

# Assessment of Brain Damage and Plasticity in the Visual System after Early Occipital Injury: Comparison of FDG-PET with Diffusion MRI Tractography

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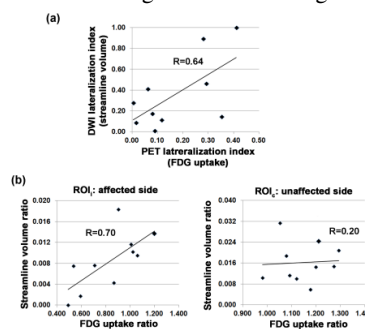
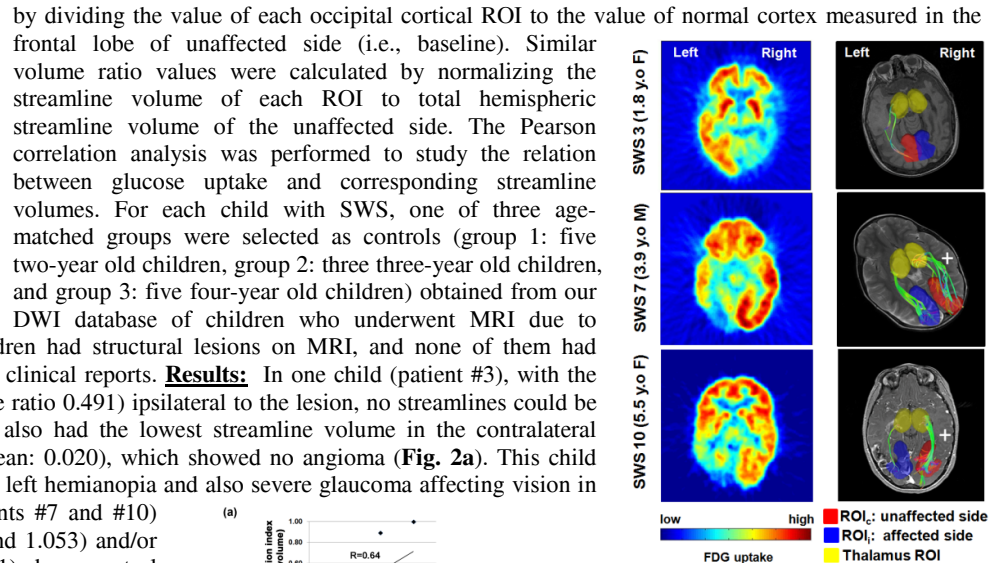
**Targeted audience:** Clinical trainees and researchers in pediatric neuroradiology. **Purpose:** Sturge-Weber syndrome (SWS) is a rare disorder associated with a variety of nervous system problems, including visual field impairment, motor deficit, cognitive decline and seizures<sup>1</sup>. In our previous PET study<sup>2</sup>, we have observed increased glucose metabolism in the unaffected occipital cortex contralateral to the severely damaged occipital lobe of SWS children. The present study combined DWI streamline tractography with FDG-PET to determine the relation between occipital cortical metabolic changes and abnormalities of the corresponding visual tracts in children with unilateral SWS. We hypothesized that decreased occipital glucose metabolism will be associated with decreased visual streamline volume on the affected side. We also hypothesized that high glucose metabolism in the contralateral occipital (visual) cortex may be associated with high DWI streamline volume of the corresponding visual pathway.

**Methods:** In 10 children with unilateral SWS (ages 1.5-5.5 years), an objective region-of-interest analysis (**Fig. 1**) was applied in the bilateral medial occipital cortex on glucose PET and used as seeding regions to track diffusion weighted imaging (DWI)-defined streamlines corresponding to the central visual pathway. Independent component analysis with ball and stick model ("ICA+BSM") tractography<sup>3</sup> was utilized to detect the central visual pathway in both hemispheres where each visual cortical ROI obtained (**Fig. 2**) was used as a seeding region, and ipsilateral thalamus was the terminating region. To investigate whether visual cortical glucose metabolism is related to streamline volume in the central visual pathway of children with SWS, we correlated glucose metabolism asymmetry with streamline volume asymmetry across the hemispheres. Lateralization index (LI) of the total streamline volume and glucose uptake was calculated from a set of two regions, ROI<sub>c</sub>: unaffected side and ROI<sub>i</sub>: affected side, as shown on **Fig. 1**, using the ratio of (ROI<sub>c</sub>-ROI<sub>i</sub>) and (ROI<sub>c</sub>+ROI<sub>i</sub>). Furthermore, in order to quantify the degree of hypo- or hypermetabolism in ROI<sub>c</sub> and ROI<sub>i</sub>, a normalized glucose uptake ratio value was calculated

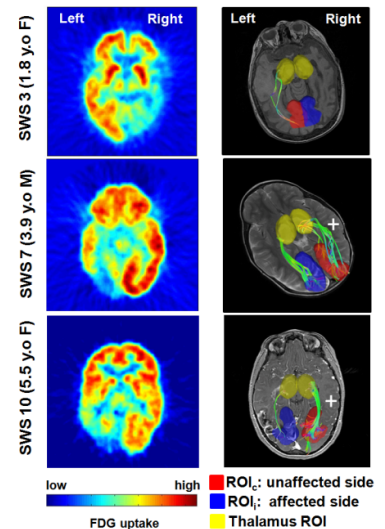
by dividing the value of each occipital cortical ROI to the value of normal cortex measured in the frontal lobe of unaffected side (i.e., baseline). Similar volume ratio values were calculated by normalizing the streamline volume of each ROI to total hemispheric streamline volume of the unaffected side. The Pearson correlation analysis was performed to study the relation between glucose uptake and corresponding streamline volumes. For each child with SWS, one of three age-matched groups were selected as controls (group 1: five two-year old children, group 2: three three-year old children, and group 3: five four-year old children) obtained from our DWI database of children who underwent MRI due to

history of seizures. None of the control children had structural lesions on MRI, and none of them had significant developmental delay based on their clinical reports. **Results:** In one child (patient #3), with the lowest occipital glucose uptake on PET (uptake ratio 0.491) ipsilateral to the lesion, no streamlines could be identified by DWI on the affected side. She also had the lowest streamline volume in the contralateral occipital lobe (volume ratio: 0.006; control mean: 0.020), which showed no angioma (**Fig. 2a**). This child showed the most severe visual symptoms, with left hemianopia and also severe glaucoma affecting vision in her right eye. In contrast, two children (patients #7 and #10) showed very prominent FDG uptake (1.293 and 1.053) and/or normalized streamline volume (0.021 and 0.031) above control mean value (0.014) in the contralateral occipital lobe (**Fig. 2b, c**). This increase was most striking (>2 standard deviations above control mean) in the contralateral visual fibers of patient #10, who had no visual field deficit at the time of the scans or at 1-year follow-up, at age 6.5 years. In cross-modal (DW-MRI/FDG-PET) analysis, a positive correlation was observed in the LI values of corresponding ROIs (**Fig. 3a**,  $R = 0.64$ ,  $p = 0.046$ ). Also, there was a positive significant correlation between the normalized ratios of ROI<sub>c</sub> and ROI<sub>i</sub> in PET and DWI. Lower metabolism was associated with lower DWI streamline volume on the affected side ( $R = 0.70$ ,  $p = 0.024$ ; **Fig. 3b**, left panel). Only a non-significant trend was observed in the unaffected occipital lobe of the SWS children (right panel of **Fig. 3b**,  $R = 0.20$ ). **Discussion and Conclusion:** The present study demonstrates that FDG-PET combined with DWI tractography can be utilized to investigate both brain damage and plasticity in children with early occipital lesion, and the findings can provide clinically meaningful data on reorganization of the visual system.

**References:** 1. Bodensteiner JB, Roach ES. Sturge-Weber syndrome, The Sturge-Weber Foundation, New York: Mt. Freedom; 2010. 2. Batista CE, Juhász C, Muzik O, et al. Increased visual cortex glucose metabolism contralateral to angioma in children with Sturge-Weber syndrome. *Dev Med Child Neurol* 2007; 49:567-73. 3. Jeong JW, Asano E, Yeh FC, et al. Independent component analysis tractography combined with a ball-stick model to isolate intra-voxel crossing fibers of the corticospinal tracts in clinical diffusion MRI. *Magn Reson Med*. 2013;70:441-53.



**Figure 3.** Positive correlations between glucose uptake and streamline volume obtained from visual areas of the children with SWS. (a) Positive correlation between lateralization index of normalized FDG uptake and streamline volume ( $R = 0.64$ ,  $p=0.046$ ). (b) Normalized ratios of FDG uptake and streamline volume in ROI<sub>c</sub> and ROI<sub>i</sub>. The correlation was particularly strong, despite the small numbers, on the affected side ( $R = 0.70$ ,  $p=0.024$ ).



**Figure 2.** Representative patients showing significant metabolic and/or visual pathway abnormalities in the central visual system. (a) Patient #3, with the lowest occipital glucose uptake on PET (uptake ratio 0.491) and no visual pathway streamlines identified by DWI on the affected right side. The contralateral streamline volume was also low; this child had severe visual symptoms. (b) An older child (patient #7, age 3.9 years) showed very prominent FDG uptake and high (about 1 standard deviation above normal average) streamline volume in the occipital lobe unaffected by SWS (marked by "+"). (c) The oldest child (patient #10, age 5.5 years) showed moderate FDG uptake but very high streamline volume (>2 standard deviations above normal average) in the occipital lobe unaffected by SWS (marked by "+"), suggesting reorganization. These latter two children had no evidence of visual field deficit.