INTRODUCTION

Episodic memory is one of the earliest types of memory decline in Alzheimer's disease (AD).

In mild cognitive impairment (MCI) patients, the degree of cognitive decline is positively associated with the strength of the BOLD response during episodic memory processing.

Increased BOLD is also reported in some but not all samples of cognitively normal older adults with the apolipoprotein E epsilon 4 allele.

Cognitively normal WRAP participants with subclinical memory decline show significant difference in neural metabolic changes and a trend toward increased activation during episodic memory processing compared to participants with no memory decline.

These findings indicate that heightened BOLD response in MCI individuals may be a useful early marker of cognitive decline.

OBJECTIVE

To investigate the contribution of subclinical episodic memory decline on functional brain activity in cognitively normal individuals.

METHODS

Participants: Cognitively normal (CN) middle-aged adults enrolled in the Wisconsin Registry for Alzheimer’s Prevention (WRAP) who underwent imaging and have been followed with cognitive assessment since 2001.

Classification: Based on the longitudinal Rey Auditory Verbal Learning Test (RAVLT) & Tustin Delayed Recognition Test, participants were classified as either Stable (n=90) or Decline (n=124).

Clinical comparison: 10 MCI patients were recruited from the Wisconsin Alzheimer’s Disease Research Center (WADRC) as a disease comparison group.

Task effect: In the first group of 107 additional CN adults from the WRAP were included as a fMRI task effect reference group.

Encoding session: Outside the scanner: 30 min prior to fMRI, subjects viewed 48 faces over 5 viewing contexts where they rated the faces across attractiveness, likability, distinctiveness, energy level, and age.

fMRI recall task: In the 3rd BOLD & MTR 30 scanner using an 8-channel head coil, subjects made "old" or "new" decisions about previously viewed (novel) and novel faces (NV) over two runs. Each run consisted of 24 NV and 24 NF faces.

CONCLUSIONS

Declines showed greater reactivation than Stables within the postero medial cortex when viewing previously viewed faces on an episodic recognition memory task. This finding was not associated with task ICBF or GMV, APOE status, fMRI task performance, or neuropsychological measures.

Hyperactivation in Decline relative to Stables and MCI demonstrates an inverted-U function, suggesting that a balance of task-induced activation patterns may reflect subclinical memory changes within a very early phase of preclinical AD.

Neuropsychological data

| Variable | Stable, n = 90 | Decline, n = 124 | MCI, n = 9 | P value | Value
|----------|----------------|------------------|-----------|----------|------
| Age      | 59.11 (8.83)   | 62.14 (5.39)     | 72.06 (9.42) | .006     |
| Education| 15.18 (3.86)   | 16.24 (2.31)     | 17.72 (2.77) | 2.41     |
| MMSE     | 73.5           | 78.2             | 70.0       | .015     |
| APOE4 positive, % | 41.1         | 47.1             | 70.0       |    ns    |

Data analyzed with ANCOVA and Geisser as appropriate.