P4-154

PROGRESSIVE WHITE MATTER ABNORMALITIES IN AUTOSOMAL-DOMINANT ALZHEIMER'S DISEASE: RESULTS OF THE DIAN STUDY

Tammie Benzinger[1], Tyler Blazey[1], Robert Koeppe[2], Clifford Jack[3], Marc Raichle[1], Beau Ances[1], Abraham Snyder[1], Daniel Marcus[1], John Ringman[4], Paul Thompson[5], Bernardino Ghetti[6], Andrew Saykin[6], Yi Su[7], Reisa Sperling[8], Stephen Salloway[9], Keith Johnson[10], Steve Correia[11], Peter Schofield[12], Nick Fox[13], Christopher Rowe[14], Krista Moulder[1], Randall Bateman[15], Chester Mathis[16], Eric McDade[17], Michael Weiner[18], Alison Goate[1], Virginia Buckles[1], Richard Mayeux[19], Colin Masters[20], Victor Villemagne[21], Morris John[1], [1]Washington University School of Medicine, St. Louis, Missouri, United States; [2]University of Michiagan, Ann Arbor, Michigan, United States; [3]Mayo Clinic, Rochester, Minnesota, United States; [4]Easton Center for Alzheimer's Disease Research, Los Angeles, California, United States; [5]University of California, Los Angeles, Los Angeles, California, United States; [6]Indiana University School of Medicine, Indianapolis, Indiana, United States; [7]Washington University School of Medicine, St Louis, Missouri, United States; [8]Harvard University, Boston, Massachusetts, United States; [9]Brown University, Providence, Rhode Island, United States; [10]MGH HMS, Boston, Massachusetts, United States; [11]Brown University, Providence, Rhode Island, United States; [12]Neuroscience Research Australia, Newcastle, Australia; [13]The National Hospital for Neurology and Neurosurgery, London, United Kingdom; [14]Neuroscience Research Australia, Melbourne, Australia; [15]Washington University, St. Louis, Missouri, United States; [16]University of Pittsburgh, Pittsburgh, Pennsylvania, United States; [17]University of Pittsburgh, Pittsburgh, Pennsylvania, United States; [18]University of California, San Francisco, San Francisco, California, United States; [19]University of Columbia, New York, New York, United States; [20]University of Melbourne, Melbourne, Australia; [21]Austin Health, Melbourne, Australia.

Background: DIAN (Dominantly Inherited Alzheimer's Network) is an international longitudinal study of autosomal dominant Alzheimer's disease, including individuals affected with, or at risk for, AD. In late onset AD it is often difficult to separate white matter disease associated with aging and diseases of aging (hypertension, diabetes, etc) from that of AD. In this young cohort, we quantified WM pathology using volumetric MRI and diffusion tensor imaging (DTI) in order to evaluate WM disease in ADAD. Methods: 71 participants from the DIAN study underwent DTI. Participants were classified into four groups based upon mutation (M+ and M-) and dementia status (CDR, Table 1). DTI was acquired using a 64 direction sequence at 3T. Image analysis was conducted with Tract Based Spatial Statistics (TBSS), a part of FSL. Group-level differences were assessed with a general linear model controlling for age, gender, and education and corrected for multiple comparisons using Threshold-Free Cluster Enhancement. Volumetric T1 (MPRAGE) studies were processed with FreeSurfer to generate white matter volumes. Results:Whitematter volumes decreasewith carrier status and progressive dementia (Figure 1). Associated loss of fractional anisotropy (FA, Figure 2) and elevated mean diffusivity (MD, not shown) are widespread. Periventricular white matter is particularly involved at very mild (CDR 0.5) andmild (CDR 1.0) dementia (Figure 2). Conclusions: These findings support the hypothesis that widespread white matter abnormalities are associated with dementia in ADAD, and that these abnormalities precede the development of dementia.

Table 1

	Non-carriers (M-) CDR 0	Carriers (M+) CDR 0	Carriers (M+) CDR 0.5	Carriers (M+) CDR >=1
n	43	44	18	15
Age*	39.90 (9.02)	34.84 (9.08)	42.17 (10.95)	47.67 (8.63)
Estimated time to dementia*	-5.48 (12.33)	-12.02 (8.47)	-1.72 (8.75)	+2.27 (8.02)
Gender	M=43%	M=36%	M=56%	M=60%
Education*	15.05 (2.49)	14.61 (2.62)	13.50 (2.31)	12.27 (1.98)

*Mean (standard deviation) in years