P1-015 BRAIN AND HIPPOCAMPAL RATES OF ATROPHY IN FAMILIAL ALZHEIMER'S DISEASEMUTATION CARRIERS: PRELIMINARY FINDINGS FROM THE DIAN STUDY

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Background: The Dominantly Inherited Alzheimer Network (http://dian-info.org/) study is an international clinical, biomarker and multi-modality imaging study of individuals at risk for autosomal dominant Alzheimer's disease and those already mildly affected. This prospective study of these individuals provides an opportunity to follow these individuals through different stages of the disease process, starting several years before symptoms are evident.We report here the first longitudinal analyses of cerebral and hippocampal atrophy rates from the DIAN cohort. Methods: All DIAN participants have T1-weighted volumetric MRI scanning at baseline. We analysed data from the first 22 participants with a follow-up MRI scan (mean6sd interval 12.760.9 months). Seventeen subjects were symptomatic mutation carriers (sMut+) with Clinical Dementia Rating (CDR) scores >0 aged 46.4 6 9.6 years; three were asymptomatic carriers (aMut+) with CDR ¼ 0; and two were non-carriers (NC). The aMut+ and NC were combined into one group for this initial analysis (age: 34.5 6 5.4 years). The whole brain and hippocampi were first delineated using an automated procedure. Annualized atrophy rates were measured by volumetric difference as well as the Boundary Shift Integral (BSI). Two sample t-tests assuming unequal variances were performed between the annualized atrophy rates of the sMut+ group and the combined NC/aMut+ group. Results: Brain BSI atrophy rates were higher (see Table) in the symptomatic subjects (1.9% vs. 0%/year; P ¼ 0.003). However, the difference in hippocampal atrophy rates was not statistically significant (2.5% vs. 0.5%/year; P ¼ 0.057 for volumetric). Conclusions: Initial analysis of atrophy rates from this cohort indicates that brain atrophy rates are higher in symptomatic mutation carriers than in asymptomatic carriers or non-carriers. The lack of a detectable difference in hippocampal atrophy rates may reflect the small sample size and that these preliminary analyses included presymptomatic mutation carriers in the control group who may have already had increasing rates of hippocampal atrophy. Over 200 subjects will be followed longitudinally,

Table 1
Mean (95%CI) brain and hippocampal atrophy rates as a percentage of baseline volume

Group	Age	Annualized Brain BSI % loss/year	Annualized Hippocampal Volume change % loss/year
NC/aMut+ (n ¼ 5)	34.5 6 5.4	0.0 6 0.8% (-1.0,1.1)	0.5 6 1.7% (-1.6,2.6)
sMut+ (n ¼ 17)	46.4 6 9.6	1.9 6 1.3% (1.2,2.5)	2.5 6 1.7% (1.6,3.3)
P-value	0.006	0.003	0.057

so as more data are acquired, we will separately analyze atrophy rates in asymptomatic carriers and non-mutation carriers, estimate sample sizes for trials and assess the relationship between atrophy rates and symptom onset.