Whole-Brain N-Acetylaspartate Concentration Comparison of Young and Elderly Healthy: Evidence for Brain Durability

W. E. Wu\textsuperscript{1}, O. Gonen\textsuperscript{1}, J. Hirsch\textsuperscript{2}, L. Achtnichts\textsuperscript{2}, K. Weir\textsuperscript{2}, A. U. Monsch\textsuperscript{2}, and A. Gass\textsuperscript{2}

\textsuperscript{1}Radiology, New York University School of Medicine, New York, NY, United States, \textsuperscript{2}Neurology, University Hospital of Basel, Switzerland, Basel, Basel, Switzerland

Introduction:
An estimated 40 million Americans are currently 65 years of age or older, with that number expected to grow to 70 million by 2030\textsuperscript{1}. Since several neurological conditions, especially Alzheimer’s Disease (AD) and the broad spectrum of ischemic disorders, afflict the elderly, the burden of these diseases to healthcare delivery will soon become staggering. Although it has been shown that AD, which affects primarily neurons, manifests in deficits of its surrogate marker – the N\textsubscript{-}acetylaspartate (NAA) concentration, it is not known whether these deficits are due exclusively to AD pathology, to the normal aging process, or to their combination. Since AD is a diffuse disorder, whole-brain NAA (WBNAA) obtained with proton MR spectroscopy (\textsuperscript{1}H-MRS) can be used as a surrogate for global neuronal dysfunction and loss (3). Because WBNAA has recently shown no significant change during a 4-year follow-up in young healthy adults (3,4), we applied it to cognitively normal elderly to ascertain the changes that result from normal aging.

Methods:
All MR experiments were done at 3 T human scanners (Magnetom, Siemens AG, Erlangen, Germany) using the standard circularly-polarized transmit-receive head-coil. Each subject’s whole brain volume was obtained from T1-weighted sagittal MP-RAGE, [TE/TR/TI: 3.49/2150/1000 ms, 7\textdegree flip angle, 144 slices, 1 mm slice thickness, 256x224 matrix, 256x256 mm\textsuperscript{2} field-of-view (FOV)] MRI using our in-house FireVoxel image-segmentation package. The amount of whole-brain NAA for each subject was obtained with a non-localizing TE/TI/ TR=0/940/10\textsuperscript{4} ms, \textsuperscript{1}H-MRS sequence described previously (3-5). Although lacking explicit spatial localization, the sequence relies on the implicit localization of NAA by its biochemistry to neuronal cells, i.e., to just the brain. Quantification was done against a reference 3 L sphere of 1.5x10\textsuperscript{-2} mole NAA in water, and peak areas were converted to absolute molar amounts by phantom replacement as described previously (6). These were normalized to specific brain-size-independent concentrations by dividing by the brain parenchymal volume.

WBNAA was obtained from 79 young healthy controls (34 men, 45 women) 34.2±10.3 years old and from 50 cognitively healthy elderly (30 men, 20 women) 69.7±8.3 years old. “Normal” for the elderly was established based on neurological and neuropsychiatric examinations as well as an age-appropriate unremarkable MRI. All subjects gave written IRB approved informed consent.

Results:
The mean subjects’ WBNAA concentration was 12.3±1.3 (mean±standard deviation) for young compared with 12.0±2.8 for elderly, as shown in Fig. 1. Despite a broader distribution (see Fig. 1), there was no statistically significant difference in WBNAA concentration between the two cohorts, nor was there a WBNAA difference with respect to gender.

Discussion:
The absence of WBNAA decline over a 30 year (median) period, despite known 0.25%/year (normal) brain atrophy, suggests brain durability. Specifically, the “quality” of the remaining brain (in the elderly) as reflected by its overall NAA concentration, is not different from that of the young. The broader spread in WBNAA values among the young subjects, probably indicates divergent (albeit “age appropriate”) processes that the elderly encountered over the years but which did not adversely affect cognition or overall neurological health.

References:

**Fig. 1.** Box plots showing the first, second (median) and third quartiles (box) and ±95% (whiskers) of the WBNAA distribution in healthy young individuals and cognitively intact elderly. Note the similar distributions, especially with respect to their medians.