
Notes: BACKGROUND: Reliable blood-oxygen-level-dependent (BOLD) functional magnetic resonance imaging (fMRI) phenotypic biomarkers of Alzheimer's disease (AD) or mild cognitive impairment (MCI) are likely to emerge only from a systematic, quantitative, and aggregate examination of the functional neuroimaging research literature. METHODS: A series of random-effects activation likelihood estimation (ALE) meta-analyses were conducted on studies of episodic memory encoding operations in AD and MCI samples relative to normal controls. ALE analyses were based on a thorough literature search for all task-based functional neuroimaging studies in AD and MCI published up to January 2010. Analyses covered 16 fMRI studies, which yielded 144 distinct foci for ALE meta-analysis. RESULTS: ALE results indicated several regional task-based BOLD consistencies in MCI and AD patients relative to normal control subjects across the aggregate BOLD functional neuroimaging research literature. Patients with AD and those at significant risk (MCI) showed statistically significant consistent activation differences during episodic memory encoding in the medial temporal lobe, specifically parahippocampal gyrus, as well superior frontal gyrus, precuneus, and cuneus, relative to normal control subjects. CONCLUSIONS: ALE consistencies broadly support the presence of frontal compensatory activity, medial temporal lobe activity alteration, and posterior midline "default mode" hyperactivation during episodic memory encoding attempts in the diseased or prospective predisease condition. Taken together, these robust commonalities may form the foundation for a task-based fMRI phenotype of memory encoding in AD


Notes: The Cache County Study of Memory in Aging (CCMS) is an epidemiological study of Alzheimer's disease (AD), mild cognitive disorders, and aging in a population of exceptionally long-lived individuals (7th to 11th decade). Observation of population members without dementia provides an opportunity for establishing the range of normal neurocognitive performance in a representative sample of the very old. We examined neurocognitive performance of the normal participants undergoing full clinical evaluations (n = 507) and we tested the potential modifying effects of apolipoprotein E (APOE) genotype, a known genetic risk factor for the later development of AD. The results indicate that advanced age and low education are related to lower test scores across nearly all of the neurocognitive measures. Gender and APOE epsilon4 both had negligible and inconsistent influences, affecting only isolated measures of memory and expressive speech (in case of gender). The gender and APOE effects disappeared once age and education were controlled. The study of this exceptionally long-lived population provides useful normative information regarding the broad range of "normal" cognition seen in advanced age. Among elderly without dementia or other cognitive impairment, APOE does not appear to exert any major effects on cognition once other demographic influences are controlled.

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