

Repurposing Clinically-Ordered Structural Magnetic Resonance Images for use in Research on Cognitive Aging: The ACT Study

Linda K. McEvoy¹; Rod L. Walker¹; Jalal B. Andre²; Patti Curl²; Nicole M. Gatto¹; Bradley Howlett²; David Hunt²; Nina LaPiana²; Samantha Murray Tuesta²; James Ralston¹; Juan Eugenio Iglesias³; Christine Mac Donald²

¹Kaiser Permanente Washington Health Research Institute, Seattle, WA, USA; ²University of Washington, Seattle, WA, USA; ³Massachusetts General Hospital and Harvard Medical School, Boston, MA, USA

Clinically-ordered brain MRIs can be repurposed for use in research, providing a cost-effective method to increase sample size and include participants who are less likely to volunteer for research studies.

Introduction

Acquiring a large database of brain MRIs in cohort studies is cost prohibitive.

MRI scans are being increasingly used in clinical care. The ability to repurpose these scans for research use would provide an efficient method for increasing sample size and allow inclusion of individuals less likely to volunteer for research MRI.

Objective

To establish suitability of use of clinical MRIs in brain aging research, determine whether regional volumetric measures from clinical MRIs show similar age-sensitivity as measures from research MRIs, and whether clinical MRI data can be used to predict incident dementia.

Study Population

The Adult Changes in Thought Study (ACT) is a longitudinal study of members of the Kaiser Permanente Washington health care system. Participants are aged 65+ and dementia-free at enrollment. They consent to use of their medical records for research, including records available prior to enrollment. Participants are followed with biennial research visits; those who experience cognitive decline undergo rigorous evaluation and consensus diagnosis of type and presence of dementia using standard criteria.

MRI Acquisition

Research MRI: A subset of participants take part in a research MRI visit in which multimodal images are obtained, including 3D MPRAGE.

Clinical MRIs: All available clinical MRIs since 2002, regardless of acquisition parameters and imaging platform, are procured from participants' medical records, as previously described (Mossa-Basha et al. BJR, 2024; PMC11027291). We used a single clinical scan per participant for the current analysis,. Time-to-event analyses used scans obtained when participants were dementia-free.

Study Sample

Characteristics of participants with clinical and research MRIs as of 04/30/2025 from visit closest to scan. Values are % unless otherwise indicated.

Characteristics	Clinical N=1195	Research Scans N=520
Age, mean (sd)	79 (8)	79 (6)
Women	57	50
Race		
White	84	87
Asian	6	5
Black or African American	5	2
Other	6	5
Hispanic, Latino	2	1
Education, yrs, mean (sd)	16 (3)	17 (2)
Hypertension	61	54
Diabetes	14	10
Coronary artery disease	22	14
Cerebrovascular disease	21	11
Fair/poor self-rated health	19	10

Participants with clinical scans were more likely to be women and to have more comorbidities and poorer self-rated health than those with research scans.

MRI Processing

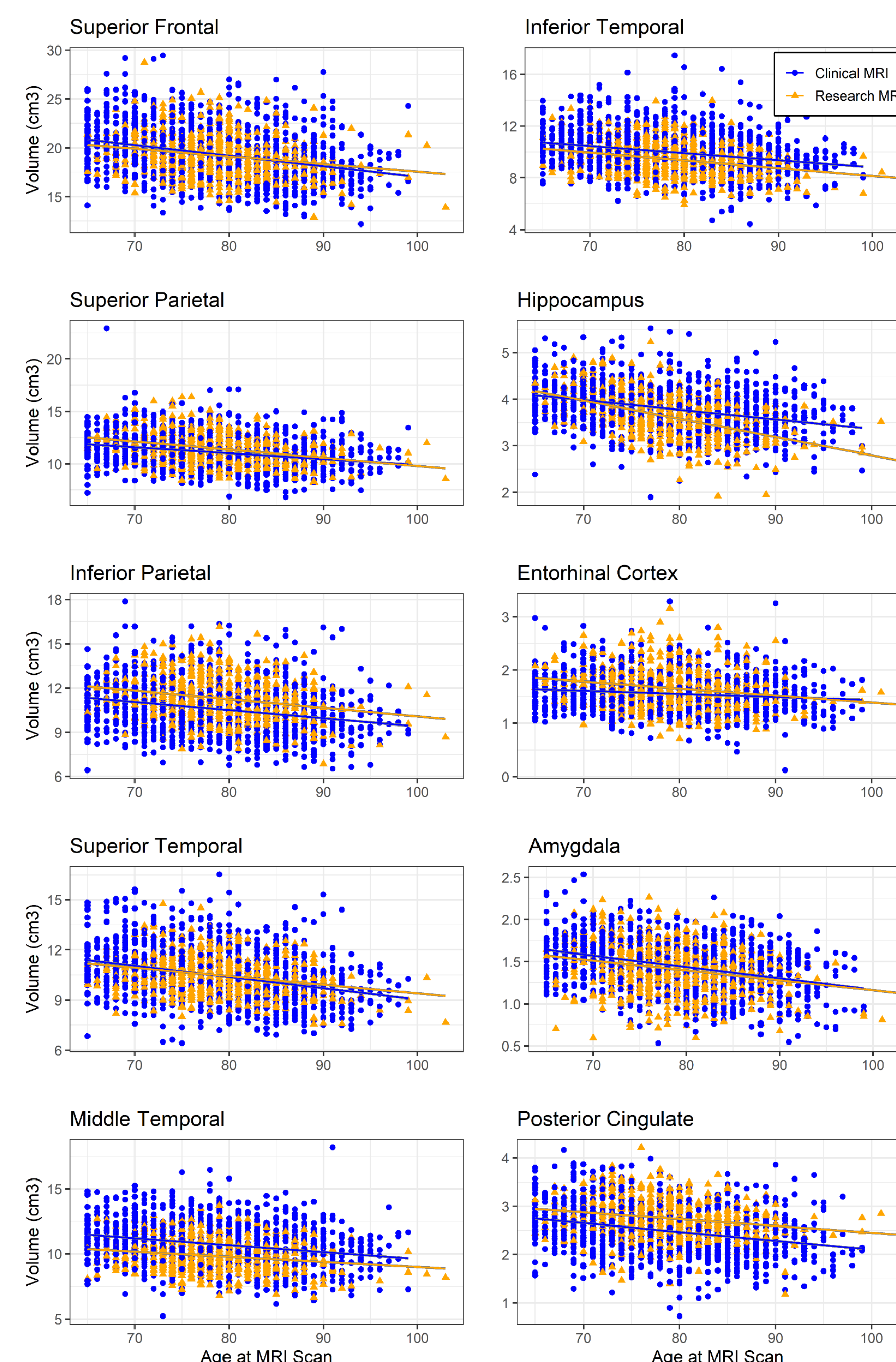
Clinical MRIs from participants' medical records were processed with SuperSynth, a validated method for creating synthetic, 1-mm isotropic 3D MPRAGE scans from MRIs obtained with a variety of acquisition parameters and imaging platforms (Billot et al. Medical Image Analysis, 2023; Iglesias et al 2023, Science Advances). Available at: <https://surfer.nmr.mgh.harvard.edu/fswiki/SuperSynth>

Synthetic scans and research 3D MPRAGE scans were processed with FreeSurfer to obtain regional volumes.

ACT data, including neuroimaging data from >1600 participants, are available for use by the research community. See <https://actagingresearch.org>

Results

Association of regional volumes, averaged across hemispheres, with age from clinical and research MRIs.



Regional volumes showed expected significant associations with age in both clinical and research MRIs, with few differences in magnitude of age-associations between scan types.

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	Research scan (N=520)	Clinical scan (N=1195)	p-value
Superior Frontal	-0.22 (-0.29, -0.16)	-0.30 (-0.34, -0.26)	0.042
Superior Parietal	-0.36 (-0.43, -0.28)	-0.25 (-0.30, -0.21)	0.018
Inferior Parietal	-0.25 (-0.32, -0.18)	-0.23 (-0.27, -0.19)	0.617
Superior Temporal	-0.25 (-0.32, -0.19)	-0.33 (-0.37, -0.28)	0.068
Middle Temporal	-0.18 (-0.24, -0.12)	-0.24 (-0.28, -0.20)	0.135
Inferior Temporal	-0.28 (-0.35, -0.21)	-0.25 (-0.29, -0.20)	0.456
Hippocampus	-0.59 (-0.67, -0.50)	-0.30 (-0.34, -0.26)	<0.001
Entorhinal Cortex	-0.27 (-0.36, -0.17)	-0.11 (-0.16, -0.06)	0.005
Amygdala	-0.29 (-0.39, -0.19)	-0.32 (-0.37, -0.27)	0.550
Posterior Cingulate	-0.21 (-0.28, -0.13)	-0.26 (-0.31, -0.22)	0.185

Coefficients from linear regression models adjusted for sex and total intracranial volume correspond to estimated change in mean volume (in standard deviation, SD, units) associated with a 1-SD increase in age (7.2 years). P-values for differences in age coefficients between research scans vs. clinical scans.

Larger hippocampal volumes on clinical scans were associated with reduced risk of incident AD and all-cause dementia:

	AD dementia (N=131)		All-cause dementia (N=153)	
	HR (95% CI)	p-value	HR (95% CI)	p-value
Hippocampus	0.71 (0.56, 0.89)	0.003	0.78 (0.63, 0.96)	0.019

Hazard ratios (HR) and 95% CIs associated with a 1-SD increase in hippocampal volume (i.e., 0.5 cm³), based on Cox regression models estimated among 629 participants, adjusted for sex, education, age at MRI scan, and total intracranial volume, over an average follow-up of 5.4 years. Because ACT's research neuroimaging collection began in 2023 there are insufficient dementia events among those with research scans to examine research MRI associations with dementia.

Conclusions

Regional brain volumes from clinical MRIs show expected differences with age. Hippocampal volumes from clinical images are predictive of dementia, in agreement with known predictive ability of hippocampal volumes from research-grade MRI scans. Thus clinical brain MRIs can be repurposed for use in research on factors associated with brain aging and dementia risk.

Repurposing clinical scans for research use is a cost-effective method for increasing samples sizes in cohort studies, and for increasing clinical heterogeneity in imaging samples.