INTRODUCTION

Structural brain alterations in grey matter volume (GMV) and cortical thickness (CT) have been previously documented in adult Crohn's Disease (CD) patients in remission\(^1\), however data is inconsistent and not available in the active disease state. The aim of this present study was to investigate anatomical brain changes in patients with active CD, and their correlation with disease activity biomarkers such as faecal calprotectin (FCP), CRP (C-reactive protein), IL-1β, IL-6 and TNFα.

METHODS

- 25 active CD patients and 25 age-, BMI- and gender-matched healthy controls (HC), underwent anatomical MRI brain scans.
- Patient inclusion criteria was active CD (Harvey Bradshaw index >5 and CRP >5mg/dl, or faecal calprotectin >250µg/g, or as assessed through ileocolonoscopy/magnetic resonance enterography (MRE).
- IL-6, IL-1β, and TNFα were measured from serum samples using solid phase sandwich ELISA and FCP was acquired at inclusion.
- Anatomical T1-weighted brain images were acquired on a 3T MR scanner (1 mm isotropic resolution).
- CT was assessed using computational anatomy toolbox (CAT) in Statistical Parametric Mapping (SPM12) to identify differences in CT between HC's and patients. Disease biomarkers were correlated with CT. Brain regions with significant differences were corrected for multiple comparisons.
- Whole brain volumetry and voxel-based morphometry (VBM) were assessed using SPM12 to identify regional differences in grey matter (GM) density between HC's and CD patients.
- A two sample t-test was carried out between HC and CD GM maps, with subjects' age and total intracranial volume (TIV) as covariates of no interest. In CD patients, disease biomarkers were correlated with the GM volume, using age and TIV as covariates of no interest.

RESULTS

Fig 2: (A) Cortical thinning in CD compared with HC (P<0.001, uncorrected) (B)ROI analysis showing bilateral thinning in the rostral middle frontal and paracentral gyrus (P<0.001 uncorrected), (C) Decrease in GMV of pre/post-central grey matter volume and anterior insula in CD patients compared with HC. (P<0.005, uncorrected)

Fig 3: (A) IL-6 negatively correlated with CT (B) ROI analysis of CT (C) IL-6 negatively correlated with GMV

CONCLUSIONS

- This is the first study to assess alterations in brain's structure in active CD patients. We found a significant reduction in CT in the rostral middle-frontal cortex in CD. This region is functionally important for executive function, including attention and working memory and was found to be negatively correlated with IL-6.
- The reduction in CT and GMV could be due to high levels of neurotoxic proinflammatory cytokines\(^1\). In addition, the negative correlation of IL-6 with GMV in CD patients in the insula region could be indicative of impaired pain processing in these patients, the insula being an integral part of the pain matrix.
- The effect of systemic inflammation on the brain may also explain symptoms of disease induced fatigue\(^2\) and symptoms like irritable bowel syndrome (IBS)\(^3\) in CD patients.
- Cortical thinning in the right superior frontal region\(^2\) and loss of GMV in the pre- and post-central gyrus\(^2\) was in agreement with previous findings in CD patients in remission.
- In conclusion, a significant reduction in CT and GMV in cortical areas was found in patients with active CD compared with HCs in this present study. This observation may be associated with a chronic inflammatory response.
- Investigating structural brain changes in active CD will aid our understanding of the cross-linking between chronic inflammation, brain morphology and changes in behaviour, cognitive function and unexplained symptoms such as fatigue in CD. This will inform new medical and psychological therapies.

REFERENCES