Longitudinal changes in brain MRI and cognition in older adults

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INTRODUCTION

Specific cognitive domains, subserved by many different brain regions, are affected by aging. There is no consensus on the precise nature of the underlying neurobiological changes. Neuroimaging findings may elucidate potential surrogate markers of cognitive impairment and help identify specific changes that underlie declines in specific cognitive functions. The majority of studies, however, are cross-sectional in nature and do not distinguish between secular changes and those directly related to aging. The application of serial imaging to study pathological changes demands a better understanding of the evolution of structural changes with normal aging as part of the normal developmental process and as distinct from pathology. The present study examines how volumetric MRI changes relate to cognitive decline in older adults from the neuroimaging sub-study of the Baltimore Longitudinal Study of Aging (BLSA) who were prospectively followed for up to 9 years.

METHODS

The present sample includes participants (age 56-86) from the BLSA neuroimaging sub-study, prospectively followed for up to 9 years (M = 6; SD = 2.78 yrs). Participants are divided into two groups: Normal (N = 131) and MCI (N = 18) based on standardized BLSA diagnostic procedures. Neuroimaging participants return for annual assessments and are in generally good health at initial evaluation. At each evaluation, participants underwent an MRI scan, a series of neuropsychological tests, a neurological exam, interval medical history, and medication review.

A standard battery of cognitive tests was administered annually (Resnick et al., 1998), including measures of language (fluency and naming), verbal and nonverbal memory (California Verbal Learning Test - CVLT and Benton Visual Retention Test - BVRT), spatial rotational ability (Card Rotations), and executive function and attention (Trails A & B).

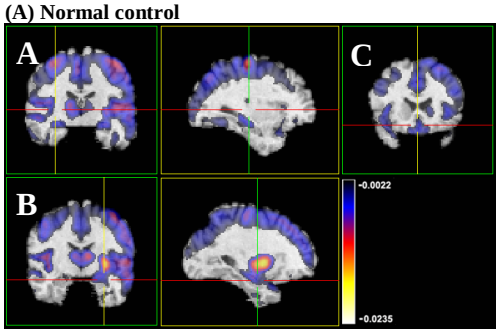
Scanning was performed on a GE Signa 1.5 Tesla scanner (Milwaukee, WI) using a high-resolution volumetric spoiled-grass (SPGR) axial series (TR = 35 ms, TE = 5 ms, FOV = 24 cm, flip angle = 45º, matrix = 256 x 256, NEX = 1, voxel dimensions 0.94 x 0.94 x 1.5mm slice thickness).

Procedures for image processing have been validated as described previously (Goldszal et al., 1998). Briefly, images are first corrected for head tilt and rotation and reformatted parallel to the anterior-posterior commissure plane. Extracranial tissue is removed using a semi-automated procedure followed by additional manual editing. Next, images are segmented into white matter (WM), gray matter (GM), and cerebrospinal fluid (CSF). The final step involves stereotaxic normalization and tissue quantitation for specific regions of interest. A template-based deformation approach is employed, using the ICBM standard MRI (Montreal Neurologic Institute) as the template and a hierarchical elastic matching algorithm for deformation and determination of regions of interest (Shen and Davatzikos, 2002; Lao et al., 2004); all images are normalized individually to the same template. Voxel-based analysis utilizes our RAVENS approach (regional analysis of volumes examined in normalized space; Goldszal et al., 1998), whereby local values of tissue density maps (one for GM, one for WM and one for CSF) reflect the amount of respective tissue in the vicinity of a voxel.

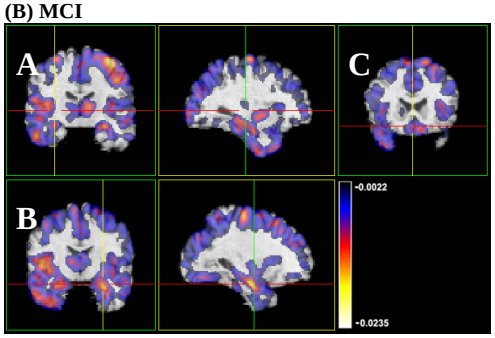
Statistical analyses were performed using SAS 9.1 (SAS Institute Inc.; Cary, NC). Rates of cognitive change were estimated using PROC MIXED for the linear model and PROC NLMIXED for the exponential mixed model. Longitudinal volumetric changes were examined by mixed effects linear regression models (PROC MIXED) based on absolute regional volume measurements adjusted for intracranial volume [ICV = GM+WM; (Regional Volume/ICV)*100] at initial MRI evaluation.

RESULTS

(A) Normal control



(B) MCI



- Volumetric MRI outcome measures include the trajectories of change for the whole brain, ventricular CSF, tc gray and white matter respectively, hippocampus, cingulate gyrus, and orbito-frontal cortex. Cognitive outc ability (verbal fluency and naming), verbal and nonverbal memory (CVLT and BVRT), spatial rotational abili (Trails A & B).
- Our previous findings suggest that the majority of global and regional volumes investigated declined sig previously reported that cognitive tests sensitive to normal aging in the BLSA include the BVRT, CVLT, verb (Driscoll et al., 2006).
- When examining the group of clinically normal older adults only, we found no significant relationships betwe rates of decline in specific aspects of cognition [except perhaps for card rotation and frontal GM (p = 0.04, unc
- When we added the longitudinal data for the 18 MCI participants to the analysis, some significant relationshi between the change in card rotation performance and whole brain (p = 0.05) and frontal GM (p = 0.03) volu ventricular CSF and CVLT (p = 0.05).
- Interestingly, these emerging relationships between cognitive decline and frontal GM atrophy specifica differential trajectories distinguishing between normal aging and MCI involve primarily frontal and temporal lo in those regions (Driscoll et al., 2007).

CONCLUSION

- Our results suggest the lack of relationships between longitudinal structural brain changes and declines in spe
- Some significant relationships begin to emerge when we include the data for the 18 MCI participants in addit
- One interpretation of the lack of relationship between cognitive decline and structural brain changes in cli threshold beyond which the change in brain structures becomes significant and results in negative functional co
- Results also have implications for underlying pathologic processes and ultimately diagnosis.

Figure 1. Linear regression map of grey matter on age. Volume loss for **(A)** Normal and **(B)** MCI groups, superimposed on a reference brain image. From A to C: coronal and sagittal sections of right hippocampus and adjacent structures; coronal and sagittal sections of left hippocampus and adjacent structures; coronal section of orbital frontal, inferior frontal region and adjacent structures. Radiology convention. Color bar displays estimated regression coefficients (from -0.0235 to -0.0022 and the unit of change is mm^3/year/voxel). The red-yellow color indicates greater volume loss.

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