Brain function mapping of pre-mild cognitive impairment

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Introduction
Subjects with Mild Cognitive Impairment (MCI) are characterized by impaired memory and preserved activities of daily living. fMRI of MCI patients has revealed reduced activation in the occipitotemporal regions and inferior frontal cortex and increased activation in bilateral portions of anterior cingulate cortex. In order to identify patients at the earliest possible stage of MCI, recent research has investigated patients with memory decline that is insufficient for MCI criteria, but who also appear to be at increased risk for developing MCI and dementia. This is termed pre-MCI. It will be important to better understand the fMRI activation patterns in such patients in order to establish its utility as a marker for treatment response. However, a memory task might not be the optimal task for this purpose due to conflicting results showing that MCI patients have increased rather than decreased fMRI activation during memory tasks. The objective of this study is to identify functional tasks and brain areas that can be used to monitor the treatment of pre-MCI patients.

Methods
Preliminary results A group of six pre-MCI patients (ages 66-82 y, 3 females/3 males) and a similar number of age matched controls (4 females/2 males) were studied. Both groups are right-handed, native English speaking subjects with matched education and IQ. The pre-MCI subjects were diagnosed with memory loss but intact activities of daily living and were selected based on the criteria defined by Storandt et al. Scanning was performed on a 3 T Achieva Philips scanner (Cleveland, OH), equipped with an 8-channel head coil. The fMRI paradigms were presented using an Invivo IFIS-SA fMRI System (Orlando FL).

Functional EPI images were acquired with an isotropic spatial resolution of 3.4 mm, TR/TE 3000/22 ms, 80° flip angle, 64×64 matrix size, 40 slices. Each subject was presented with four block design functional tasks: [1] Attention tasks where the subject is required to respond to indicate if a dot was seen to the right or left side of a vertical bar. [2] Verbal fluency where the subject is asked to generate words starting with a given displayed letter. [3] Visuospatial problem solving (VPS) where the subject is asked to solve simple geometrical problems. [4] Memory task where the subject is presented with a series of pictures and asked to memorize for later testing then after the MRI session. A high resolution T1 weighted image was also acquired: TR/TE 8.1/3.7 ms, 1×1×1 mm3 voxel resolution, 3D acquisition. Outside the scanner immediately following the MRI, subjects repeated the same verbal fluency, VSP and memory tasks and scoring was performed. Functional images were motion corrected and unwarped using the B0 field map and FSL software utilities. All images were registered to the MN1152 standard using nonlinear registration. Single subject and group functional analysis was performed using FSL tools using cluster analysis with a Z-score threshold of 2.0 and a cluster p<0.05.

Results
The patient group showed decreased performance on the, verbal fluency, VPS and attention tasks. Figure 1A shows a reduction in the VPS of the pre-MCI group compared to the controls when tested outside the MR scanner. The corresponding reduction in the activation map of the frontal lobe is shown in Figure 2. In addition, we found that the pre-MCI group showed an activation reduction in the visual cortex during the attention task and in the frontal lobe during the verbal fluency task. Correspondingly there was a reduction in the verbal fluency test score of the pre-MCI group compared to controls (Figure 1B). The activation during the memory task did not show a significant difference between the two groups, which indicate that the disease was mild in these patients and/or may be due to the small size of the groups. Testing the subjects immediately after the MR study to see if they remember the pictures preset during the memory task, showed an insignificant difference between the groups as shown in Figure 1C.

Conclusions
The study showed that the fMRI scan is sensitive to differentiate the pre-MCI patients from matched normals, which may serve as a way to monitor potential pre-MCI treatment effects.