ORIGINAL CONTRIBUTION

MRI-Guided SPECT Perfusion Measures and Volumetric MRI in Prodromal Alzheimer Disease

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Objective: To identify group differences in the prodromal phase of Alzheimer disease (AD) using quantitative single-photon emission computed tomography (SPECT) perfusion and magnetic resonance imaging (MRI) volume measures within specific volumes of interest.

Setting: Gerontology research unit.

Participants: There were 17 healthy controls, 56 nondemented patients with memory problems who did not develop AD during 3 to 5 years of follow-up (questionables), and 27 nondemented patients with memory problems who developed AD during follow-up (converters).

Methods: A Tc 99m hexamethylpropyleneamine oxime SPECT study and an MRI were performed in each participant at baseline. Mean SPECT activity concentration and MRI volume were estimated within 9 structures: rostral anterior cingulate, caudal anterior cingulate, posterior cingulate, hippocampus, entorhinal cortex, basal forebrain, temporal horn, amygdala, and the banks of the superior temporal sulcus. Data were analyzed using overall and pairwise discriminant analysis, and performance in pairwise group discrimination was measured using correlated receiver operating characteristic curve analysis.

Results: The overall (3-group) discriminant function was significant for SPECT (F test, $P<.001$) and MRI (F test, $P<.0001$). For the SPECT analysis, the ranking of structures for discriminating among the 3 groups was, in order of decreasing discriminating power, caudal anterior cingulate, temporal horn, superior temporal sulcus, entorhinal cortex, hippocampus, rostral anterior cingulate, amygdala, basal forebrain, and posterior cingulate. For the MRI analysis, this ranking was entorhinal cortex, superior temporal sulcus, temporal horn, hippocampus, amygdala, caudal anterior cingulate, rostral anterior cingulate, basal forebrain, and posterior cingulate. Combining the 2 modalities yielded significantly better discrimination performance than did either alone. Furthermore, the correlation between SPECT and MRI measures was low.

Conclusion: Measures of structure activity concentration and volume carry independent information; both reveal group differences in prodromal AD.

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SINGLE-PHOTON EMISSION computed tomography (SPECT) reveals perfusion abnormalities in patients with established Alzheimer disease (AD).[1-4] The most consistent finding reported in these studies is decreased perfusion in the temporoparietal association neocortex in mildly and moderately impaired patients with probable AD compared with healthy controls. More recently, several research groups have attempted to identify brain perfusion patterns that predict subsequent development of AD. These efforts have practical, as well as theoretical, significance, because early prediction of AD would make it possible to implement strategies to prevent or delay dementia. Johnson et al[5] used principal component analysis to identify decreased perfusion in the hippocampal-amygdaloid complex and in the anterior and posterior cingulate in prodromal AD. This approach does not require a priori assumptions about the locations of discriminating regions, but it may not yield insight into the role of particular brain structures in the development of AD. Other SPECT studies[6,7] targeted specific volumes of interest (VOI) and reported that perfusion in the posterior cingulate declines in prodromal AD. None of these studies targeted all of the small brain regions believed to be involved in prodromal AD. Several magnetic resonance imaging (MRI) studies[8-13] have, similarly, sought to determine whether decreased volume in certain brain structures characterizes prodromal AD. Significant volume changes in the entorhinal cortex

Representative Results:

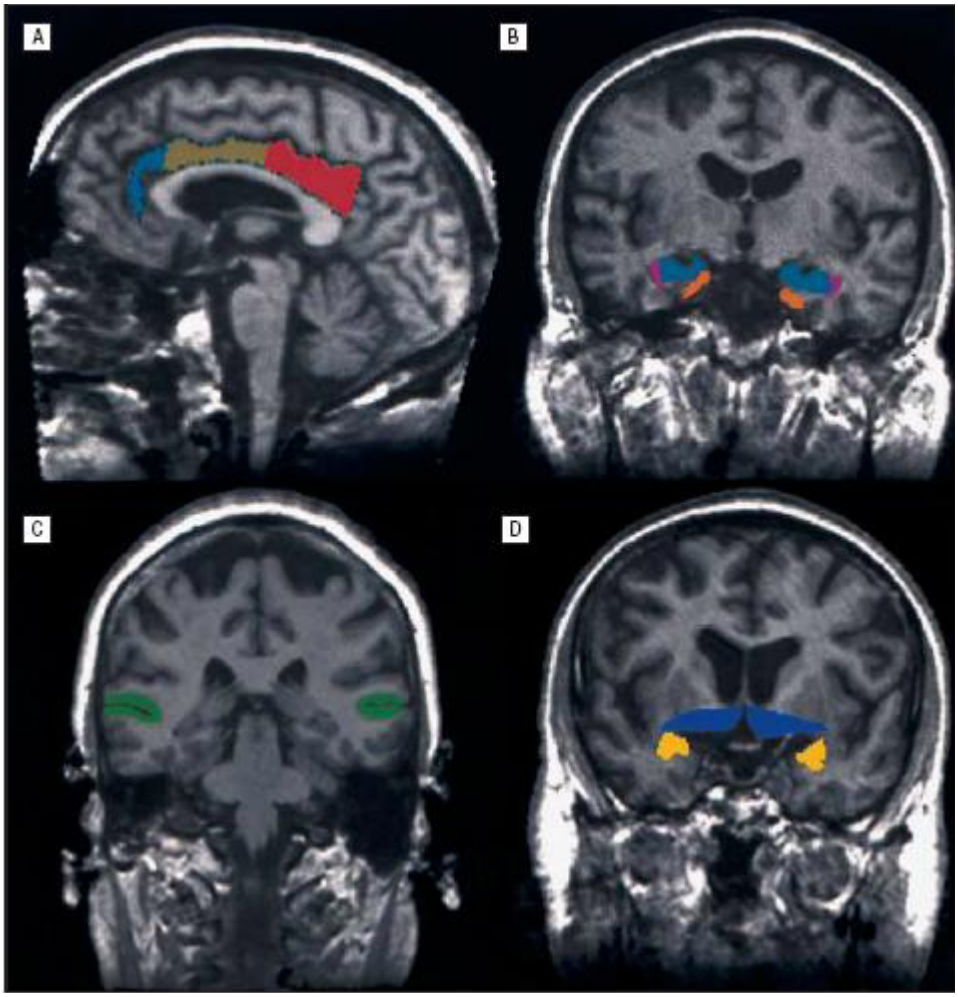

Figure 1. The locations of the 9 volumes of interest used for the magnetic resonance imaging and magnetic resonance imaging-guided single-photon emission computed tomography data: rostral anterior cingulate (blue), caudal anterior cingulate (green), and posterior cingulate (red) (A); temporal horn (purple), hippocampus (blue), entorhinal cortex (orange) (B); basal forebrain (blue) and amygdala (yellow) (C); and the banks of the superior temporal sulcus (green) (D).

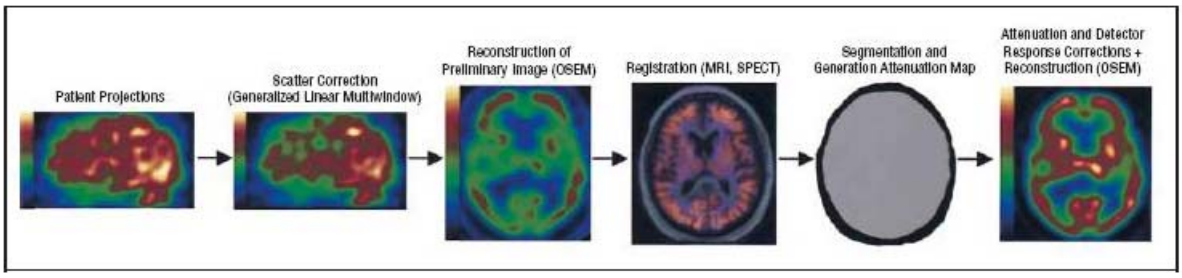

Figure 2. An outline of the procedure for estimating the magnetic resonance imaging (MRI)-guided single-photon emission computed tomography (SPECT) measures, including corrections for scatter, nonuniform attenuation, and variable collimator response. OSEM indicates ordered subset expectation maximization.