Published in final edited form as:
Cephalalgia. 2011 October ; 31(14): 1452–1458. doi:10.1177/0333102411421025.

Absence of changes in cortical thickness in patients with migraine

Ritobrato Datta, **John A Detre**, **Geoffrey K Aguirre**, and **Brett Cucchiara**
University of Pennsylvania, USA

Abstract

Objective—Previous studies have reported gray matter alterations in patients with migraine, particularly thinning of the cingulate gyrus, and thickening of the somatosensory cortex (SSC) and visual motion processing areas (V3A/MT+). We attempted to replicate these findings in a larger patient population.

Methods—Brain anatomy was collected with 3T MRI. Surface-based morphometry was used to segment each brain volume, reconstruct and inflate the cortical sheet, and estimate gray matter thickness.

Results—Eighty-four age and sex-matched participants (28 migraine with aura, 28 migraine without aura, and 28 controls) were studied. No significant differences in somatosensory, cingulate gyrus, or V3A/MT+ cortical thickness were found between the groups, including analysis of specific subregions previously reported to be affected. Whole brain analysis found no regions of differential gray matter thickness between groups. A highly significant inverse correlation between age and whole brain and regional cortical thickness was identified. Power analyses indicate that even a small difference (~0.07 to 0.14 mm) in cortical thickness could have been detected between groups given the sample size.

Interpretation—Using highly sensitive surface-based morphometry, no differences in cortical thickness between patients with migraine and controls could be identified.

Keywords

Migraine; morphometry; cortical thickness; brain structure

Introduction

The recent demonstration of interictal structural changes in brain morphology in patients with migraine, particularly alterations in cerebral gray matter, has supported a shifting perception of migraine from an episodic neurovascular disorder to a chronic, progressive brain disease. However, as other authors have pointed out, studies of structural alterations in the brain must be interpreted with caution (1). For instance, there is a considerable amount of data suggesting that structural changes in migraine and other pain disorders are reversible and can be relatively transient responses to acute pain stimuli (1, 2).

Corresponding author: Brett Cucchiara, Department of Neurology, University of Pennsylvania, Medical Center, 3400 Spruce Street, Philadelphia, PA 19104, USA cucchiar@mail.med.upenn.edu.

Conflicts of interest
There are no conflicts to disclose.

Anatomical comparisons between populations have generally been made with voxel-based morphometry (VBM). After volumetric registration to a standard template, T1-weighted MR image intensities are compared between the populations at each voxel, often segregated by tissue type (e.g. gray matter and white matter) (3). While a productive approach, VBM is prone to known artifacts introduced by anatomical registration and is dependent on a number of assumptions about the data to be analysed (4, 5). Surface-based morphometry (SBM) is an alternative approach that provides a direct measure of gray matter thickness (6). An automated routine identifies the continuous, gray matter cortical sheet and estimates gray matter thickness at each point with sub-voxel accuracy. Registration of anatomical images between participants is accomplished by matching of gyral and sulcal geometry within an inflated, cortical spherical atlas. This reduces susceptibility to registration artifacts induced by global volume changes, and has been shown to reduce variability in structure–function matching between participants as compared to volumetric approaches (7).

Several previous studies using VBM have demonstrated decreases in gray matter in small cohorts of migraine patients in a number of different focal brain regions, most consistently in the cingulate cortex (1). In contrast, a study using SBM found an increase in gray matter thickness in the somatosensory cortex (SSC) in patients with migraine (8). In addition, an increase in gray matter thickness in visual motion processing areas (V3A and MT+) has also been identified using SBM in patients with migraine (9).

The purpose of the present study was 1) to attempt to independently replicate the reported findings of increased cortical thickness in the SSC and visual motion processing areas in migraineurs using a similar surface-based morphometric method, 2) to attempt to confirm previous VBM observations showing gray matter decreases in the cingulate cortex using a SBM method, and 3) to identify any regional changes in cortical thickness using a whole brain analysis on an exploratory basis.

Methods

Participants

Participants were recruited both from the neurology clinic at the University of Pennsylvania and by advertisements in the wider University of Pennsylvania community. Participants were eligible for inclusion if they were 25–50 years old, had a diagnosis of migraine with aura (MWA) or without aura (MwoA) using International Headache Society criteria, or were headache- free healthy controls. Patients with a previous history of cerebrovascular disease, significant neurological illness other than migraine, atrial fibrillation, carotid stenosis, thrombotic disorder, or contraindication to MRI were excluded. Headache-free healthy controls could not have any history of potentially migrainous headaches (including ‘sinus’ headaches or any type of headache requiring medication) and could not have tension-type headache unless it occurred exceedingly rarely (defined as less than once a year). Isolated infrequent provoked headaches associated with excessive alcohol consumption or transient illness other than reported sinusitis were allowed. Family history of migraine was not an exclusion criterion for control participants. All participants were screened and examined by a single study neurologist (BC) to ensure that they met inclusion/exclusion criteria. This analysis was a substudy of an ongoing larger MRI study comparing patients with migraine to healthy controls designed to evaluate brain and vascular structure and function. For the present study, all MWA participants from the overall study with imaging data suitable for analysis were included. MwoA and control participants were randomly selected from the overall cohort in an iterative manner until optimal age and sex-matching with MWA participants was achieved. This was done prior to any analysis being performed. The study was approved by the University of Pennsylvania Institutional Review Board and all participants provided written informed consent.

Anatomical imaging and cortical thickness analysis

MRI was performed using a 3.0T Siemens Trio scanner with a Siemens 8 channel head coil. Anatomical images were acquired using a standard T1-weighted high resolution anatomical scan of magnetization prepared rapid gradient echo (MPRAGE) (160 slices, 1mm×1mm×1 mm, repetition time=1.62 s, echo time=3.09 ms, inversion time=950 ms, field of view=250 mm, flip angle=15°). For all participants, brain surfaces were reconstructed, inflated and parcellated into anatomical regions from the MPRAGE images using the FreeSurfer toolkit (http://surfer.nmr.mgh.harvard.edu/) as described previously (6, 10, 11) This approach matches morphologically homologous cortical areas based on the cortical folding patterns with minimal metric distortion and allows sampling at subvoxel resolution and detection of cortical thickness differences at the sub-millimeter level. Cortical thickness was estimated at each point across the cortical mantle by calculating the distance between the gray/white matter boundary and the cortical surface. Gray matter thickness was compared using measurements of cortical thickness in anatomical regions of interest most relevant to the hypotheses and from previous reports and a whole-brain surface-based morphometric analysis.

Analysis of specific regions of interest

Several regions of interest (ROIs) were examined for focal changes in gray matter thickness. First, we attempted to replicate the finding of increased thickness in the sensorimotor cortex (SMC) adhering as closely as possible to the methodology described in the previous report describing this finding (8). For this analysis, anatomical ROIs were identified in each participant's reconstructed brain surface-based on automated parcellations consisting of 1) the sensorimotor cortex (SMC), comprising the central sulcus, precentral gyrus, postcentral sulcus and precentral gyrus, which are involved with somatosensory processing, and 2) the precentral sulcus (PCS), which served as a control region not involved in somatosensory processing. Two additional ROIs consisting of distinct subregions within the SMC were identified as areas of increased thickness in the previous report, one in MWA participants and a separate region in MwoA participants (8). These were studied by manually mapping comparable ROIs on a participant's inflated surface and applying these to participants in the corresponding MWA or MwoA groups and comparing with controls.

Second, we used a participant-specific ROIs defined as the SSC alone parcellated by FreeSurfer (12). Subregions of the anterior cingulate cortex (ACC), including the anterior cingulate gyrus and sulcus and mid-anterior cingulate gyrus and sulcus, were examined using this same approach, as was the visual area MT+ (13). Cortical area V3A was defined using the PALS-B12 cortical surface atlas (14).

Mean cortical thickness values for all ROIs were measured in each participant using FreeSurfer; values were averaged across the two hemispheres within each participant. Population differences in thickness between the three groups (MWA, MwoA, controls) for the ROIs were compared using a two-tailed Student t-test.

Whole-brain surface-based morphometric analysis

In addition to the directed, region specific analyses described above, whole-brain analysis was also performed to detect any change in thickness between the three groups across the entire cortical mantle. For this analysis, individual whole brain cortical thickness maps were registered to a common FreeSurfer template surface (fsaverage) using FreeSurfer spherical registration system and smoothed with a 10mm 2D Gaussian smoothing kernel (15). Smoothing was restricted to the cortical surface. Using an in-house VoxBo toolkit (http://www.voxbo.org), whole brain random-effect models using t-test determined whether the three groups differed in mean cortical thickness at each vertex. Additional covariates

modeled the effects of age and gender. The analysis yielded surface t-maps comparing MWA with control, MwoA with control, and the independent effect of participant age. The last of these maps served as a positive control, as the association between cortical thinning and advancing age is well established (11).

Permutation analyses correcting for multiple comparisons were used to determine map-wise false discovery rate (FDR) thresholds (q=0.05) separately for each statistical map (16).

Power analysis

A retrospective power analysis was performed to assess the degree of difference in cortical thickness (in mm) that could be detected with 80% power at $p<0.05$ for n=28 (the number of participants in each group) using the measurements available from specific ROIs. For this analysis, the mean thickness values and their respective standard deviations were used for each population within the ROIs for which significant differences had been previously reported by others using SBM (SSC, SMC, V3A, and MT+).

Results

A total of 84 participants were included: 28 MWA (4 males/24 females), 28 MwoA (4 males/24 females), and 28 controls (4 males/24 females). Mean age was not significantly different between controls (age 33±6 years) and those with MWA (age 35±6 years, p=0.22 vs controls) and MwoA (age 35±7 years, p=0.25 vs controls). The mean age of onset of migraines was 15.9±7 years for the MWA group and 20.0±8 years for the MwoA group. The median headache frequency reported in an average month was 3 (intraquartile range 1–4) per month for the MWA group and 2 (intraquartile range 1–5) per month for the MwoA group. Mean headache frequency reported in an average month was 4.1±5.6 per month for the MWA group and 3.4±3.8 per month for the MwoA group. The median headache frequency in the month immediately preceding scanning was 2.5 (intraquartile range 1–5) per month for the MWA group and 1 (intraquartile range 1–4.5) per month for the MwoA group.

Comparison of cortical thickness across groups in specific regions of interest

Initial analysis examined cortical thickness in the SMC and PCS using methods and ROI definitions replicating those reported by DaSilva et al (8). We found no significant differences in mean thickness of the SMC or PCS between the MWA, MwoA, and control groups (Table 1). We then analysed two subregions of the SMC that had been identified by DaSilva et al. (8) as differing between patients with MWA and controls (subregion 1) and between patients with MwoA and controls (subregion 2). No difference was seen in cortical thickness across groups in this analysis. In addition, we analysed the visual motion processing areas (V3A and MT+), which had previously been reported by Granziera et al. (9) to differ between participants with migraine and controls. No difference was seen in cortical thickness across groups in this analysis (Table 1).

To further analyse potential differences across groups in specific brain regions, we measured the thickness of the SSC and ACC as defined using FreeSurfer-based participant-specific anatomic parcellation of these regions. In this analysis, no significant differences were observed in mean cortical thickness of the SSC or ACC (including subregions of the ACC) between the three groups (Table 2).

A retrospective power analysis was performed to quantify the ability to detect differences in cortical thickness in our population. This indicated that a difference in cortical thickness in specific ROIs in the range of 0.07–0.14mm could be detected with 80% power.

Whole brain analysis comparing cortical thickness across groups

A comparison between groups of the regional thickness of the entire cortical mantle was conducted using whole brain analysis. At map-wise FDR thresholds of q=0.05, no differences in thickness were found over the entire cortical surface between either of the migraine groups or control participants. As FDR is an adaptive threshold that reflects the degree of signal contained within the dataset, calculated thresholds will vary depending on the data and may be undefined in the absence of any signal. Indeed, for several of the comparisons of migraine groups with control no FDR threshold could be identified (finite calculated thresholds were: MWA – controls, left hemisphere=3.4; MwoA – controls, right hemisphere=3.11). Additional analysis using a 15 and 20mm full width half maximum smoothing kernel did not change any of the above results.

Whole brain analysis of the relationship between age and cortical thickness in all participants

To confirm the sensitivity of the whole brain analysis to changes in cortical thickness, the effect of age on cortical thickness was tested. The mean age for the overall population of 84 participants was 34±7 years. The threshold for age determined by FDR (q=0.05) was 2.66 for the right hemisphere and 2.63 for the left hemisphere. Using these map-wise thresholds, older age was significantly associated with decreasing cortical thickness at multiple cortical locations.

Additional exploratory analysis

The correlation between cortical thickness and migraine frequency and duration was analysed and no significant associations were found. Analysis using a 15 and 20 smoothing kernel did not significantly change any of the above results. A comparison of control participants with a combined cohort including both MWA and MwoA did not demonstrate any statistically significant differences in cortical thickness in any ROI, although in this analysis there was now a possible trend towards reduced cortical thickness in the SSC and SMC in migraine compared with control participants (Table 3).

Discussion

A number of previous studies have suggested structural differences in gray matter in migraine patients compared with healthy controls. However, the identified differences have been quite variable across studies. Using SBM, thickening of a subregion of the SSC in migraine patients compared with controls was reported in a recent small study of 24 patients with migraine and 12 controls (8). Viewed in light of other morphological studies of brain plasticity associated with learning, particularly those that have shown an association between experimentally induced repeated painful stimulation and increase in the gray matter of the SSC, this finding of a difference in the SSC in migraine patients is intuitively appealing (2, 17). Increased gray matter thickness in visual motion processing areas of the visual cortex (V3A and MT+) has also been reported using SBM in one study (9). This, too, is intuitively appealing given previous reports of visual motion processing alterations interictally in patients with migraine (18,19).

However, it should be noted that other studies assessing gray matter alterations in migraine, which have used VBM not SBM, have not reported similar changes. Although not all VBM studies in migraine have reported gray matter changes, those that have found changes have almost exclusively identified reductions in gray matter (20–25). Affected regions that have been identified in individual reports have included the ACC, insular cortex, superior temporal gyrus, inferior frontal gyrus, precentral gyrus, prefrontal cortex, posterior parietal cortex, and orbitofrontal cortex (21–25). As this list emphasizes, consistently reproducible

findings across studies have not generally been reported, with the possible exception of reduction in gray matter in the ACC, which has been identified in five of six VBM studies analysed in a recent summary review (1). VBM estimations of cingulate cortex gray matter may be particularly prone to artifacts from the differences in ventricular size between populations, thereby mistaking global differences in brain size with focal changes in cingulate morphology. In addition, these VBM studies have been relatively small and thus with limited power for whole-brain studies, with the largest enrolling 35 patients with migraine and 31 healthy controls (23).

In contrast to previous studies, we found no significant difference in cortical thickness in patients with migraine (with or without aura) compared with age and sex-matched headache-free controls. Strengths of our study include a relatively large sample size compared with earlier studies and optimal matching by age and sex. Further, SBM has been shown to be a reliable and highly sensitive method of assessing gray matter thickness, and has been validated with both histological and manual measurements (26,27). As an example of the sensitivity of SBM, our study had sufficient power to identify a change in gray matter thickness of 0.07 to 0.14 mm, which represents a change of 3.4–6.7% in the thickness of SSC. This is well below the size of changes in cortical thickness that have been reported in other conditions. For example, a 0.30mm difference in occipital cortex gray matter thickness was reported comparing early blind participants with sighted controls, and a 0.20mm difference in temporal- prefrontal gray matter comparing patients with schizophrenia with controls (28,29). In the study by Granziera et al. of the visual cortex, the difference in gray matter thickness between migraine and control participants was about 0.23mm for MT+ and 0.17mm for V3A cortical regions (9).

SBM measurements of cortical thickness seem to be very stable in test-retest comparisons, but results can be affected by variations in MR field strength, pulse sequences, and the parameters used in data processing (30). As a positive control in our study, we examined the relationship between participant age and cortical thickness across the entire study population. It is well established that cortical thickness is inversely correlated with age, and even relatively small overall changes in age distribution across populations can result in clear, measurable changes in cortical thickness (11). We were able to clearly detect cortical thinning associated with increasing age in our population even though the age range of our population spanned only 25 years, with most patients clustered within an approximately 15 year age range, demonstrating the robust sensitivity of the SBM method as used in our study.

A number of factors might account for the discordant findings between our studies and those done previously. One possible explanation is that differences in migraine frequency and duration, which have been correlated with extent of gray matter changes in VBM studies, might have varied between study populations (24,25). Compared to the population studied by Valfre et al. using VBM, our participants had substantially lower headache frequency (25). However, comparing our population with those studied using SBM by DaSilva et al. and Granziera et al. (8, 9), headache frequency and lifetime duration of migraine were very similar in our MWA cohort, and only slightly lower headache frequency and lifetime duration were present in our MwoA group. Furthermore, our analysis showed no correlation between cortical thickness measures and headache frequency or duration. In the American Migraine Study II, a large-scale epidemiological study of almost 30,000 people, 38% of those who reported migraine had a headache frequency of <1 per month, and 37% of 1–3 per month (31). The headache frequency of our population would therefore be representative of above average migraine frequency overall compared with the general migraine population. It is also possible that headache severity differed in our population compared with the populations studied in previous reports, and that this could have affected our results. We did

not record average headache severity owing to concerns about the reliability of retrospective recall of this measure, and so we are unable to comment directly on what the role of this might have been.

Another, perhaps more intriguing possibility, is that short-term headache burden in the month preceding imaging might affect measured cortical thickness. A previous study of experimentally delivered repetitive painful stimulation in healthy participants demonstrated that an increase in gray matter in the SSC from baseline could be seen using VBM at day 8 and day 22 after initiating the stimulation, and that these changes receded at 1 year follow-up (2). These findings suggest that brain structure, particularly in terms of cortical thickness, may be much more dynamic than commonly believed. Unfortunately, data on short-term headache burden immediately preceding imaging have not been systematically reported in previous studies.

Particular to the comparison of our study results and the previous results reported using VBM are the important differences between these two measurement methods. VBM provides an assessment of gray matter that is affected not only by cortical thickness, but also by cortical surface area and cortical folding, whereas SBM assesses only cortical thickness (32). For example, in a direct comparison of VBM and SBM in a study comparing patients with schizophrenia with controls, a number of regions of altered gray matter were found with VBM but not SBM, which the authors interpreted as suggesting that changes in local surface area of the gray matter but not alterations in cortical thickness may indicate neurodevelopmental structural differences in cortex (33). Therefore, the fact that our analysis with SBM failed to confirm the changes seen with VBM in migraine patients could still be consistent with gray matter changes other than alterations in cortical thickness in migraine patients.

Finally, it is possible that no focal alterations of gray matter occur in migraine patients, at least at the population level, and that previously reported findings were due to chance. Future studies directed at applying both SBM and VBM concurrently within populations might provide greater confidence in the reliability and robustness of identified gray matter abnormalities in the case of concordant results, or in the case of discordant results might provide further insight into the specific strengths and limitations of each morphometric technique. Additional investigations further comparing MWA and MwoA in terms of brain morphology and response to pain stimuli would also be informative.

Acknowledgments

Funding

This work was supported by grants from the National Institute of Neurological Disorders and Stroke (NS061572 to BC; NS058386, NS045839, RR002305 to JD).

References

1. May A. Morphing voxels: The hype around structural imaging of headache patients. Brain. 2009; 132:1419–1425. [PubMed: 19443629]
2. Teutsch S, Herken W, Bingel U, Schoell E, May A. Changes in brain gray matter due to repetitive painful stimulation. Neuroimage. 2008; 42:845–849. [PubMed: 18582579]
3. Ashburner J, Friston KJ. Voxel-based morphometry–the methods. Neuroimage. 2000; 11:805–821. [PubMed: 10860804]
4. Bookstein FL. “Voxel-based morphometry” should not be used with imperfectly registered images. Neuroimage. 2001; 14:1454–1462. [PubMed: 11707101]

5. Thacker NA, Williamson DC, Pokric M. Voxel based analysis of tissue volume from MRI data. Br J Radiol. 2004; 77:S114–S125. [PubMed: 15677353]
6. Fischl B, Dale AM. Measuring the thickness of the human cerebral cortex from magnetic resonance images. Proc Natl Acad Sci U S A. 2000; 97:11050–11055. [PubMed: 10984517]
7. Hinds OP, Rajendran N, Polimeni JR, Augustinack JC, Wiggins G, Wald LL, et al. Accurate prediction of v1 location from cortical folds in a surface coordinate system. Neuroimage. 2008; 39:1585–1599. [PubMed: 18055222]
8. DaSilva AF, Granziera C, Snyder J, Hadjikhani N. Thickening in the somatosensory cortex of patients with migraine. Neurology. 2007; 69:1990–1995. [PubMed: 18025393]
9. Granziera C, DaSilva AF, Snyder J, Tuch DS, Hadjikhani N. Anatomical alterations of the visual motion processing network in migraine with and without aura. PLoS Med. 2006; 3:e402. [PubMed: 17048979]
10. Dale AM, Fischl B, Sereno MI. Cortical surface-based analysis. I. Segmentation and surface reconstruction. Neuroimage. 1999; 9:179–194. [PubMed: 9931268]
11. Salat DH, Buckner RL, Snyder AZ, Greve DN, Desikan RS, Busa E, et al. Thinning of the cerebral cortex in aging. Cereb Cortex. 2004; 14:721–730. [PubMed: 15054051]
12. Destrieux C, Fischl B, Dale A, Halgren E. Automatic parcellation of human cortical gyri and sulci using standard anatomical nomenclature. Neuroimage. 2010; 53:1–15. [PubMed: 20547229]
13. Fischl B, Rajendran N, Busa E, Augustinack J, Hinds O, Yeo BT, et al. Cortical folding patterns and predicting cytoarchitecture. Cereb Cortex. 2008; 18:1973–1980. [PubMed: 18079129]
14. Van Essen DC. A population-average, landmark- and surface-based (pals) atlas of human cerebral cortex. Neuroimage. 2005; 28:635–662. [PubMed: 16172003]
15. Fischl B, Sereno MI, Tootell RB, Dale AM. High-resolution intersubject averaging and a coordinate system for the cortical surface. Hum Brain Mapp. 1999; 8:272–284. [PubMed: 10619420]
16. Nichols T, Hayasaka S. Controlling the familywise error rate in functional neuroimaging: A comparative review. Stat Methods Med Res. 2003; 12:419–446. [PubMed: 14599004]
17. May A, Hajak G, Ganssbauer S, Steffens T, Langguth B, Kleinjung T, et al. Structural brain alterations following 5 days of intervention: Dynamic aspects of neuroplasticity. Cereb Cortex. 2007; 17:205–210. [PubMed: 16481564]
18. McKendrick AM, Badcock DR. Motion processing deficits in migraine. Cephalalgia. 2004; 24:363–372. [PubMed: 15096225]
19. Ditchfield JA, McKendrick AM, Badcock DR. Processing of global form and motion in migraineurs. Vision Res. 2006; 46:141–148. [PubMed: 16257032]
20. Matharu MS, Good CD, May A, Bahra A, Goadsby PJ. No change in the structure of the brain in migraine: A voxel-based morphometric study. Eur J Neurol. 2003; 10:53–57. [PubMed: 12534993]
21. Kim JH, Suh SI, Seol HY, Oh K, Seo WK, Yu SW, Park KW, Koh SB. Regional grey matter changes in patients with migraine: A voxel-based morphometry study. Cephalalgia. 2008; 28:598–604. [PubMed: 18422725]
22. Rocca MA, Ceccarelli A, Falini A, Colombo B, Tortorella P, Bernasconi L, et al. Brain gray matter changes in migraine patients with t2-visible lesions: A 3-t MRI study. Stroke. 2006; 37:1765–1770. [PubMed: 16728687]
23. Schmidt-Wilcke T, Ganssbauer S, Neuner T, Bogdahn U, May A. Subtle grey matter changes between migraine patients and healthy controls. Cephalalgia. 2008; 28:1–4. [PubMed: 17986275]
24. Schmitz N, Admiraal-Behloul F, Arkink EB, Kruit MC, Schoonman GG, Ferrari MD, et al. Attack frequency and disease duration as indicators for brain damage in migraine. Headache. 2008; 48:1044–1055. [PubMed: 18479421]
25. Valfre W, Rainero I, Bergui M, Pinessi L. Voxel-based morphometry reveals gray matter abnormalities in migraine. Headache. 2008; 48:109–117. [PubMed: 18184293]
26. Kuperberg GR, Broome MR, McGuire PK, David AS, Eddy M, Ozawa F, et al. Regionally localized thinning of the cerebral cortex in schizophrenia. Arch Gen Psychiatry. 2003; 60:878–888. [PubMed: 12963669]

27. Rosas HD, Liu AK, Hersch S, Glessner M, Ferrante RJ, Salat DH, et al. Regional and progressive thinning of the cortical ribbon in Huntington's disease. Neurology. 2002; 58:695–701. [PubMed: 11889230]

28. Jiang J, Zhu W, Shi F, Liu Y, Li J, Qin W, et al. Thick visual cortex in the early blind. J Neurosci. 2009; 29:2205–2211. [PubMed: 19228973]

29. Kuperberg GR, Broome MR, McGuire PK, David AS, Eddy M, Ozawa F, et al. Regionally localized thinning of the cerebral cortex in schizophrenia. Arch Gen Psychiatry. 2003; 60:878–888. [PubMed: 12963669]

30. Han X, Jovicich J, Salat D, van der Kouwe A, Quinn B, Czanner S, et al. Reliability of MRI-derived measurements of human cerebral cortical thickness: The effects of field strength, scanner upgrade and manufacturer. Neuroimage. 2006; 32:180–194. [PubMed: 16651008]

31. Lipton RB, Stewart WF, Diamond S, Diamond ML, Reed M. Prevalence and burden of migraine in the united states: Data from the American migraine study II. Headache. 2001; 41:646–657. [PubMed: 11554952]

32. Hutton C, De Vita E, Ashburner J, Deichmann R, Turner R. Voxel-based cortical thickness measurements in MRI. Neuroimage. 2008; 40:1701–1710. [PubMed: 18325790]

33. Voets NL, Hough MG, Douaud G, Matthews PM, James A, Winmill L, et al. Evidence for abnormalities of cortical development in adolescent-onset schizophrenia. Neuroimage. 2008; 43:665–675. [PubMed: 18793730]

Table 1

Cortical thickness in previously reported regions of interest across groups

ROI and group	Thickness (mm) ± SD	*p* value vs control
SMC – MWA	2.27 ± 0.11	0.13
SMC – MwoA	2.27 ± 0.10	0.11
SMC – controls	2.32 ± 0.12	
PCS – MWA	2.52 ± 0.12	0.33
PCS – MwoA	2.50 ± 0.11	0.11
PCS – controls	2.56 ± 0.14	
Manually mapped SMC subregion 1 – MWA	2.36 ± 0.21	0.14
Manually mapped SMC subregion 1 – controls	2.44 ± 0.18	
Manually mapped SMC subregion 2 – MwoA	2.12 ± 0.12	0.23
Manually mapped SMC subregion 2 – controls	2.16 ± 0.13	
V3A – MWA	2.16 ± 0.17	0.54
V3A – MwoA	2.12 ± 0.18	0.75
V3A – controls	2.13 ± 0.18	
MT+ – MWA	2.47 ± 0.15	0.46
MT+ – MwoA	2.43 ± 0.14	0.81
MT+ – controls	2.44 ± 0.13	

Mean cortical thickness combining right and left hemispheres for each ROI across groups (n=28 per group). Manually mapped SMC subregions refer to corresponding regions described in DaSilva et al. (8). SMC: sensorimotor cortex, PCS: precentral sulcus, MWA: migraine with aura, MwoA: migraine without aura, V3A: visual cortex area V3A, MT+: visual cortex area MT+.

Table 2

Somatosensory and anterior cingulate cortical thickness across groups

ROI and group	Thickness (mm) ± SD	*p* value vs control
SSC – MWA	2.05 ± 0.10	0.20
SSC – MwoA	2.05 ± 0.09	0.13
SSC – controls	2.09 ± 0.11	
ACC – MWA	2.86 ± 0.17	0.78
ACC – MwoA	2.83 ± 0.15	0.67
ACC – controls	2.85 ± 0.15	
mACC – MWA	2.86 ± 0.14	0.33
mACC – MwoA	2.87 ± 0.14	0.98
mACC – controls	2.90 ± 0.19	

Mean cortical thickness combining right and left hemispheres for each ROI across groups (n=28 per group). SSC: somatosensory cortex, ACC: anterior cingulate cortex, mACC: mid-anterior cingulate cortex, MWA: migraine with aura, MwoA: migraine without aura.

Table 3

Cortical thickness in regions of interest comparing control participants to all migraine participants (migraine with and without aura combined)

ROI and group	Thickness (mm) ± SD	*p* value vs control
SMC – migraine	2.27 ± 0.10	0.06
SMC – controls	2.32 ± 0.12	
PCS – migraine	2.51 ± 0.11	0.12
PCS – controls	2.56 ± 0.14	
V3A – migraine	2.14 ± 0.17	0.86
V3A – controls	2.13 ± 0.18	
MT+ – migraine	2.45 ± 0.15	0.77
MT+ – controls	2.44 ± 0.13	
SSC – migraine	2.05 ± 0.10	0.09
SSC – controls	2.09 ± 0.11	
ACC – migraine	2.84 ± 0.16	0.95
ACC – controls	2.85 ± 0.15	
mACC – migraine	2.86 ± 0.14	0.28
mACC – controls	2.90 ± 0.19	

Mean cortical thickness combining right and left hemispheres for each ROI across groups (n=28 controls, 56 migraine participants). SMC: sensorimotor cortex, PCS: precentral sulcus, V3A: visual cortex area V3A, MT+: visual cortex area MT+, SSC: somatosensory cortex, ACC: anterior cingulate cortex, mACC: mid-anterior cingulate cortex.