Regionally specific cortical thinning in paediatric sickle cell disease

R. A. Jones[1,2], G. Kirk[3], M. R. Haynes[4], S. Palasis[5], and C. Brown[6]

[1]Radiology, Children's Healthcare of Atlanta, Atlanta, GA, United States, [2]Radiology, Emory University, Atlanta, GA, United States, [3]Radiology, Children's Healthcare of Atlanta, Atlanta, United States, [4]Biomedical Engineering, Georgia Institute of Technology, Atlanta, United States, [5]Radiology, Children's healthcare of Atlanta, Atlanta, United States, [6]Haematology, Children's Helathcare of Atlanta, Atlanta, United States

Introduction. It has become clear that some sickle cell (SC) patients show cognitive deficits and are at risk of intellectual decline, with patients with overt or covert infarcts being at greater risk. While the lesions are often unilateral, small, and focal, the cognitive deficits are widespread, involving different functional domains, including verbal and non-verbal intelligence, and cognitive deficits have also been found in children without obvious lesions. We hypothesize that there may be additional, relatively extensive damage that is not seen on conventional imaging. Cortical thickness measures have been applied to study a variety of neurological disorders and have been able to detect differences between groups which were not apparent on radiological evaluations of the individual patients. We hypothesized that significant differences in cortical thickness may exist between SC patients and a control population and that the spatial distribution of differences may be indicative of the etiology of specific deficits.

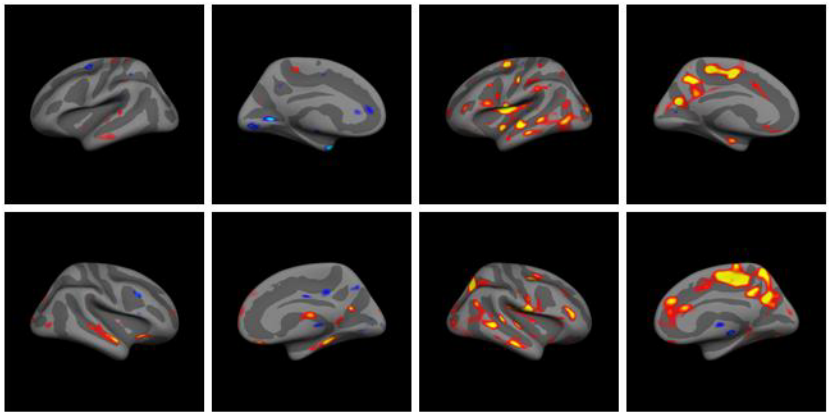
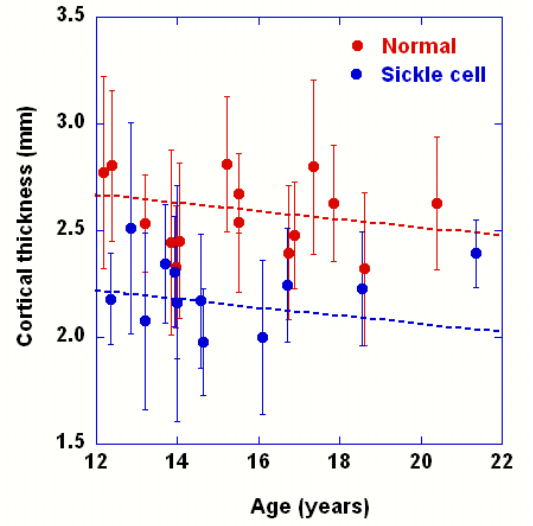


Fig. 1:Parametric maps were calculated on the null hypothesis of no significant difference between the thickness intercept (i.e. age=0); a lower threshold of P<0.05 and a saturation point of P<0.001 were applied. Significant cortical thinning in red (and thickening in blue) in SC patients superimposed on a group averaged, inflated, cortical surface. Columns 1 and 2 show the younger children (5-12 years) while columns 3 and 4 show older children (12-21 years). The upper row shows the left hemisphere, the lower row the right hemisphere with the medial and lateral surface being shown for each hemisphere.

Methods. We performed cortical surface based morphometry using Freesurfer (http://surfer.nmr.mgh.harvard.edu) to study brain development and performed a retrospective study of 29 paediatic SC patients who did not exhibit any ischaemia, atrophy or other abnormalities on MRI scans, and 29 age matched volunteers. Volumetric MR data from 1.5T scanners with 1mm isotropic spatial resolution was used as a starting point for the calculation of cortical thickness. The standard Freesurfer methodology, which provides accurate matching of morphologically homologous cortical locations amongst subjects while minimising metric distortion, was applied to the volumetric data to derive parametric maps of cortical thickness. The results from the SC and control groups were then compared using a general linear model. The groups were split into two components by age. The first group consisted of all SC patients and normal controls < 12 years of age, and the second group all subjects >=12 years of age. Separate group analyses were performed on each of the two groups. There were several reasons for splitting the study cohort into two groups and performing separate analyses. First, we planned to determine if thinning progresses with age. Second, there is limited knowledge of growth trends in the development of the pediatric cerebral cortex and this may pose a problem considering the wide range of ages included in the study. We decided that comparing thickness over a smaller age range would lead to more accurate results, even though the effect of age is regressed out in the linear model. Finally, in a smaller age range the variance in folding patterns should be reduced allowing a more representative average pial and grey/white surface to be computed, affording a more accurate allignment of the folding patterns of the subjects.



Results and conclusion. In the younger group only limited differences were apparent, while in the older children extensive areas with bilateral areas of thinning are apparent (see figure 1). Figure 2 shows a plot of the mean cortical thickness in the area of cortical thinning with the largest spatial extent in the right hemisphere. A very clear difference in thickness between the control and sickle cell groups can be seen, suggesting that the gray matter is abnormal in children with sickle cell disease and that this difference is age related.