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BRAIN VOLUME CHANGES IN RECENTLY MENOPAUSAL WOMEN IN A HORMONE REPLACEMENT TRIAL

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Objective: Estrogens are thought to enhance neurological function and exert neuroprotective effects. The Kronos Early Estrogen Prevention Study (KEEPS) gave us the unique opportunity to assess the neuroprotective effects of hormone replacement with magnetic resonance imaging (MRI) based brain volumetric measurements. Our objective in this study was to quantify the rates of brain volume and ventricular volume change in newly menopausal women in the KEEPS trial.

Design & Method: 106 women (40-55 years of age), who were enrolled to the KEEPS trial at the Mayo Clinic, underwent brain MRI at baseline and were randomly assigned to one of the three treatment arms (oral conjugated estrogen with active progesterone, transdermal 17- β estradiol skin patch with active progesterone, and placebo). 30 of these women (mean \pm SD age at baseline = 54.5 ± 2.8) underwent a follow-up MRI exam at 18 months. The investigators were blinded to the treatment groups. All MRI studies were performed on a single 1.5T system using 3D Magnetization Prepared Rapid Acquisition Gradient-Echo acquisition. Rates of change in whole brain and ventricle volumes were calculated using a home-built software algorithm which computes change in brain and ventricular volume from baseline to follow-up MRI exam. (Gunter *et al.* 2003).

Results: On average, the brain volumes decreased and the ventricular volumes increased at 18 months. The mean \pm SD annual percent decline in the brain volume was $0.3\% \pm 0.35\%$ and the mean \pm SD annual percent expansion in ventricular volume was $3.59\% \pm 3.72\%$. There was a significant correlation between the annual percent decline in the whole brain volume and the expansion in the ventricular volume ($R^2=0.35$, $p<0.001$). The rate of decrease in brain volume in KEEPS subjects was comparable to the brain volume decrease we previously observed in cognitively normal elderly with a median (range) age of 79 (56,93) (Jack *et al.* 2004) (0.4% in elderly subjects vs. 0.35% in KEEPS subjects). However, the ventricular volume increase was more than twice as high in KEEPS subjects (1.7% in elderly subjects vs. 3.7% in KEEPS subjects).



Conclusion: The changes in brain structure in KEEPS subjects, were as much as the changes observed in individuals two decades older than KEEPS subjects. Because we are blinded to the treatment information at this time, it is unknown to us whether there is accelerated atrophy of the brain during menopausal transition, or if hormone replacement modifies the change in brain structure.

Key words: KEEPS, brain, magnetic resonance imaging