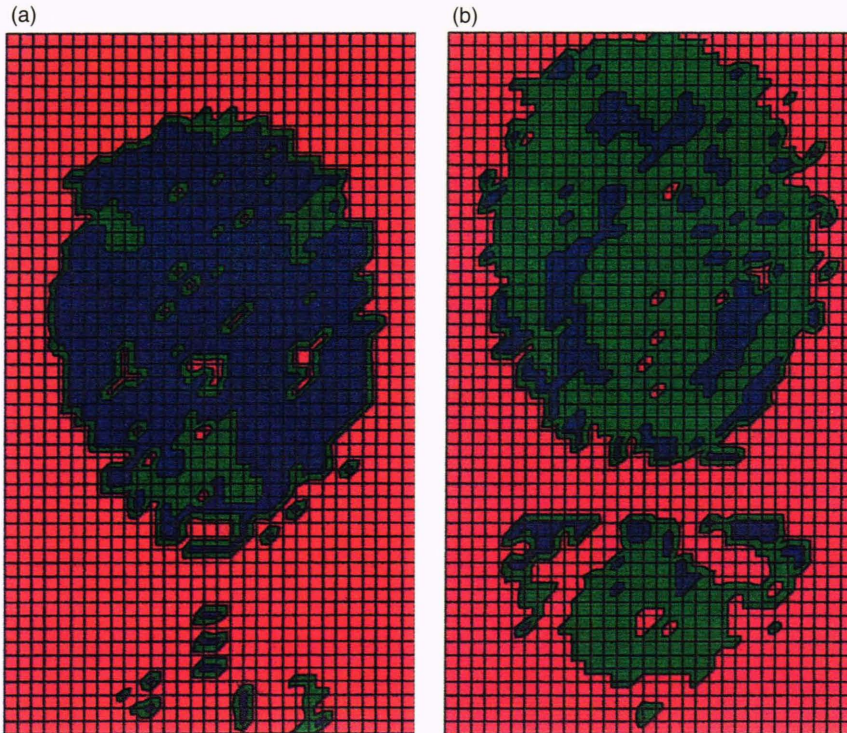
layer. Resonance therefore exists without any input. This phenomenon is known as hallucination, and is prevented by the input check system. That system has two inputs and one output. The inputs are the input data in an excitatory mode and the F2 activity in an inhibitory mode. If F2 activity occurs without any F1 activity, there is negligible output from the input check system.

The similarity check system (Fig. 2) determines how different two patterns can be and still be placed in the same category. This system has two inputs and one output. The two inputs are the input signal in an excitatory mode and the activity in F1 in an inhibitory mode. The output goes to F2 as a reset wave. When an input pattern is similar to what has been input before, the input pattern and the top-down activity from F2 to F1 are similar, so the signals to this system cancel each other out and there is no reset wave. When a new pattern is input, an F2 neuron is activated. If this category is not similar to the input, the resulting F2 to F1 top-down activity differs from the input activity, and a reset wave is sent to the F2 layer. The active F2 neuron is made inactive, a previously unused neuron of F2 is made active, and a new category is formed. A vigilance parameter controls how similar a pattern must be to the category template to prevent a reset wave from being sent. The higher the vigilance, the more similar patterns must be to be in the same category.

## RESULTS

Blocked and unblocked time series for each pixel were fed into an ART neural network and categorized. The F1 layer had 13 neurons, 1 for each time step in the series. Since the F2 layer had 15 neurons, 15 categories were possible. One run through the data consisted of all of the blocked and unblocked data (4096 time series).

Figures 3a and b show the results for the unblocked and blocked time series, respectively. They demonstrate that the neural network puts most of the brain portion of



**Figure 3.** ART neural network categorization. (a) Unblocked time series. (b) Blocked time series. The pixel time histories were broken into two main categories, shown in green and blue. Pixel time histories that were given a different category or were outside the brain are shown in red.

the pixel time series into one of two categories. The vigilance parameter for this run was 0.999, which is very high. The neural network was first run with a vigilance parameter of 0.95 and did not separate the data into categories at that value. The vigilance value was increased until more than one category was obtained. Category 1 in Fig. 3a (blue) corresponds to category 1 in Fig. 3b. The neural network put the blue pixels in Fig. 3a (unblocked brain) in the same category as the blue pixels in Fig. 3b (blocked brain), and likewise for the green pixels.

## CONCLUSIONS

Figures 3a and b show a marked difference in the blocked and unblocked category maps created by the neural network. In the unblocked state, most of the temporal cortex is put into one of two categories, and most of the cerebellum shows only a small portion in either of the two categories. Since the cerebellum has very few histamine  $H_1$  receptors, it is expected to act differently than the upper brain when the histamine  $H_1$  receptors are unblocked. In the blocked state, most of the brain, including the cerebellum, is put into the other of the two categories. When the histamine  $H_1$  receptors are blocked, the temporal cortex and cerebellum are expected to look the

same. Thus, the ART neural network seems to be able to identify receptor-rich and receptor-poor regions, since the temporal cortex and the cerebellum are categorized differently in the unblocked state. It also appears that the ART neural network categorizes fewer pixels in the receptor-rich category when the brain is in the unblocked state.

This method may help to assess the effectiveness of histamine blockers. We undertook the study described to determine the feasibility of applying neural networks to PET analysis. To determine if a neural network can, in general, assess the effectiveness of the histamine blocker, this study should be expanded to analyze additional sets of data. The results from the ART neural network should then be compared with results obtained using other approaches.

## REFERENCES

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**THE AUTHORS**



CHERYL L. RESCH obtained B.S. and M.S. degrees in mechanical engineering from the University of Maryland. She joined APL in 1988 and worked until 1991 primarily on aerodynamic heating and ablation models of the Standard Missile radome, IR dome, motor case, and fuze antenna. Ms. Resch currently works in the Applied Intelligent Systems Section of the Aeronautics Department's Engineering Group, where she is applying neural networks to ballistic missile defense.



ZSOLT SZABO is a board certified physician of nuclear medicine who obtained his M.D. and Ph.D. degrees at the University of Dusseldorf, Germany. He works in the positron emission tomography (PET) research team of the Johns Hopkins Hospital. His main interest is investigation of the histamine receptors and serotonin transporters of the brain and the use of pattern recognition in the analysis of PET image sequences.