Whole Brain N-Acetylaspartate Quantification Comparison between Healthy Elderly, Mild Cognitively Impaired and Alzheimer's Patients: Evidence For Different Clinical Cohorts

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INTRODUCTION:

Alzheimer's disease (AD) is a progressive fatal neurological disorder affecting over five million Americans. Although it is "only" the sixth leading cause of death in the US (1), it is the third costliest to treat (2). Alzheimer's disease is believed to progress via mild cognitive impairment (MCI), characterized by below par memory performance compared with age-appropriate memory loss (3). Since over 10% of MCI patients progress to AD (4), early detection of the former is critical to avert or defer the onset of the later, which is clearly a critical public health focus. Since both AD and MCI are diffuse pathologies affecting neuronal cells, the study of their marker, the N-acetylaspartate (NAA) could provide a non-invasive window onto the disease progression. Whole-brain NAA (WBNAA) – a proton MR spectroscopy approach could therefore facilitate a quantitative assay of the overall brain health.

METHODS:

Absolute whole-brain NAA amount was obtained with non-localizing proton MR spectroscopy (5) from 224 subjects (123 males, 101 females) 72.5±8.5 years of age. A clinical psychologist administered cognitive and memory tests which were used, along with a physical exam, to categorize all incoming subjects as either healthy, MCI, or with probable Alzheimer's disease. According to these diagnostic criteria, there were divided into controls (*N*=116), MCI (*N*=48), and AD (*N*=60) subjects. The absolute whole-brain NAA amount was converted into WBNAA concentration by dividing by their brain's parenchymal volume obtained from MRI image segmentation. All subjects gave written informed consent.

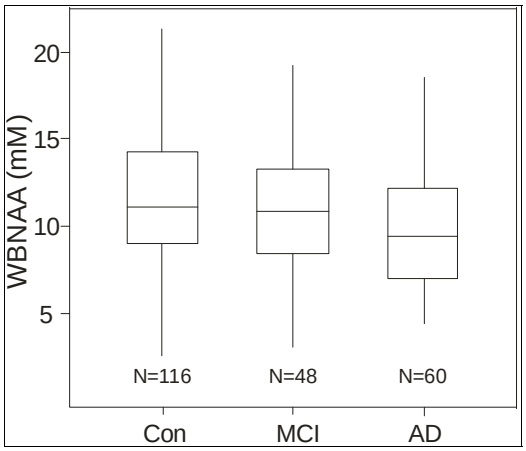

Fig. 1: Box plots showing the first, second (median) and third quartiles (*box*) and ±95% (*whiskers*) of the WBNAA distribution of the three subject groups. Note the WBNAA decline between the controls and MCI versus AD patients

RESULTS:

The mean WBNAA concentration was 11.6±3.7 for the healthy, 11.1±3.7 for MCI, and 9.7±3.3 mM for AD patients, as shown in Fig. 1. The three groups were significantly different (F=6.1, p=0.01). A significant 2.06±1.17 mM WBNAA difference was observed between the healthy and AD subjects (p=0.001) and between MCI and AD: 1.5±1.4 mM (p=0.037), but none between healthy and MCI: 0.56±1.2 mM (p=0.366).

CONCULSION: The significant WBNAA decrease from healthy to AD probably reflects accumulating widespread neuronal damage. The significant decline between MCI and AD subjects underscores the underlying progressive neuronal pathogenesis. Although no significant decline was observed between healthy and MCI subjects, the trend in Fig. 1 warrants further investigation of the concept that MCI is an intermediate stage. It could also be attributed to the lack of consensus on the proper diagnostic criteria of MCI.

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