Effects of metabolic risk factors in Type 2 Diabetes and Hypertension on cortical thickness in the brain

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Introduction

Type 2 Diabetes Mellitus (T2DM) is a multi-organ disease that includes the brain and is associated with an increase in global and regional brain tissue atrophy. With the increased prevalence of T2DM worldwide, there is an impetus to improve our understanding on how T2DM impacts the brain. To date the majority of this research has involved anatomical brain imaging, often involving a comparison of T2DM vs. healthy controls. In this study we examined the effects of physiological factors, i.e. glucose and insulin levels in subjects with and without diabetes, on global and regional cortical thickness. Given the sensitivity of cortical thickness measures that has been observed in other neurological populations we hypothesize that these measures can be used to quantify the impact of T2DM on brain regions. An additional voxel-based morphometry (VBM) analysis is also performed. To improve the specificity in this analysis, hypertensive T2DM (T2DM+HT) individuals are compared with age-matched non-T2DM hypertensives (HT).

Methods: Twenty-two participants were scanned using a Siemens Trio 3T MRI system (7 with T2DM+HT, 9 HT, 4 healthy older controls (HC) and 2 older adults with mild cognitive impairment (MCI), mean age: 72.1±6.1 years). High resolution T1-weighted magnetic resonance imaging parameters included: 3D magnetization prepared rapid acquisition gradient echo (MPRAGE), FOV= 256x192mm, TR/TE/TI=2000/2.63/1100ms, flip angle=9˚, in-plane resolution =1 x1x 1mm, acquisition matrix 64x64.

Thirteen participants (7 HT, 4 HC and 2 MCI) were scanned on two separate days to assess the reproducibility of the global cortical measurement in our population. The average time between two scans was 13±6.9 days. For the 7 T2DM+HT and 9 HT adults blood was drawn several days prior to the scan to measure the levels of hemoglobin A1C [% of hemoglobin A bound to glucose] and plasma insulin [pmol/l]. A third physiological variable, fasting glucose [mmol/l], was also obtained using a glucometer on the morning of the MRI. All 16 subjects had a history of high blood pressure and 7 of those were diagnosed with T2DM at least 2 years prior to the study and managed their diabetes with diet and/or oral medications.

Cortical thickness was measured using FreeSurfer software[1]. Global thickness was taken as the median value of all regions weighted by the surface area of each hemisphere. Regional analysis was corrected for multiple comparisons using a Monte Carlo simulation method with $p<0.05$ threshold. VBM analysis was performed using the tools available in FSL [2]. Correction for multiple comparisons in VBM analysis was done using threshold-free cluster enhancement (TFCE) approach with 4mm Gaussian smoothing[3]. For reproducibility assessment in N=13, the cortical thickness maps from two sessions were co-registered and differenced. The difference images were registered to an average template and smoothed with a 10mm FWHM kernel before calculating the mean of the absolute difference images.

Results and Discussion

Reproducibility analysis produced a median inter-session difference of 2% (range: 0.08 - 6.2%), (Figure 1a), which is in line with other studies [4]. Regional assessment indicated a higher inter-session variability in superior parietal region and temporal pole regions (Figure 1b).

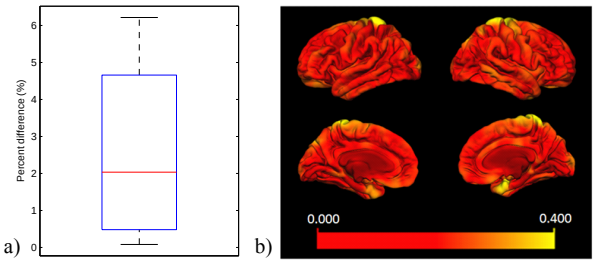

Figure 1. a) Global cortical thickness reproducibility (%) b) Regional cortical thickness reproducibility (mm)

Global median cortical thickness was significantly correlated with fasting glucose and hemoglobin A1C (Figure 2a and 2b), but not insulin levels (R^2=0.04, p=0.46). Regional analysis of cortical thickness identified several significant regions that were correlated with fasting glucose level: bilateral superiortemporal, left- precuneus and pars opecularis and right - supramarginal and superior frontal regions (Figure 3). No significant regions were identified when considering hemoglobin A1C or insulin (data not shown).

Cortical thickness and VBM group comparison analyses between T2DM+HT and HT were performed, but were not significant. For the correlation assessment using VBM, only a small region in left anterior cingulate reached significance, $p<0.05$, in correlation with fasting glucose measures (results not shown).

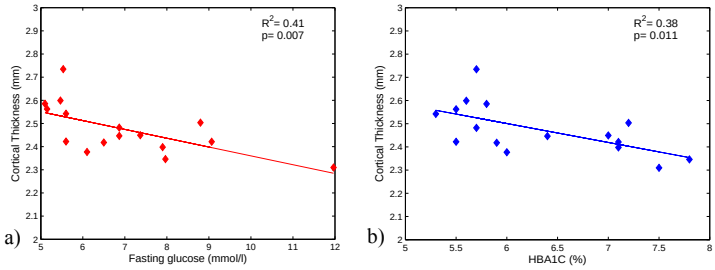

Figure 2. a) Global cortical thickness correlation with fasting glucose b) Global cortical thickness correlation with hemoglobin A1C

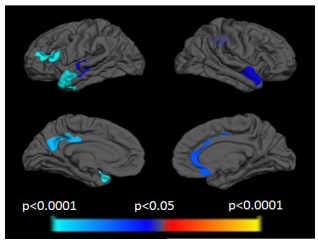

Figure 3. Regional cortical thickness correlation with fasting glucose

Conclusion

We have found that both global and regional cortical thickness measures were significantly correlated with fasting blood glucose levels in our cohort of hypertensive and T2DM older adults. VBM results were found to be less sensitive. These finding suggest that measures of vascular health and glucose tolerance impact the cortical thickness in a linear and continuous fashion. Our observed changes in the temporal lobe support previous suggestion of the link between diabetes and neurological conditions including dementia and Alzheimer's disease[5].

References

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