

Factor VIII deficiency is associated with abnormal brain volumes

Staber, Janice; Al-Huniti, Ahmad; Novak, Marci; Harshman, Lyndsay; Nopoulos, Peggy

Submission Group

Clinical Research/Clinical Trials

Abstract

Objective: Factor VIII (FVIII) deficiency (hemophilia A) leads to bleedings events requiring prophylactic FVIII replacement therapy. While significant progress has been made in prevention and treatment of hemophilia-related joint and muscle disease with prophylaxis, people with hemophilia (PWH) continue to demonstrate increased rates of anxiety, depression, and executive dysfunction more frequently than the general population. Unfortunately, there is paucity of data to understand, treat or prevent brain disease in PWH. Therefore, our study aims to evaluate brain structure and cognitive function in pediatric patients with severe FVIII deficiency in order to improve outcomes. **Methods:** Ten pediatric patients with severe FVIII deficiency were recruited from the Iowa Hemophilia and Thrombosis Center and compared to 23 healthy controls. Inclusion criteria included males aged 6 – 16 years for both groups and confirmed diagnosis of FVIII deficiency for PWH. All subjects with known diagnosis of traumatic brain injury, major chromosomal anomalies, or intellectual disability were excluded. PWH with known diagnosis of intracranial bleed or FVIII inhibitor were excluded. Behavior and cognitive data collected included Behavioral Regulation Index of Executive Function and Wechsler Intelligence Scale for Children. Magnetic resonance imaging sequences were completed and included T1, T2, and diffusion tensor imaging. Freesurfer and BrainTools programs were used to preprocess imaging and generate volumetric data. **Summary:** Mean age for PWH was 10.2 yrs and 11.8 yrs for controls ($p = 0.24$). Both groups had similar height, weight, socioeconomic status, and maternal education level. Controls had slightly higher levels of paternal education level compared to PWH; however this was not associated with difference in group IQ scores. Despite normal IQ, PWH demonstrated a worsened behavioral regulation score indicating executive dysfunction. Relative to controls, PWH group had overall lower whole brain volume. **Conclusions:** PWH demonstrated abnormal brain structure and function compared to healthy controls. Further evaluation is warranted to understand why and how FVIII deficiency and its treatment alter neurological outcomes.