Title: Brain MRI Abnormalities in Patients with Infantile Spasms and Down Syndrome

Authors: Sara K. Trowbridge¹, Christopher J. Yuskaitis², Nicole Baumer¹,³, Sanjay P. Prabhu⁴, Chellamani Harini²
¹Department of Neurology, Boston Children’s Hospital, Harvard Medical School, Boston, MA ²Division of Epilepsy and Clinical Neurophysiology, Department of Neurology, Boston Children’s Hospital, Harvard Medical School, Boston, MA ³Down Syndrome Program, Developmental Medicine Center, Boston Children’s Hospital, Boston, MA ⁴Neuroradiology Division, Department of Radiology, Boston Children’s Hospital, Harvard Medical School, Boston, MA

Introduction: Down syndrome (DS) accounts for five to six percent of infantile spasms (IS) cases (1,2), and IS is the most common epilepsy syndrome seen in children with DS (3,4). Brain magnetic resonance imaging (MRI) is recommended in new onset IS to aid in identifying the underlying etiology (1,2,5), but clinicians do not undertake MRI routinely in IS associated with DS, as DS is a recognized genetic etiology for IS (2). Nevertheless, available information from the literature shows that neuroimaging is obtained in many patients with DS who have presented with IS (6,7). No study to date has systematically addressed the clinical utility of neuroimaging in children with IS who have DS.

Methods: The clinical research tool I2B2 was used to identify patients with IS and DS cared for at Boston Children’s Hospital (BCH) between 2001 and 2016. Retrospective chart review confirmed the diagnosis of IS and DS, identified timing, indication and type of imaging done, and determined any significant imaging findings that directly impacted medical decision-making. All available images were independently reviewed by a pediatric neuro-radiologist, who was blinded to the prior MRI reports. We classified the MRI as normal/normal variant, acquired structural abnormalities, relevant or potentially relevant congenital structural abnormalities, and non-specific abnormalities.

Results: Of 52 patients with IS in DS, the majority (43 patients, 83%) underwent neuroimaging. Neuroimaging was abnormal in 21 (58%) of the 36 patients with scans available for review, but in 15 patients (42%) the abnormalities were non-specific (prominence of extra-axial spaces and/or Sylvian fissures; isolated inferior vermian hypoplasia) and not felt to be explanatory of the patients’ epilepsy. Six patients (16%) had acquired (hypoxic ischemic injury) or potentially relevant structural congenital abnormalities (small brainstem; under-sulcation of the inferior frontal lobes; shallow pontomedullary sulcus; thinned or thickened callosum; simplified gyral pattern; gray matter heterotopia), suggesting an additional or compound etiology for the epilepsy. We did not find any change in medical treatment or management of IS secondary to neuroimaging findings. Interestingly, at last follow-up, when compared to the normal/normal variant group, patients with acquired structural or potentially relevant congenital structural abnormalities were more likely to have refractory epilepsy (3 of 14 in normal/normal variant group versus 5 of 6 in acquired/congenital structural abnormality group, p = 0.04) and to be on at least one AED (4 of 14 in normal/normal variant group versus 6 of 6 in acquired/congenital structural abnormality group, p = 0.02).

Discussion: Overall, our study provides the first detailed review of neuroimaging findings in a cohort of DS patients with IS. The findings noted on MRI in the current study are consistent with brain abnormalities previously reported in DS patients (8,9). Therefore, some of the MRI findings in our patients may be intrinsic developmental neuroanatomic findings related to DS, whether or not associated with epilepsy. However, it is interesting that our data suggests an association between congenital/acquired imaging abnormalities and refractory epilepsy in DS patients. Whether this is related to other genetic or anatomic variables remains to be determined.

The clinical relevance of neuroimaging is an important consideration, as imaging usually requires general anesthesia, and the DS population is known to be a higher risk group for general anesthesia (10). Ultimately, we believe that the risks and benefits of sedated neuroimaging should be carefully weighed. Our data suggests that neuroimaging does not alter treatment course but might offer some prognostic information. For some families and clinicians, this could be an argument in favor of deferring imaging, while others might prefer to obtain neuroimaging at time of IS diagnosis.
References/Citations:


