



Test-Retest of fMRI Activity in Hippocampus and Default Network in Non-demented Elderly Subjects



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INTRODUCTION

- Few studies have assessed fMRI signal reliability in older and cognitively impaired subjects over time periods typically used in clinical trials.
- In this study, we assessed the reliability of fMRI signal over 4-6 weeks in a memory network consisting of the hippocampus and precuneus regions, during full and abbreviated memory paradigms. We examined older subjects who were either cognitively normal (NC) or who have mild cognitive impairment (MCI).

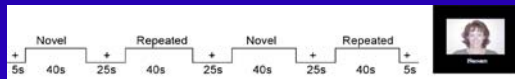
METHODS

Subjects

- 27 older subjects recruited from aging study and clinics and classified on the basis of the Clinical Dementia Rating Scale.
 - 18 subjects classified as CDR 0 (MMSE= 29.2); 9 subjects as CDR 0.5 (MMSE= 28.8)
 - Age (years): 73 +/- 9; Gender: 10 M/ 17 F; Education (years): 17.5 +/- 3
 - Average inter-scan interval (weeks): 5.15 +/- 1.5
- Time 1 refers to subjects' Baseline Scan and Time 2 is a follow-up scan, between 4-6 weeks later.

Face-name associative memory task

- 7 novel face name pairs/block, 2 blocks/run (84 total, each seen once)
- 2 repeated face name pairs/block, 2 blocks/run (each seen 42 times)
- Total of 6 experimental runs
- Timing of the images jittered within the blocks
- Subjects instructed to make a subjective decision as to whether the name "fit" the face and to remember the associated name



RESULTS

Whole-brain activation at Time 1 and Time 2

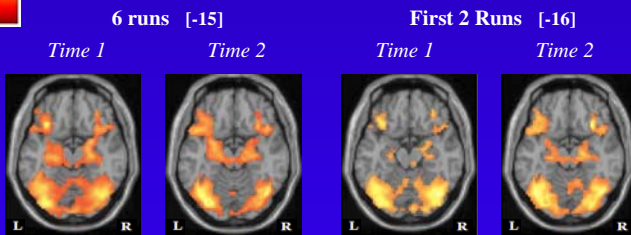
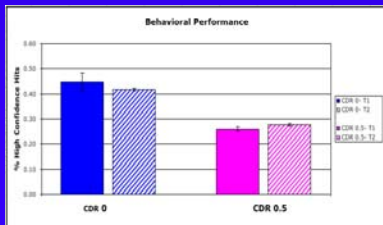


Figure 1. Whole Brain SPM2 axial maps of N > R for all 27 subjects with foci at [29 -17 -16]. Thresholded at $p < 0.001$, extent = 5 contiguous voxels.

Behavioral performance at Time 1 and Time 2



	% HCH
CDR 0 : T1	45
CDR 0 : T2	42
CDR 0.5 : T1	26
CDR 0.5 : T2	28

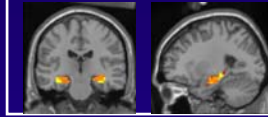
Imaging methods and data analysis

- 3.0T Siemens Trio; Gradient echo EPI: TR=2000, TE=30, FA= 90;
- 30 oblique slices (5mm, skip 1mm), perpendicular to AC/PC
- Data preprocessed in SPM2
- SPM2 whole brain repeated measures and region of interest (ROI) analyses utilized to explore magnitude of activation in the hippocampus

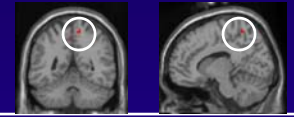
ROI analyses

e.g. Union T1, T2; constricted with MNI anatomical ROI

Hippocampus



Precuneus



Hippocampal activation is reliable in both block- and event-related paradigms

6 runs: N > R

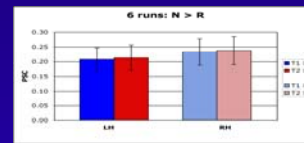


Figure 2. 6 runs: N > R - Paired-T test (T1-T2): LH- $p=0.90$, RH- $p=0.90$.
 ICC- LH: 0.43 (0.60) ; RH: **0.69 (0.81)**.

6 runs: HCH > F

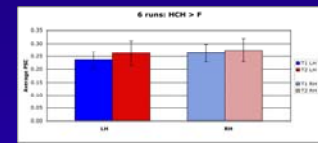


Figure 3. 6 runs: HCH > F - Paired-T test (T1-T2): LH- $p=0.57$, RH- $p=0.73$.
 ICC- LH: 0.40 (0.56); RH: **0.67 (0.80)**.

Analyses were repeated by CDR subgroup, showing similar results, with more variance in the CDR 0.5 group. ICC (N>R) - CDR 0: LH 0.65 (0.78), RH 0.64 (0.78); CDR 0.5: LH 0.20 (0.34); RH 0.74 (0.85).

Hippocampal activation in full and abbreviated paradigms are comparable in reliability

First 2 runs: N > R

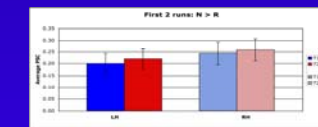


Figure 4. N> R - Paired-T test (T1-T2): LH- $p=0.69$, RH- $p=0.68$.
 ICC- LH: 0.37 (0.54) ; RH: **0.69 (0.81)**

First 2 runs: HCH > F

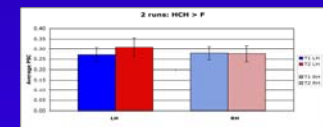


Figure 5. HCH > F - Paired-T test (T1-T2): LH- $p=0.35$, RH- $p=0.95$.
 ICC- LH: 0.54 (0.70) ; RH: **0.53 (0.69)**

Analyses were repeated for CDR subgroup. ICC (N > R) - CDR 0: LH 0.56 (0.71), RH 0.66 (0.80) ; CDR 0.5: LH 0.08 (0.16); RH 0.74 (0.85).

Deactivation in precuneus is less reliable

6 runs: F > ALL

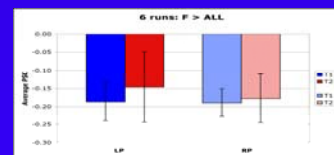


Figure 6. F > ALL - Paired-T test (T1-T2) : LH- $p=0.62$, RH- $p=0.87$.
 ICC- LH: 0.47 (0.67); RH: 0.13 (0.23).

• First 2 runs: Not enough power for deactivation ROI analyses in either the precuneus or lateral parietal regions.

• Elderly subjects showed great between- and within-subject variance in location and magnitude of deactivation.

• Several mildly impaired elderly subjects demonstrate failure of deactivation.

CONCLUSIONS

- Hippocampal activation, especially in the right hemisphere, demonstrates good test-retest reliability for cognitively normal and mildly impaired elderly subjects.
- The full and abbreviated face-name paradigms demonstrate comparable reliability, suggesting possible use of the task as cognitive "proof of concept" in clinical trials.
- Activation in the hippocampus demonstrates higher test-retest reliability than deactivation in the precuneus and default mode areas of the brain, potentially due to spatial and temporal variance inherent in deactivation for elderly subjects.

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