

O2-06-02 FDG METABOLISM IN THE DIAN STUDY OF AUTOSOMAL DOMINANT ALZHEIMER'S DISEASE

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Background: Abnormal brain glucose metabolism has been reported in individuals with genetic risk factors for AD. In order to evaluate the natural history of these changes, participants in the Dominantly Inherited Alzheimer's Network (DIAN) study underwent 18F FDG PET, and we report here an initial assessment of the current baseline FDG-PET DIAN data set. Objective: To evaluate the association of FDG metabolism with age and mutation status in cognitively normal (CDR  $\geq$  0) and symptomatic (CDR  $<$  0.5) individuals. Methods: FDG data sets from 91 CDR0 (47 carriers/44 non-carriers), 20 CDR0.5 (all carriers) and 13 CDR  $>$  1 (all carriers) subjects were spatially normalized to an MNI-space template using SPM8, resampled in regions defined by the MNI-based LONI probabilistic atlas, and scaled to cerebellum. Linear regression was used to model the associations of regional average FDG with age, time-to-familial-age-of-onset (TFAO), mutation status and group membership. Results: Compared to CDR0 non-carriers and controlling for age, FDG uptake was significantly low

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Network (DIAN) study underwent 18F FDG PET, and we report here an initial assessment of the current baseline FDG-PET DIAN data set. Objective: To evaluate the association of FDG metabolism with age and mutation status in cognitively normal (CDR  $\geq$  0) and symptomatic (CDR  $<$  0.5) individuals. Methods: FDG data sets from 91 CDR0 (47 carriers/44 non-carriers), 20 CDR0.5 (all carriers) and 13 CDR  $>$  1 (all carriers) subjects were spatially normalized to an MNI-space template using SPM8, resampled in regions defined by the MNI-based LONI probabilistic atlas, and scaled to cerebellum. Linear regression was used to model the associations of regional average FDG with age, time-to-familial-age-of-onset (TFAO), mutation status and group membership. Results: Compared to CDR0 non-carriers and controlling for age, FDG uptake was significantly lower in CDR0.5 subjects globally (P  $<$ 0.01) and in AD-vulnerable regions in CDR0.5 subjects globally (P  $<$ 0.01) and in AD-vulnerable regions including angular gyrus (P  $<$ 10<sup>-5</sup>), middle temporal (P  $<$ 0.004), supramarginal (P  $<$ 0.003) and precuneus (P  $<$ 10<sup>-5</sup>) (Figure 1). Greater decreases in metabolism were seen in CDR  $>$  1 subjects in a similar set of regions (P  $<$ 10<sup>-5</sup>). Significant negative associations of FDG metabolism with age, controlling for CDR group, were also seen in these regions (P  $<$ 0.04). While lower mean regional FDG uptake in CDR0 carriers compared to non-carriers did not reach statistical significance, there was a significant inverse relation between TFAO and carrier FDG uptake measured in an AD-vulnerable aggregate region (P  $<$ 0.05) and in the angular gyrus (P  $<$ 0.05) (Figure 2). Conclusions: In symptomatic DIAN participants, FDG metabolism was reduced in a regional pattern similar to sporadic AD. In asymptomatic mutation carriers, a similar pattern of FDG hypometabolism was associated with increasing proximity to their family's median age of symptom onset.