

White Matter Integrity in Tanzanian Children with Sickle Cell Anemia: A Diffusion Tensor Imaging Study

Mboka Jacob¹, Hanne Stotesbury², Jamie Kawadler², Dawn Saunders², Raphael Sangeda¹, Clara Chamba¹, Ramadhan Kazema¹, Julie Makani¹, Julie Kirkham², Chris Clark²

¹Muhimbili University of Health and Allied Sciences, Dar Es Salaam, Tanzania

²Institute of Child Health-University College London, London, United Kingdom

Background: Widespread reductions in white matter (WM) integrity are associated with cognitive dysfunction in sickle cell anemia (SCA). Silent cerebral infarction (SCI), vasculopathy (VSC), and low hemoglobin concentration (Hb) are implicated; we aimed to determine independent contributions to microstructural WM injury and whether WM integrity differs across arterial territories.

Methods: Sixty two children with SCA aged 6-19 years were prospectively studied at Muhimbili National Hospital, Tanzania. SCI+/- and VSC+/- were identified on MRI/MRA scans by two neuroradiologists. Tract-based spatial statistics (TBSS) tested for voxel-wise differences in DTI metrics (i.e. fractional anisotropy [FA], mean diffusivity [MD], radial diffusivity [RD], and axial diffusivity [AD]) between SCI+/- and VSC+/- groups, with correlations between DTI metrics and Hb. In TBSS analyses, potentially mediating factors (i.e., age, gender, as well as Hb, SCI, and/or vasculopathy) were covariates. Differences in mean DTI metrics across regions of interest in arterial territories were explored.

Results: Compared with SCI- patients (n=45), SCI+ patients (n=17) exhibited increased RD in multiple regions; negative relationships were observed between MD, AD, and Hb ($p < 0.005$). Compared with VSC- patients (n=49), mild (n=6) or moderate (n=7) VSC+ patients exhibited reduced FA in widespread regions ($p < 0.05$), including the anterior longitudinal fasciculi, corpus callosum, internal capsule, corona radiata, and corticospinal tracts. Overall, the posterior cerebral arterial territory (PCA) had higher mean MD and mean RD than the anterior (ACA) and middle cerebral arterial (MCA) territories. However, no patient had vasculopathy in this area. There was an interaction between territory and vasculopathy.

Conclusions: SCI, vasculopathy, and Hb are independent risk factors, and thus treatment targets, for diffuse WM injury in SCA patients. Exacerbation of hemodynamic stress may play a role.

