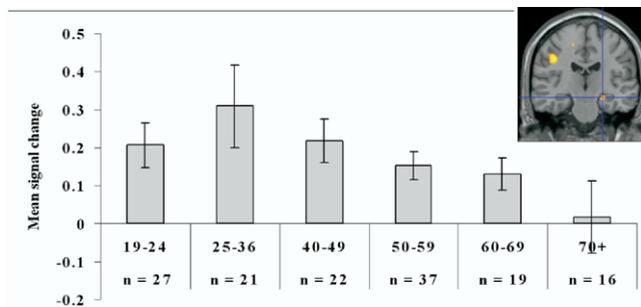


medial temporal lobe (MTL) structures that display pathological changes in AD. Recent evidence suggests that young individuals display significantly greater functional activation in the MTL relative to elderly individuals during episodic encoding. To date, few studies have included middle-aged individuals (i.e., 35-60 years) to determine whether these individuals also display reduced hippocampal activation during episodic encoding relative to younger individuals. **Objective:** The present study used functional MRI to test the hypothesis that there would be an age-related decline in MTL activation during episodic encoding in 142 individuals between 19 and 83 years of age using a task sensitive to reduced hippocampal activation in individuals with mild cognitive impairment (MCI). **Methods:** Participants were divided into 6 different groups: 19-24 years ($n = 27$), 25-36 years ($n = 21$), 40-49 years ($n = 22$), 50 - 59 years ($n = 37$), 60-69 years ($n = 19$), and 70 years or greater ($n = 16$). Individuals with psychiatric/neurological disease were excluded, and all participants received a detailed neuropsychological evaluation to exclude subjects with cognitive impairments. **Results:** We found a linear, parametric decline in right hippocampal and bilateral ventral temporal cortex activation during episodic encoding as a function of increasing age (FDR-corrected $p < 0.05$). In contrast, a similar pattern was not observed in the left MTL as a function of increasing age. Furthermore, no brain regions displayed a significant parametric increase in activation as a function of increasing age. **Conclusions:** These results suggest that increasing age is associated with a decline in medial and ventral temporal lobe activation during memory encoding, despite intact cognitive function on standardized neuropsychological measures. Since increasing age is a major risk factor for AD, hippocampal activation paradigms might be useful in studying individuals with risk factors for AD (e.g., MCI, APOE $\epsilon 4$ allele, or parental-history of AD). More studies that better characterize changes in hippocampal activation across the entire age spectrum are needed before fMRI is to be used in the early diagnosis of MCI or AD.



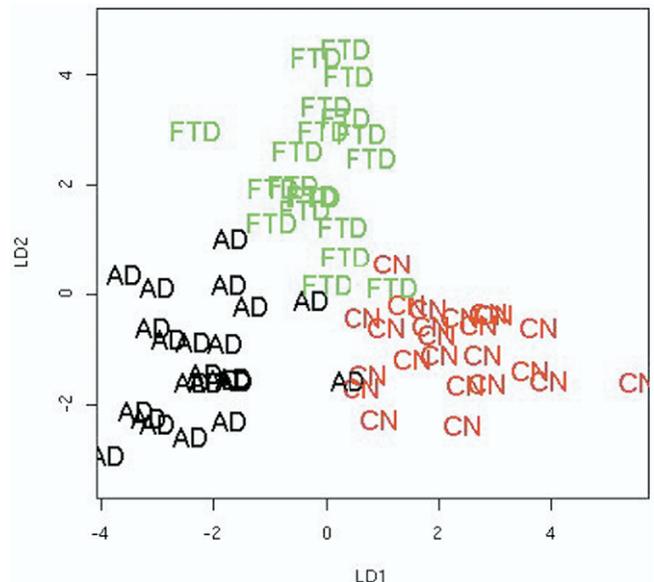
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DETECTION AND CLASSIFICATION OF DEMENTIAS USING GENERALIZED COMPLEXITY ESTIMATES

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Background: Although quantitative neuroimaging studies of neurodegenerative diseases have identified several promising markers for detecting and classifying dementias, their usefulness for diagnosis is hampered by large numbers of structural, physiological and neurochemical outcomes that are hard to summarize and interpret. In particular measurements of cortical thinning, brain volume loss and cerebral hypoperfusion and hypometabolism depend critically on the choice of processing parameters, exacerbating the problem. Generalized complexity estimates (GCE) constitute sensitive, interpretable summary information that can be extracted from images and are easy to generate. **Objectives:** We hypothesized that GCE of structural magnetic resonance images (MRI) produce robust, sensitive separation between cognitive normal (CN), Alzheimer's disease

(AD) and Frontal Temporal Dementia (FTD) subjects. **Methods:** An initial test applied GCE to structural, segmented MRI from 50 ICBM database subjects, 25 with the cortex artificially thinned in the right superior temporal gyrus (RSTG). For tests on experimental data, GCE were also obtained from structural MRI from 21 AD, 20 FTD, and 25 CN subjects. Statistical significance was estimated using MANOVA and linear discriminant analysis, and specificity and sensitivity were estimated using 10 fold, 10 times cross validation. **Results:** MANOVA analysis of the GCE for cortical thinning showed significant separations between the populations for all regions containing the RSTG (with $p = 4.1e-09$, sensitivity of .91 and specificity of .85 for the RSTG itself). MANOVA for the experimental data also produced a highly significant ($p = 2.4e-08$) separation between AD, FTD, and CN subjects, using GCE for the hippocampus, subiculum, and putamen. The LDA for GCE from 13 brain regions achieved a classification accuracy of 0.96. Projection onto the first 2 linear discriminants is shown in the figure. **Conclusion:** Preliminary studies indicate that easy to apply and interpret GCE summary information provides robust classifications between AD, FTD, and CN subjects, and could be useful in classification and early detection of dementias. GCE should in fact be of general utility for producing sensitive and interpretable summary information from multimodal imaging studies in a variety of contexts.



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REDUCED MEDIAL PARIETAL ACTIVITY IN COGNITIVELY-HEALTHY MIDDLE-AGED INDIVIDUALS WITH A PARENTAL HISTORY OF ALZHEIMER'S DISEASE

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Background: Medial parietal regions are vulnerable to some of the earliest structural and functional changes associated with Alzheimer's disease (AD). A growing body of research suggests that neuropathological changes occur in individuals at risk for AD, decades prior to symptom-onset. **Objective:** The current study employed functional MRI methods to examine function of medial parietal brain regions (i.e., posterior cingulate cortex and precuneus) in asymptomatic, middle-aged individuals who varied in their risk for AD. **Methods:** Prior fMRI research in healthy young adults indicates that medial parietal regions are active during both episodic retrieval and self-referential processing. Therefore, we administered an fMRI task that would allow examination of medial parietal function under both conditions. Participants included six at-risk individuals with a parental