Insulin Sensitizers Cut Cognitive Decline in AD

BY ROBERT FINN
San Francisco Bureau

A mmentic mild cognitive impairment (MCI) is neurophysiologically the same entity as early Alzheimer’s disease and represents a transition from the normal aging brain to the profound pathology of Alzheimer’s, according to Dr. William Markesberry of the University of Virginia, Charlottesville.

The transition appears to be marked more by an increase in neurofibrillary tangles than in dendritic or neuritic plaques, wrote Dr. Markesberry of the University of Virginia, Charlottesville, and his associates.

The researchers followed 43 elderly subjects who were cognitively normal at baseline, until their deaths: 23 of them remained cognitively normal, 10 developed amnestic MCI, and 10 developed early Alzheimer’s disease (EAD).

All of the brains were available for autopsy via prior arrangement with the subjects (Arch. Neurol. 2006;63:18-46).

Comparison of the brains from patients with EAD to normal brains found significant increases in neuronal and pathologic hallmarks of the disease (dendritic plaques, neuritic plaques, and neurofibrillary tangles) in all of the neocortical and ventromedial regions.

There were no significant differences in the number of dendritic plaques between the controls and those with MCI, nor between the MCI brains and the EAD brains. “Because dendritic plaques were so common in normal control subjects, our data suggest that they are not critical neuropathologic determinants of the transition from normal to MCI, or MCI to EAD,” the investigators wrote.

Neuritic plaques were significantly more common in the MCI brains than in the control brains. But when the MCI brains were compared with EAD brains, the plaques only increased significantly in the amygdala and subiculum.

“This indicates that the pathologic deposition of insoluble β-amyloid peptide and formation of neurofibrillary tangles in the neocortex progress from normal to MCI, but do not distinguish MCI from EAD,” the researchers said.

The most striking difference between the brains was the amount of neurofibrillary tangle. Compared with normal controls, the MCI brains showed significant increases in the inferior parietal lobule, amygdala, entorhinal cortex, and subiculum. When compared with MCI brains, EAD brains showed an expansion of the tangles, with significantly more in the middle temporal gyrus, middle temporal gyrus, amygdala, and subiculum.

These changes imply neuropsychologic progression, the researchers wrote. “The increase in tangles in all of the neocortical and ventromedial lobe structures in EAD, compared with controls, further supports a gradual increase in [tangle] formation from normal aging to having MCI to having EAD.”

The conclusions argue for a change in the diagnostic criteria of early Alzheimer’s and MCI. Dr. John Morris of Washington University, St. Louis (Arch. Neurol. 2006;63:13-16).

“Revised criteria should permit the diagnosis of AD at these early stages, because the pathology is already established. Moreover, the earliest stages of AD may be the optimal time for intervention with drugs now in development that have the potential to retard or even arrest the AD process.”

Pathology Shows Amnestic MCI Is Same Entity as Early Alzheimer’s

BY MICHELE G. SULLIVAN
Mid-Atlantic Bureau

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Atrophy of Hippocampus and Amygdala Linked to Dementia

BY MARTHA KERR
Contributing Writer

H hippocampal and amygdalar atrophy are predictive of dementia in the cognitively intact elderly. Dutch researchers reported.

The investigators studied 511 community residents aged 60-90 years and free of dementia at baseline. The objective of the study, conducted by Dr. Tom den Heijer of Erasmus Medical Center in Rotterdam, the Netherlands, and his colleagues, was to assess whether atrophy of the hippocampus and amygdala was present before the onset of dementia. All of the participants were part of The Rotterdam Study, a prospective, population-based study launched in 1990.

In the current investigation, volumetric assessment of the hippocampus and amygdala was evaluated by MRI. The investigators also performed extensive neuropsychological testing and questioned participants about daily memory problems (Arch. Gen. Psychiatry 2006;63:57-62). During a mean follow-up of 6 years, 35 of the participants developed dementia, 26 of whom were diagnosed with Alzheimer’s disease. The investigators found that those participants who developed dementia had much smaller hippocampal and amygdalar volumes at baseline than did those without incident dementia.

Furthermore, they found that volume reduction at baseline was inversely associated with time until the onset of dementia. This was true “even in persons without memory complaints or low cognitive performance at baseline,” the investigators reported.

Dr. den Heijer and his colleagues said that MRI findings have been validated by previous autopsy studies of brain tissue showing neuronal loss and Alzheimer’s disease.

Decreases in hippocampal and amygdalar volumes of 15-17% were found, depending on how far in advance of dementia the MRI was done. For individuals with Alzheimer’s disease, Dr. den Heijer’s team found reductions ranging from 25% to 40%, a range that suggests that the atrophy rate accelerates in patients with Alzheimer’s disease.

The investigators concluded that “structural imaging can help identify people at high risk for developing dementia, even before they have any memory complaints or measurable cognitive impairment.” They have intended that, however, that most people with atrophy failed to develop dementia, even after 6 years.