377.7/MM4
0

The effects of aging and Alzheimer's disease on medial temporal lobe: A quantitative morphometric study of entorhinal perirhinal and parahippocampal cortex

Eric Feczko[2], Jenni Pacheco[3,4], Bruce Fischl[3,4], Randy L. Buckner[3,4,5], Jon C. Morris[6], Jean Augustinack[3,4], Bradford C. Dickerson[1,7]
Departments of Neurology[1], Psychiatry[2], Radiology[3], and the Athinoula A. Martinos Center for Biomedical Imaging[4], Massachusetts General Hospital HHMI at Harvard University[5]
Washington University School of Medicine[6]
Department of Neurology, Brigham & Women's Hospital[7]

INTRODUCTION

Background

- Quantitative MRI-based protocols have been developed that enable the measurement of entorhinal cortical (ERC) volume in vivo, and have been applied to the detection of ERC atrophy in very early Alzheimer's disease (AD).
- Dickerson et. al. (2001), Juottonen et. al (1998), and Bobinski et.al. (1999) showed volumetric ERC atrophy in early AD subjects when compared with healthy aged subjects.
- However, little MRI data exist on the effects of normal aging on the structure of ERC(Du et. al. (2006), Raz et. al. (2004))
- Du et. al. (2006) and Raz et. al. (2004) suggest minimal ERC atrophy occurs in aging.
- Furthermore, data are lacking on the quantitative MRI-based measurement of nearby medial temporal(MTL) cortex, including perirhinal (PRC) and parahippocampal cortex (PHC) in normal aging or AD.

Objective

•Past research has not examined thickness and surface area atrophy in MTL subregions: PRC, ERC, and PHC.

•Study the effects of healthy aging and AD on thickness and surface area of medial temporal neocortical regions.

METHODS

Subjects

•87 healthy right-handed volunteers(ages 18-90 57 f/30m)
•20 patients diagnosed with dementia of alzheimer's type(ages 50-96, 10 f/ 10m, CDR = 0.5 or 1.0)

•No other major medical, neurologic, or psychiatric illnesses

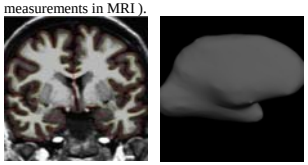
•All subjects provided informed consent in accordance with Human Research Committee guidelines of Massachusetts General Hospital

Imaging Parameters

•Siemens 1.5 T Vision
•Acquired 3-4 T1-weighted MPRAGE acquisitions per subject(1x1x1.25mm resolution; see Buckner RL et. al, Neuroimage 2004 for details)

Imaging Analysis

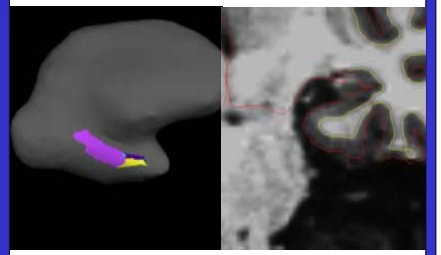
•Data were analyzed using the Freesurfer processing stream(http://surfer.nmr.mgh.harvard.edu); cortical white matter and pial surfaces were generated.
•Thickness measurements were determined through Freesurfer's semi-automated processing stream(See Han et. al. 2006, Kuperberg et. al. 2003 for validity of measurements in MRI).



•Dura layer was removed manually in order to ensure reliable ERC thickness measurements

Imaging Analysis(cont'd)

•A novel parcellation protocol was developed, based in part on Dickerson et. al. (2001), using visualization of surface and volume features to delinate ERC, PRC, and PHC, boundaries.



•Protocol was manually performed on data from all subjects
•Reliability of manual edits was assessed through reapplication of protocol to six subjects (two AD, two young, two elderly) by a rater, who was blind to each subject's identity
•Intraclass correlation coefficients were calculated to assess the level of reliability for the rater
•3-way ANOVAs were calculated to assess significance between the three groups for volume, thickness, and surface area
•Surface area and volume were covaried with estimated intracranial volume measurements (eTIV) in order to control for head size.

RESULTS

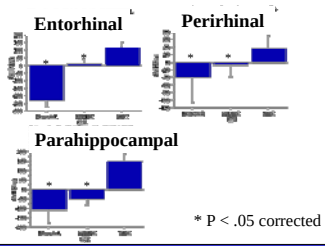
Reliability

•Reliability of dura edits was assessed by calculating an intraclass coefficient for ERC thickness, the primary region that is affected by dura edits.
•Reliability of surface label edits was assessed by determining intraclass correlation coefficients for ERC,PRC, and PHC surface area.

Measurements	ICC
ERC thickness	0.807
ERC surface area	0.8587
PRC surface area	0.9431
PHC surface area	0.9227

Volume

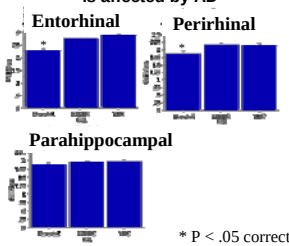
Volume is affected by both AD and aging



* P < .05 corrected

Thickness

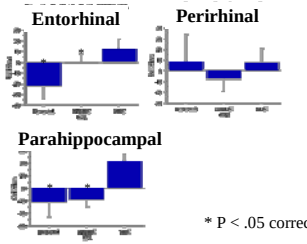
Thickness is affected by AD



* P < .05 corrected

Surface Area

Surface area is affected by aging



* P < .05 corrected

FUTURE DIRECTIONS

•Further investigate the effects of AD and aging on the PRC. As the surface area of the PRC appears to be equal to or greater in AD than normal subjects.
•Further investigate and categorize anatomic, sulcal, and gyral variance in the PRC and ERC.

CONCLUSIONS

These findings suggest that aging and AD have disparate effects on MTL subregional volumes. Surface area atrophy is associated with aging, whereas cortical thickness atrophy is associated with AD.

REFERENCES

- Daselaar SM, et al. Common Pathway in the medial temporal lobe for storage and recovery of words as revealed by event-related functional MRI. Hippocampus. 2004; 14:163-169.
- Eldridge LL, et al. A dissociation of encoding and retrieval processes in the human hippocampus. J. of Neuroscience. 2005; 25:3280-3286.
- Fischl B, et al. Whole brain segmentation: automated labeling of neuroanatomical structures in the human brain. Neuron 2002; 33:341-55.
- Lepage M, et al. Hippocampal PET activations of memory encoding and retrieval: the hiper model. Hippocampus. 1998; 8:313-322.
- Schacter DL & Wagner AD. Medial temporal lobe activations in fMRI and PET studies of episodic encoding and retrieval. Hippocampus. 1999; 9:7-24.
- Strange BA & Dolan RJ. Adaptive anterior hippocampal responses to oddball stimuli. Hippocampus. 2001; 11:690-698.

ACKNOWLEDGMENTS

This study was supported by the National Institute on Aging (K23-AG22509 P50-AG05681 P01-AG03991 P41-RR14075 U24-RR021382).

Disclosures: Dr. Dickerson received research support from Pfizer. Other authors have nothing to disclose.

Contact: bradd@nmr.mgh.harvard.edu