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Project Summary
Priming in Mild Cognitive Impairment and Alzheimer's Disease
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Mild cognitive impairment (MCI) is defined as a precursor syndrome to Alzheimer's disease (AD) (Petersen, et al., 1999), but not all patients with MCI will go on to develop AD (Mandzia, et al., 2001). Better prediction is essential for providing treatment before irreversible cognitive decline takes place. Diagnosis is currently mainly based on neuropsychological assessment (McKhann, et al., 1984; Drzezga, 2008), although neuropathological changes are known to precede the onset of cognitive symptoms by many years (Braak, et al., 1999). Changes in fMRI have in fact been detected in those at risk of developing AD (Bookheimer, et al., 2000; Smith, et al., 2002), so that functional imaging may come to play an important role in early diagnosis of AD (Scheltens and Korf, 2000).

While deterioration of explicit memory is a well-recognised hallmark of AD (Craik and Jennings, 1992), implicit memory, including priming, can be preserved in aging and dementia despite explicit memory impairment (Lustig and Buckner, 2004). Furthermore, perceptual processing is impaired in AD but often remains intact in MCI (Fleischmann, et al., 1999; Akdemir, et al., 2007). Perceptual priming can be investigated using a word stem completion (WSC) paradigm, in which a word series is presented and encoded at a shallow level of processing by participants judging the number of syllables in the words (Richardson-Klavehn and Gardiner, 1998). Participants later complete 3-letter word stems with the first word that comes to mind, stating whether the word was on the original list. Priming has occurred when an old word is used, but the participant says that it is new. WSC priming in particular has been shown to be preserved in MCI, but impaired in AD (LaVoie and Faulkner, 2008).

There is both fMRI and EEG evidence that the neural correlates of explicit and implicit memory differ (e.g. Schott, et al., 2002; Schott, et al., 2005; Duezel, et al., 2005; Schott, Richardson-Klavehn, et al., 2006). At encoding of primed words, decreased activation is found bilaterally in the extrastriate cortex, in the left fusiform gyrus, and bilaterally in the inferior prefrontal cortex (PFC) (Schott, Richardson-Klavehn, et al., 2006), and at retrieval, bilateral frontal and occipital areas, and the left fusiform gyrus show reduced activation (Schott, et al., 2005). The reduction in activity is thought to result from an increased neural efficiency. While participants with MCI show a preserved behavioural pattern, neuropathological changes are expected to be detectable in alteration of the activation pattern seen on fMRI. Some early preservation of behavioural performance in MCI in explicit memory tasks is thought to result from compensatory neural activity, which may involve increased activation of the areas involved in normal participants or recruitment of different brain regions (Drzezga, 2008). As priming is associated with reduced activation, it is hypothesised that compensation would occur by way of a greater reduction in activity. Of particular interest here are prefrontal areas, which are both involved in priming and affected by MCI and AD. Changes in prefrontal activity have in fact been detected in studies of explicit memory (e.g. Yetkin, et al., 2006), and prefrontal compensation may also be important during priming.

The main aims of the study are to investigate whether the pattern of activity associated with priming in normal participants is altered in those with MCI to show similar patterns to those who already have mild AD, which could lead to development of a new early diagnostic tool, and to investigate the importance of prefrontal regions in establishing implicit memory. The proposed project would require use of the 3T fMRI scanner. A total of 30 participants would be required, including 10 participants with MCI, 10 with AD, and 10 age and educationally-matched controls.