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Original Research Article

Regional Cerebral Blood Flow in Alzheimer's Disease: Classification and Analysis of Heterogeneity

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Key Words

- Alzheimer's disease
- Artificial neural networks
- Cerebral blood flow
- Heterogeneity, regional cerebral blood flow

Abstract

Neural networks have been successfully applied to brain perfusion images to classify patients with Alzheimer's disease from normal or other patient populations. Given the recognition that Alzheimer's disease constitutes a heterogeneous disorder, the identification of subgroups sharing common functional brain deficits would constitute a further improvement in the utility of such methods. Therefore, we aimed to investigate whether neural networks could discriminate cortical perfusion deficits of patients with Alzheimer's disease from normal brain perfusion. A second step was to identify subgroups of patients sharing similar perfusion deficits. The study population consisted of one group of 92 normal healthy subjects and one group of 132 patients with mild-to-moderate Alzheimer's disease. The patients were diagnosed according to established criteria (DSM-IV and NINCDS-ADRDA). Regional cerebral blood flow was assessed by the non-invasive ^{133}Xe inhalation method, using a 64-detector system for measurements of blood flow in superficial cortical areas. The regional blood flow values were used as the only input to artificial neural networks with multilayer Perceptron architecture. The networks were trained using the back-propagation updating algorithm. A fourfold cross validation procedure was used in order to obtain the most reliable performance of the networks. The performance of the neural network, measured as the area under the receiver-operating characteristic curve, was 0.94, with a sensitivity for Alzheimer's disease of 86% at a

specificity of 90%. An analysis of the relative importance of cortical areas in the discrimination showed that left parietal areas were more important than the right homologous ones. A clustering analysis of the Alzheimer patients identified three or four subgroups of patients with clearly different combinations of blood flow pathology. A consistent finding in all subgroups was a significant deficit in temporoparietal blood flow of both hemispheres. Distinct group differences were seen in frontal, central and occipital areas with different combinations of involvement. This is the first study in which neural networks have been applied to brain perfusion images obtained with the ^{133}Xe inhalation method. The results demonstrate that a classification of patients with Alzheimer's disease obtained with this method is compatible with the best results obtained with other brain imaging methods. The identification of clearly distinguishable patterns of blood flow pathology in subgroups of patients lends further support to the notion that Alzheimer's disease is a heterogeneous disorder.

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