



Effects of pulse sequence, voxel geometry, and parallel acceleration on the reliability of cortical and subcortical neuroanatomic measures

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Background

- Development of sophisticated tools for the analysis of MRI data has led many researchers to adopt rapid, semi-automated methods for obtaining morphometric measurements, such as cortical thickness and volume.
 - Technological advances in MRI hardware and acquisition techniques have resulted in a push toward obtaining higher resolution images and the use of multispectral sequences for improved contrast.
 - Further, the use of parallel acquisition techniques, such as GRAPPA, have enabled substantially faster collection of structural neuroimaging data, while decreasing the adverse effects of motion artifact.
- This advance is especially beneficial to researchers studying subjects prone to motion, such as patients with movement disorders or children.
- While these advances are largely welcomed, it is important to understand how differences in image geometry, sequence parameters, and the use of parallel acquisition techniques influence subsequent processing steps and, ultimately, morphometric measurements.
 - To address this question, we examined the reliability of cortical thickness and volume measures as a function of different acquisition parameters and imaging techniques.

Methods

Participants

- 5 young adults (21.4 ± 3.8 years; 1 male / 4 female)
- 6 older adults (64.3 ± 12.2 years; 3 male / 3 female)

Parameters & Sequences

- Scans collected on a Siemens 3T Trio scanner with 12-channel TIM head coil
- Sequences were permutations of the T1-weighted Magnetization-Prepared Rapid Gradient Echo (MP-RAGE) (see pulse sequences)
- For the multiecho MP-RAGE, a final volume was generated from the RMS average of all echoes collected
- Parallel acquisition implemented by Generalized Autocalibrating Partially Parallel Acquisition (GRAPPA)
- Two scans were collected per sequence during each session
- Two scanning sessions approximately two weeks apart

Image Preprocessing

- Surface and morphometric measures with FreeSurfer and associated Montreal Neurological Institute tools
- Multiple within-session acquisitions of each sequence were averaged after motion correction to generate a single volume for reconstruction
- Volumes underwent semi-automated processing for Talairach transformation, skull stripping, subcortical registration and segmentation, and white/pial surface generation¹⁻⁴
- We derived measures of global cortical thickness and volumes of cortical grey matter (GM), white matter (WM), hippocampus, amygdala, thalamus, pallidum, caudate, and putamen

Reliability Measures

- We examined two aspects of variability: (1) the magnitude of within-subject test-retest variability of morphometric measurements ("reliability"), and (2) systematic differences in the magnitude of morphometric measures as a function of sequence ("bias"). We computed intra-class correlation coefficients (ICC) to assess session-to-session reliability for each sequence.⁵

Pulse sequences

Sequence	TR (ms)	TI (ms)	TE (ms)	Flip angle (°)	Bandwidth (Hz/pixel)	Voxel size (mm)	IPAT	Scan time (min)
Anisotropic MP-RAGE (MPR)	2530	1100	3.39	7	195	1.3 x 1.0 x 1.3	No	8:07
Isotropic MP-RAGE (ISO)	2530	1100	3.48	7	195	1.0 x 1.0 x 1.0	No	10:49
Accelerated isotropic MP-RAGE (ISH)	2530	1100	3.48	7	195	1.0 x 1.0 x 1.0	Yes (x2)	6:03
Multiecho MP-RAGE (MEM)	2530	1100	1.58 + (n x 1.74), n = 0...3	7	698	1.0 x 1.0 x 1.0	Yes (x2)	5:53

Sample anatomical data

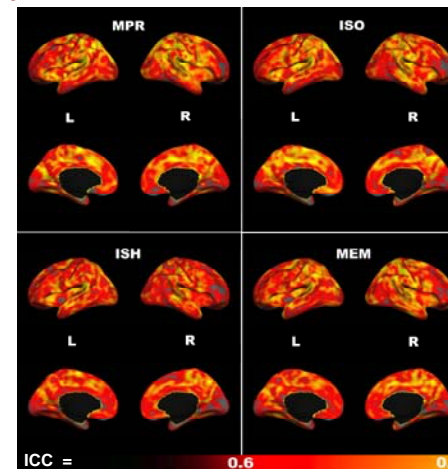


Left: WM/GM (yellow line) and GM/CSF (red line) boundaries.
Right: automatic segmentation of cortical gray matter (red), white matter (white), caudate (blue-gray), putamen (pink), globus pallidus (light blue), hippocampus (brown), and amygdala (teal)

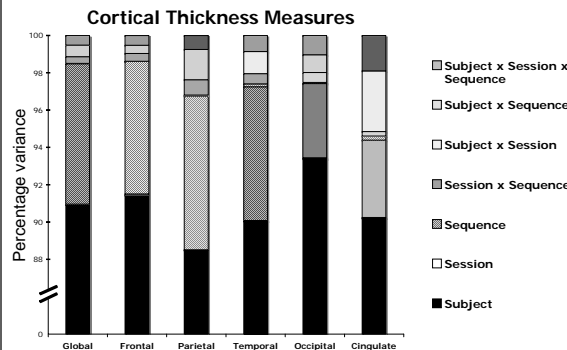
Intra-class correlation coefficients for morphometric measures across sessions

Measure	Brain Area	MPR	ISO	ISH	MEM
Cortical thickness	Global	0.994	0.987	0.960	0.986
	Frontal	0.988	0.983	0.970	0.979
	Temporal	0.989	0.975	0.969	0.975
	Parietal	0.960	0.985	0.922	0.979
	Occipital	0.987	0.982	0.946	0.959
	Cingulate	0.972	0.975	0.926	0.944
Volume	White matter	0.999	0.999	0.999	0.999
	Gray matter	0.997	0.996	0.989	0.996
	Whole brain	0.999	0.999	0.999	0.999
	Amygdala	0.942	0.874	0.949	0.856
	Caudate	0.988	0.991	0.994	0.994
	Hippocampus	0.955	0.969	0.989	0.979
	Pallidum	0.876	0.570	0.706	0.854
	Putamen	0.956	0.951	0.971	0.921
Thalamus	0.966	0.964	0.984	0.981	

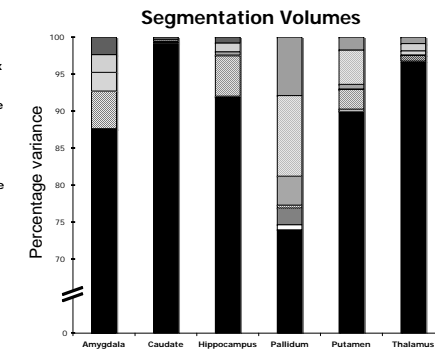
- Surface maps (figure on right) of cortical thickness reliability revealed high local ICC values across most of the cortex.
- We found minimal effects of voxel size (e.g., comparing MPR to the three isotropic sequences) and acceleration (e.g., comparing ISO to ISH) on the reliability of most morphometric measures.
- Reliability for multiecho (MEM) measures was generally high and comparable to anisotropic MP-RAGE (MPR) measures.



Percentage variance explained by sequences, sessions, and subjects

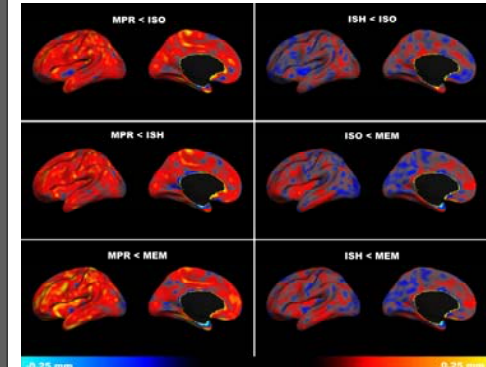


For cortical thickness measures, the percentage variance explained by differences between subject means was near or above 90% for all measures, indicating a high degree of overall reliability.



Precision of subcortical volume measures varied by structure: Caudate and thalamus were among the most reliable, while pallidum volumes were the least reliable.

Cortical thickness differences



- We found a bias towards higher cortical thickness measures using the isotropic MP-RAGE sequences compared to the anisotropic MP-RAGE. This bias was relatively consistent across the cortex, with a mean bias of 0.09 mm.
- This bias was most evident between the anisotropic and multiecho MP-RAGE sequences, especially in frontal regions.
- Between isotropic sequences, cortical thickness differences were more limited with no perceptible bias towards one sequence or another.

Summary and conclusions

- Reliability of morphometric measures was generally high and largely unaffected by small differences in voxel geometry, the use of conservative parallel acceleration factors, or the use of high-bandwidth multiecho techniques.
- Thus, acceleration may prove particularly useful when studying individuals that are prone to movement or experience discomfort in the scanner.
- Surface-based measures of cortical thickness, WM volume, and GM volume tended to be more precise than segmentation-based measures of subcortical volumes.
- The precision of subcortical volumes was likely affected by intrinsic tissue contrast properties and by the contrast between surrounding tissue types.
- Larger, anisotropic voxel sizes resulted in a significant measurement bias for surface-based measures and some volume-based measures compared to smaller, isotropic voxel sizes.
- Image geometry should, therefore, be considered carefully in protocol design.

References

- Dale AM, Fischl B, Sereno MI. (1999). *NeuroImage* 9: 179-194.
- Fischl B, Sereno MI, Dale AM. (1999). *NeuroImage* 9: 195-207.
- Fischl B, et al. (2001). *IEEE Trans Med Imaging* 20: 70-80.
- Fischl B, et al. (2004). *Cereb Cortex* 14: 11-22.
- Shrout PE & Fleiss JL. (1979). *Psych Bull* 86: 420-428.

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