Elevated Brain Iron Concentrations in Subjects with Sickle Cell Anaemia Measured using MRI Susceptibility Mapping

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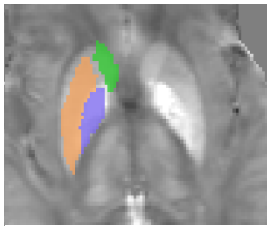
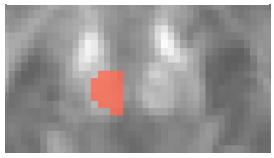
Introduction: In Sickle Cell Anaemia (SCA) the sickled red blood cells (RBC) break down more prematurely than healthy RBCs causing haemolytic anaemia. However, the effect of SCA upon iron concentrations in the brain has not been comprehensively studied. This information is clinically relevant as treatment of SCA includes chronic blood transfusions, which expose patients to high levels of iron deposits in tissue. In this study we use MRI Susceptibility Mapping (SM) to compare regional brain iron concentrations in a SCA population and healthy control subjects. SM can be used to examine regional iron concentration in the deep iron-rich regions of the brain, as tissue susceptibility values (χ) are directly proportional to iron content[1].

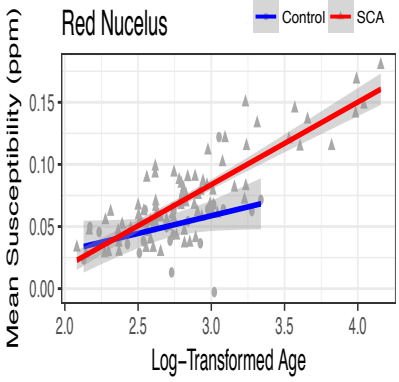
Methods: 86 SCA subjects (mean age:19.03y $\pm$ 10.84) and 25 healthy controls (16.19y $\pm$ 5.02) were recruited from the Sleep and Asthma Cohort, and Prevention of Morbidity in Sickle Cell Disease clinical trials. Susceptibility maps were calculated from multi-echo Gradient Recalled Echo (GRE) images acquired on a 3T Siemens Magnetom Prisma. Acquisition Parameters: Res: 1.15x1.15x 1.15mm^3 FOV: 180x220x166mm^3, TE1/ΔTE/TR: 3ms/4ms/38ms, 8 echoes. SM Pipeline: B0 field maps were obtained from a nonlinear fit of the complex GRE images[2]. Field maps were unwrapped using a Laplacian-based method[3]. Background field removal performed via Projection onto Dipole Fields[4]. Field to χ inversion achieved using Tikhonov regularization[5]. Regions of Interest (ROIs) examined: Red Nucleus (RN), Caudate Nucleus (CN), Putamen (PT) and Globus Pallidus (GP). ROIs were segmented based on co-registration with the Eve QSM atlas[6] using NiftyReg[7]. Age regression was carried out on log-transformed age values to remove any effect of iron accumulation. ANCOVA analysis was applied to examine differences in regional χ between SCA and control subjects.



Example Susceptibility Map showing segmented ROIs CN–Green. PT–Orange. GP-Purple. RN–Red.



Results and Discussion: Significant iron accumulation with age was observed in each of the ROIs examined. Significantly higher susceptibility values were found in the RN of SCA subjects compared to the healthy controls (difference:0.016$\pm$ 0.005ppm, p-value:0.001). There were no significant differences observed in any of the other ROI examined. The higher iron concentrations found in SCA subjects may be caused by tissue damage arising from by poor perfusion due to the sickled RBCs. Further acquisition of control data is ongoing, acquiring subjects across a broader range of ages. This will allow the rate of iron accumulation to be compared across the entire life span of the SCA subjects in relation to prior and current hypoxic and blood transfusion exposures.



SCA subjects (red) showed greater rate of iron accumulation compared to healthy control subjects (blue).

References: *1.Shmueli et al. Magn Reson Med. 2009. 2.Liu et al. Magn Reson Med. 2013. 3.Schweser et al. Magn Reson Med. 2013 4.Liu T et al. NMR Biomed. 2011. 5.Kressler et al. Trans on Med Im. 2010. 6.Lim et al. Neuroimage. 2013. 7.Modat et al. Comput Methods Programs Biomed. 2010.*