



Measurement of cortical thickness asymmetry in carotid occlusive disease



Iris Asllani^{a,*}, Pamela Slattery^a, Alexander Fafard^a, Marykay Pavol^b, Ronald M Lazar^b, Randolph S Marshall^b

^aRochester Institute of Technology, New York, USA

^bColumbia University Medical Center, USA

ARTICLE INFO

Article history:

Received 29 July 2016

Received in revised form 16 September 2016

Accepted 17 September 2016

Available online 19 September 2016

Keywords:

Atrophy
Carotid occlusion
Carotid disease
Cortical thickness
High-resolution MRI
Primary motor cortex
Primary visual cortex

ABSTRACT

Despite being considered an important anatomical parameter directly related to neuronal density, cortical thickness is not routinely assessed in studies of the human brain *in vivo*. This paucity has been largely due to the size and convoluted shape of the human cortex, which has made it difficult to develop automated algorithms that can measure cortical thickness efficiently and reliably. Since the development of such an algorithm by Fischl and Dale in 2000, the number of studies investigating the relationship between cortical thickness and other physiological parameters in the brain has been on the rise. There have been no studies however that have validated cortical asymmetry against known vascular anatomy. To this aim, using high-resolution MRI, we measured cortical thickness and volume in the primary motor (M1) and primary visual (V1) cortex in patients with unilateral, high-grade carotid occlusive disease ($n = 29$, age = 74 ± 10 years). These regions were selected based on the hypothesis that there will be thinning of the cortical thickness of M1 in the territory supplied by the occluded carotid artery, whereas V1 will show no asymmetry since its blood supply is provided by unaffected posterior arteries. To test for an effect of handedness, cortical thickness and volume were also measured in healthy volunteers ($n = 8$, age = 37 ± 13 years). In patients, we found thinner cortex in M1 on the occluded side (mean = 2.07 ± 0.19 mm vs 2.15 ± 0.20 mm, $p = 0.0008$) but no hemispheric difference in V1 (1.80 ± 0.17 mm in occluded vs 1.78 ± 0.16 mm in unoccluded, $p = 0.31$). Although the mean cortical volume of M1 in the occluded hemisphere was also lower, the difference did not reach statistical significance ($p = 0.09$). Similarly, in healthy controls, the results showed no hemispheric asymmetry in either cortical thickness or volume in either region ($p > 0.1$). To test for an orientation bias in the method, the analysis was repeated with images flipped from neurological to radiological orientation. While the algorithm did not yield identical results for the two orientations, the effect did not alter the findings of the study. These results provide a method for within-subject validation of a pathophysiological effect of carotid occlusive disease on the human cortex and warrant further investigation for underlying mechanisms.

© 2016 The Authors. Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

1. Introduction

Imaging studies have consistently shown that normal aging and disease are associated with structural changes in the cerebral cortex. These changes are commonly assessed as changes in volume rather than in cortical thickness despite indications that cortical thinning might represent a more specific marker of post-injury or degenerative processes (Fotiadis et al., 2016; Geisseler et al., 2016; Hwang et al., 2016).

Cortical thickness is typically defined as the average distance between the white matter surface and the pial surface, which can be computed locally, over a region of interest (ROI), or globally, over a hemisphere and the entire brain (Fischl and Dale, 2000). Historically, *in vivo* measurement of cortical thickness of functional regions in the brain has been difficult because of the complexities of the shape and

size of the human cortex. Until relatively recently, the most viable option was manual delineation of the cortical regions, a method both time-consuming and unreliable for cross-study comparisons (Desikan et al., 2006).

In 2000, Fischl and Dale developed Freesurfer, an automated surface-based method (Fischl and Dale, 2000) for measuring cortical thickness that has since been validated against histological analysis (Rosas et al., 2002) as well as manual measurements (Kuperberg et al., 2003; Salat et al., 2004). In addition, the method has been shown to produce reliable test-retest estimates across scanner types and field strengths (Han et al., 2006; Reuter et al., 2012). In tandem with the validation studies, an increasing number of studies have used the cortical thickness measurement as a correlate of physiological changes in the brain in normal aging and disease (Han et al., 2006; Kuperberg et al., 2003; Sailer et al., 2003; Rosas et al., 2003).

Nonetheless, the method is relatively new, and further independent studies are needed to test its reliability and clinical usefulness. In

* Corresponding author.

E-mail address: icabme@rit.edu (I. Asllani).

particular, although cortical thinning has been reported in several recent studies with focal pathology (Cheng et al., 2015; Duering et al., 2015), there have been no controlled studies for cerebrovascular diseases that take advantage of known vascular anatomy.

In this study, we used high-resolution anatomical MRI images to test for hemispheric asymmetry in cortical thickness in asymptomatic patients with unilateral carotid occlusive disease. This condition provides a robust model for testing regional cortical thinning in the vascular territory directly affected by the occlusion. We tested the hypothesis that there would be thinning of the primary motor cortex (M1) on the side of the occluded artery, but no hemispheric asymmetry in cortical thickness of V1, since the visual cortex receives its blood supply from the unoccluded posterior cerebral arteries. Such a finding would validate cortical thickness measurements as a biomarker for regional or focal vascular disease, providing support for future studies of vascular pathophysiology and its functional correlates.

2. Methods

2.1. Study participants

2.1.1. Patients

Twenty-nine patients, age 50–93, 19 male, 26 right-handed, with unilateral 80–100% ICA occlusion but no stroke were enrolled in the study. Out of the 29 patients, 16 (55%) had their occlusion on the left side. Inclusion criteria were: $\geq 80\%$ carotid stenosis or complete occlusion by carotid Doppler, MRA, or CTA, with $< 40\%$ stenosis in the contralateral ICA. Other inclusion criteria were: asymptomatic status or TIA-only referable to the ICA stenosis, fluent in English, and able to give informed consent. Exclusion criteria included prior clinical stroke, diagnosis of dementia, history of moderate-severe head trauma, current substance abuse, major psychiatric disease, NYHA Stage 3/4 congestive heart disease, or contraindication to MRI.

2.1.2. Healthy controls

As an additional control for hemispheric asymmetry in the selected ROIs, we analyzed images acquired on eight right-handed healthy volunteers, age 21–56, 4 male, enrolled for a different study conducted by one of the authors (IA) at the Leiden University Medical Center.

All participants signed the consent form approved by the respective institutions' ethics review board.

2.2. Image acquisition and processing

Imaging was performed on 3T Philips Achieva scanners in the medical centers of Columbia University (patients) and Leiden University (healthy controls). A high-resolution 3D T1-weighted (MPRAGE) image was acquired on each participant with the following parameters: TE = 3 ms, TR = 6.7 ms, in plane resolution $0.9 \times 0.9 \text{ mm}^2$, slice thickness = 0.9 mm, 120 slices. An in-house SPM12 (Wellcome Trust Centre for Neuroimaging, London, UK) based script was used to flip the orientation of the images such that they were available in both neurological and radiological orientations. This was done to test for any orientation bias in Freesurfer's performance of cortical thickness estimation.

Volumetric tissue segmentation and inference of cortical structure were obtained from each patient's MPRAGE (neurological and radiological orientation, independently) using the Freesurfer software (Fischl and Dale, 2000).

Briefly, the Freesurfer approach involved: (1) removal of non-tissue voxels using a hybridized watershed/surface deformation algorithm (Ségonne et al., 2004), (2) computation of forward and inverse transforms into Talairach space, (3) volumetric segmentation of subcortical white matter and deep gray matter structures (Fischl et al., 2002; Fischl et al., 2004), (4) intensity normalization (Sled et al., 1998), (5) tessellation of the boundary between gray and white matter, (6) automated topology correction (Fischl et al., 2001; Ségonne et al., 2007),

and (7) surface deformation, which is conducted along intensity gradients such that transitional borders are positioned along the greatest shift in signal intensity aligned with the border to the next tissue class (Dale et al., 1999; Dale and Sereno, 1993; Fischl and Dale, 2000).

Following the registration to a spherical brain atlas utilizing cortical folding patterns of subjects to match cortical geometry across subjects (Fischl et al., 1999), the cerebral cortex was parcellated into different regions based on the structure of the gyri and sulci (Desikan et al., 2006; Fischl et al., 2004). With both the inner and outer cortical surfaces identified and isolated, the cortical thickness of a subject was calculated as the Euclidean distance between the two surfaces (Fischl and Dale, 2000).

The cortical thickness maps are created through the use of spatial intensity gradients across tissue classes and are therefore largely invariant to absolute signal intensity.

Based on the parcellation results, regions of interest were selected for the cortical thickness map of the primary motor cortex (M1) and primary visual cortex (V1). Data from these ROIs were used to compute cortical thickness and volume, which were subsequently used in the analysis described below.

2.3. Data analyses

The cortical thickness (CT) coefficient of asymmetry between hemispheres was defined as

$$C_a = \frac{(CT_{unoccl} - CT_{occl})}{(CT_{unoccl} + CT_{occl})} \cdot 100 \quad (1)$$

where CT_{unoccl} and CT_{occl} denote cortical thickness in the unoccluded and occluded hemispheres, respectively. The coefficient of asymmetry (Eq. (1)) looks at the difference between hemispheres normalized to the sum so that it is not dependent on the mean values of each hemisphere. C_a can take positive values (meaning the cortical thickness of occluded hemisphere is lower), zero (meaning no hemispheric difference) or negative (meaning the cortical thickness is higher in the occluded hemisphere.)

A paired *t*-test (Bonferroni corrected for multiple comparisons, $n = 2$, with two tailed $\alpha = \alpha_{uncorr}/2 = 0.025$) was run for cortical thickness and volumetric data in M1 and V1 from each group, independently. The corrected *p*-values are reported as p_{corr} . The analysis was run twice, once each for neurological and radiological orientations.

3. Results

There was considerable variation in size and shape of both the primary motor (M1) and primary visual (V1) cortex within the same hemisphere across participants as well as between hemispheres on the same participant. Qualitatively, this variation is reflected in Fig. 1, which shows 3D surface rendering of M1 (Fig. 1A) and V1 (Fig. 1B) from six randomly selected patients.

The average cortical thickness of M1 in the hemisphere on the side of the occluded carotid was significantly lower than in the unoccluded hemisphere: $2.07 \pm 0.19 \text{ mm}$ vs $2.15 \pm 0.20 \text{ mm}$ ($t_{28} = 3.9$, $p_{corr} = 0.0008$.) Although on average the volume of M1 was also lower in the occluded hemisphere ($3399 \pm 791 \text{ mm}^3$) compared to the unoccluded ($3496 \pm 825 \text{ mm}^3$), the effect did not reach statistical significance ($p_{corr} = 0.4$).

In V1 there was no statistical difference in either cortical thickness ($1.80 \pm 0.17 \text{ mm}$ in occluded vs $1.78 \pm 0.16 \text{ mm}$ in unoccluded, $t_{28} = -1.05$, $p_{corr} = 0.4$) or volume ($3410 \pm 747 \text{ mm}^3$ vs $3503 \pm 698 \text{ mm}^3$, $t_{28} = -0.6$, $p_{corr} = 0.6$).

To give a sense of the hemispheric differences at the individual patient level, the distribution of the coefficient of asymmetry, C_a , across all patients is shown in Fig. 2 for both ROIs. Of the 23 patients with a $> 1\%$ asymmetry in M1, 19 had lower cortical thickness values on the occluded side.

Download English Version:

<https://daneshyari.com/en/article/8688966>

Download Persian Version:

<https://daneshyari.com/article/8688966>

[Daneshyari.com](https://daneshyari.com)